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ABSTRACT BOOK

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PREDAVANJA PO POZIVU
PLENARY LECTURES

EVROPSKI REGISTAR ZA MELANOM- PODACI CENTARA IZ SRBIJE

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Uvod. Put pacijenata obolelih od melanoma značajno se izmenio u 21. veku. Mere prevencije, ranog otkrivanja ali i nove terapijske mogućnosti omogućile su da ovi pacijenti imaju mnogo bolju prognozu. Uvođenje imuno i target terapija značajno je doprineo produženju preživljavanja kod obolelih od melanoma što je i dokazano kroz brojne studije. Međutim, selekcija pacijenata u studijama značajno se razlikuje od opšte populacije te su podaci iz realne kliničke prakse neophodni. Evropski melanomski registar (EUMELAREG) formiran je 2014 godine i imao je za cilj da prikupi podatke iz realne kliničke prakse. Inicijalno je uključivao podatke iz nemačkog, danskog i holandskog registra i obrađivani su podaci vezani za pacijente sa uznapredovalim stadijumima melanoma. Danas učestvuje ukupno 16 zemalja uz podatke koji uključuju sve stadijume melanoma, sa planom da se pridodaju i nemelanomski tumori kože. Srbija je deo tog programa od 2019 godine u saradnji sa centrima iz Hrvatske, Bosne i Hercegovine i Crne Gore, a u okviru podregistra za centralnu i jugoistočnu Evropu (CSEEREG).

Rezultati. U Republici Srbiji se podaci aktivno unose u tri referentna centra za melanom Vojnomedicinskoj akademiji, Univerzitetskom kliničkom centru u Nišu i Univerzitetskom kliničkom centru u Kragujevcu. U narednom periodu očekuje se nastavak aktivnog učešće Instituta za onkologiju i radiologiju Srbije i Instituta za onkologiju Vojvodina. Aktuelno, broj unetih pacijenata iznosi 1674 i uključuje pacijente sa melanom svih kliničkih stadijuma, sa posebnim fokusom na pacijente koji su na aktivnom tretmanu. U komparaciji sa podacima sa kraja 2022 godine broj pacijenata se povećao za 406 novih unosa što prestavlja povećanje od 27%, uz značajno ažuriranje prethodno unešenih podataka. Broj novounetih pacijenata prestavlja skoro četvrtinu (23.38%) svih novounetih pacijenata (N=1736) EuMelareg-a u periodu od novembra 2022 do novembra 2023. Najveći porast novih unosa viđen je na Vojnomedicinskoj akademiji (N=278; +56.5%), potom Univerzitetskom kliničkom centru Niš (N=66; +19.2%) i Univerzitetskom kliničkom centru Kragujevac (N=62; +27%).

Zaključak. Planovi CSEEREG-a u narednom periodu jesu uključivanje novih centara, kompletiranje svih kliničkih stadijuma melanoma kao i razmatranje mogućnosti zajedničkih publikacija, u cilju unapređenja svakodnevne kliničke prakse i poboljšanja ishoda lečenja pacijenata obolelih od melanoma.

Ključne reči: melanom, registar, podaci iz realne kliničke prakse

TREATMENT AND FOLLOW-UP OF ORGAN TRANSPLANT RECIPIENTS WITH SKIN CANCER

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Organ transplant recipients are at an increased risk of developing malignancies with the predominance of skin cancers, especially non melanoma skin cancers. The main cause is considered to be long term administration of immunosuppressive therapy, along with ultraviolet radiation exposure and human papilloma virus infections.

Heart, pancreas and lung transplant recipients are at the higher risk of developing skin cancer comparing to kidney and liver transplant recipients, due to intensity of required immunosuppression. Besides being significantly more frequent comparing to general population, skin cancers in organ transplant recipients are usually more aggressive with less favorable outcome. Therefore, treatment of skin cancers in organ transplant recipients is often challenging and proper follow-up is essential.

Surgical excision with adequate surgical margins of surrounding tissue is mainstay of skin cancer treatment and in selected cases use of radiotherapy may be beneficial. In patients who develop multiple skin cancers per year or individual high-risk skin cancers, mild reduct ion of immunosuppression or modification of immunosuppression in a form of multidrug regimen and switching immunosuppressive drug classes is recommended. Precancerous lesions need to be detected and treated with topical application of fluorouracil, imiquimod or diclofenac, cryotherapy or photodynamic therapy. Chemoprophylactic measures, such as oral acitretin or nicotinamide, are not widely accepted due to potential adverse effects, need for long term administration and effectiveness only during administration with possible rebound of skin cancer development on cessation of acitretin.

The frequency of follow-up visits depend on estimated skin cancer risk in individual patients, but definitive guidelines have not yet been established. Initial dermatologic assessment is necessary before transplantation for the purpose of detecting and treating all suspicious skin lesions prior to immunosuppression. In low risk patients with no history of cancer follow up may be performed at two years, in high risk patients with no history of cancer once yearly, and in patients with skin cancer at 3 to 6 months depending on the type of skin malignancy. Each follow-up visit should include complete skin examination of the organ transplant recipients, and proper education of the patients with emphasis on applying sun protection strategies and self skin examinations.

UPDATE ON MERKEL CELL CARCINOMA TREATMENT

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Merkel cell carcinoma (MCC) is a rare cutaneous tumor with a complex etiology, histopathology and aggressive nature. It is characterized by high mortality rates, ranging from 33-46% and a rapidly increasing incidence rate of approximately 8% per year. [1,2] Despite being 30 times less common than melanoma, MCC poses a significantly higher risk of fatal outcomes. Over half of the tumors are initially misdiagnosed as benign lesions such as cysts, atheromas, phlegmons, chalazia etc leading to various interventions before accurate identification. In 15% of cases, the disease manifests directly with metastatic lymph nodes and/or visceral metastases, without detection of a primary tumor. While MCC is generally responsive to tumor chemotherapy, the lasting positive effects are rare. The best results so far have been achieved with immune checkpoint inhibitors and anti-PD-L1 antibody (Avelumab), which received approval from the EMA in 2017 as a first-line treatment. Registration studies report an ORR of 62.1% in the 1st line treatment and 33% in the 2nd line, with a CR of 13.8% in the 1st line and a partial response of 48.3%, alongside an acceptable and manageable safety profile.[3]

Despite the availability of immunohistochemistry, early diagnosis of the disease remains challenging. Most patients present with locally advanced or metastatic disease, necessitating flexible strategies and a comprehensive therapeutic approach. Clinical cases from our practice illustrate successful complete response and disease control by combining the tumor's advantages, namely, radiation sensitivity and immunogenicity. Sensitizing the body through initial antibody infusion followed by radiation in our patients significantly enhances the local response and accelerates the systemic response, providing a basis for recommending the routine application of this approach.

Keywords: Merkel cell carcinoma, immune checkpoint inhibitors, radiotherapy

SYSTEMIC TREATMENT OF ADVANCED BCC: OUR EXPERIENCE

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In most cases of BCC, local treatment is sufficient, but in a smaller number of cases, patients also have locally advanced disease or, exceptionally, distant metastases can develop. In advances disease systemic treatment is used, however chemotherapy is ineffective. Changes in systemic treatment were brought by the knowledge of abnormal activation of the Hedgehog signaling pathway and the development of the agents vismodegib and sonidegib, which are oral selective inhibitors of the Hedgehog signaling pathway. By selectively binding to the transmembrane protein, SMO inhibits the signaling process through the HH signaling pathway and inhibits tumor growth. Several clinical trials have been conducted where patients with advanced or metastatic BCC, including patients with Gorlin syndrome, were treated with vismodegib or sonidegib. For patients with locally advanced or metastatic BCC who are ineligible for further curative locoregional therapy (eg, surgery or RT) and whose BCC has progressed or who are intolerant to a hedgehog pathway inhibitor, treatment with cemiplimab enables responses, prolongs the time to disease progression and has manageable side effects.

We performed a retrospective analysis of the clinical characteristics, vismodegib treatment patterns and adverse events in 40 patients with laBCC, multiple BCC and nevoid basal cell carcinoma syndrome (NBCCS) treated at the Oncology institute between November 2012 and May 2020. NBCCS, also known as Gorlin syndrome, is a hereditary condition characterized by multiple BCC and other abnormalities, and as such was analyzed separately from laBCC+multiple BCC. Population of 40 patients represents all vismodegib treated patients in Slovenia since vismodegib EMA approval with the exception of one pediatric patient treated at the Pediatric clinic. Results During 93-month period, 40 patients were diagnosed with laBCC (22), multiple BCC (12) and NBCCS (6), all inappropriate for surgery or radiotherapy. Baseline characteristics: median age was 72.6 years in laBCC + multiple BCC group and 51.3 years in NBCCS group. The overall response rate (ORR) was 79% in laBCC + multiple BCC and 83% in NBCCS group. Disease control rate (DCR) was 94% in laBCC + multiple BCC and 100% in NBCCS group. Median duration of treatment (DoT) was 9.0 months (range: 1.0-36.3) in laBCC + multiple BCC group and 27.2 months (range: 11.3-91.2) in NBCCS group. Majority of treatment emergent adverse events (TEAEs) in laBCC or multiple BCC group were grade 1 or 2 (96%), only 4% of AEs were grade 3: muscle cramps in three patients, respiratory infection, vomiting and anemia in one patient each. Majority of TEAEs in NBCCS group were also grade 1 or 2 (87%), 13% of AEs were grade 3: muscle cramps in two patients, decreased weight and diarrhea in one patient each. No grade 4 or 5 vismodegib related AEs were reported. Conclusion Vismodegib has shown meaningful efficacy with manageable safety profile in patients with laBCC, multiple BCC and NBCCS in real-world setting.

Keywords: basal cell carcinoma, vismodegib, Hedgehog pathway inhibitors

UPDATE ON CUTANEOUS SQUAMOUS CELL CARCINOMA TREATMENT

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Cutaneous squamous cell carcinoma (CSCC) is the second most common form of skin cancer. CSCC incidence rates have increased in the last thirty years, ranging from 50% to 200% increase. The majority (80-90%) occur on the head and neck. It is caused by cumulative skin exposure to UV light. Actinic keratosis is the premalignant precursor for CSCC, although it may appear *de novo*. More than 95% of CSCCs have excellent prognosis and are usually cured by surgical resection. However, sometimes, mainly if neglected, it can progress to locally advanced and/or metastatic disease. Locally advanced CSCC, especially if it invades lymph nodes or adjacent vital structures, or metastatic CSCC have both poor prognosis.

The risk factors for the advanced/metastatic disease include comorbidities, ignoring the disease until the advanced stage, and immunosuppression. Immunocompromised patients (e.g., patients with organ transplants) have a higher risk of recurrent disease and higher mortality rates.

Radiation therapy is used in older patients or those who will not tolerate surgery, when it has not been possible to obtain surgical clear margins, or in the adjuvant setting in locally/locoregionally advanced tumors. If surgical or radiation therapies are not possible, advanced CSCC may require systemic treatment. Chemotherapy and, later on, epidermal growth factor receptor (EGFR) inhibitors in CSCC have been used but are generally of limited benefit, with responses often short-lived and with toxicity issues.

Due to the high immunogenicity, driven by the high mutational burden of CSCC, the ultraviolet signature, and the overexpressed tumor antigens, immunotherapy has been recently broadly investigated in this patient population. Immunotherapeutic agents have shown significant benefit in patients' outcomes, leading to their approval by regulatory agencies. Currently, two anti-PD-1 antibodies, cemiplimab and pembrolizumab, have been approved for the treatment of advanced CSCC that is not curable by surgery or radiation. Both have shown durable responses with good tolerability in patients in phase II trials.

Adjuvant immunotherapy has been investigated in high-risk, completely resected CSCC. Also, based on the strong biological rationale and on data from melanoma studies, neoadjuvant use of checkpoint inhibitors is underway. In both adjuvant and neoadjuvant setting, the first results are very encouraging but require further investigation and longer follow-up.

Intralesional neoadjuvant administration of immunotherapeutics (e.g., cemiplimab, daromun) has shown positive results with a high percentage of significant pathologic responses. It is a promising option, especially in organ transplant recipients or in patients with a history of autoimmunity.

Anti-PD-1 therapy is now the standard of care for locally advanced and metastatic CSCC.

However, some CSCCs develop early or late resistance to immunotherapy; therefore, new drugs and new combinations are needed to overcome the resistance mechanisms and further improve the outcomes in this patient population.

PD-1 checkpoint inhibition is currently being assessed for CSCC in combination with other modalities, including oncolytic viruses (e.g., RP1) and EGFR inhibitors, where checkpoint inhibitors are used as sensitizers for EGFR inhibitors.

IMMUNE CHECKPOINT INHIBITION FOR SKIN CANCERS: A NOBEL PRICE-WINNING INNOVATION!

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For decades, the treatment of metastatic melanoma and advanced non-melanoma skin cancers has not led to significant survival improvements. The introduction of modulators to the so-called "immune checkpoint" changed treatment strategies and guidelines completely. Inhibitors to immune checkpoint regulators like PD-1, CTLA-4, or LAG-3 can induce anti-tumoral T-cell responses, sometimes going along with the induction of various autoimmune disorders as adverse events. Despite some rare and potentially life-threatening side effects immune checkpoint inhibitors (ICI) are generally tolerated well in the majority of patients.

In the post-chemo era, the median overall survival of stage IV melanomas has increased from 9 months to 5 years in our days. Also, the issue of curing advanced melanoma patients became relevant. The PD-1 antibodies pembrolizumab and nivolumab as well as the combination of ipilimumab/nivolumab are standards of care yet. Additionally, the PD-1 antibodies have been introduced as new gold standards in the adjuvant treatment of disease-free with stage IIB/C and stage III melanomas.

The outstandingly good results of cemiplimab as a PD-1 antibody in advanced squamous cell carcinomas (CSCC) are underlined by long-lasting responses in 50% of treated patients, but also a long progression-free and overall survival as compared to conventional chemo. In advanced basal cell carcinomas (BCC), which failed to hedgehog inhibitors, cemiplimab got another approval recently.

The treatment of choice for metastatic Merkel cell carcinomas (MCC) is no longer chemotherapy, but the PD-ligand 1 antibody, avelumab, with a response rate of roughly 50% and longer response duration. Moreover, the neoadjuvant/perioperative use of ICI might be able to replace aggressive surgery even in the nearer future.

In November 2018, James Allison (USA) and Tasuko Honjo (Japan) got the Nobel Price for their basic research on ICI, which entered the field in 20 different cancer entities meanwhile. It´s nice to know that dermato-oncology was the door opener of this innovative approach!

SIDE EFFECTS OF IMMUNE CHECKPOINT INHIBITORS IN DERMATOONCOLOGY

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Immune checkpoint inhibitors (ICIs) are a type of immunotherapy used to treat various types of cancer by blocking certain proteins that inhibit the immune system's ability to recognize and attack cancer cells. While ICIs can be effective in boosting the immune response against cancer, they can also result in immune related adverse events affecting various organ systems, manifesting as colitis, pneumonitis, hepatitis, myocarditis, encephalitis and endocrinopathies. Dermatologic adverse events are among the most prevalent irAEs arising in up to 34% of patients on PD-1 inhibitors and 43% to 45% on CTLA-4 inhibitors. These cutaneous adverse events often manifest as maculopapular rash, pruritus, vitiligo, psoriasiform and lichenoid rashes, autoimmune bullous disorders and rare, potentially life-threatening reactions, necessitating discontinuation of ICI therapy. Interestingly, the presence and severity of cutaneous irAEs have been associated with better treatment outcomes in several cancers. Management of irAE involves the use of topical corticosteroids for mild to moderate (grades 1-2), while systemic corticosteroids remain the cornerstone for managing grade 3 and 4 cutaneous toxicities. In cases resistant to corticosteroids, classic immunosuppressive drugs and biologic agents serve as second-line options. It's essential for patients receiving immune checkpoint inhibitors to promptly report any adverse events to their healthcare providers. While these side effects can be bothersome, they are usually manageable, and healthcare professionals may recommend adequate treatments or adjustments to the ICI treatment plan. Severe cutaneous reactions may require discontinuation of the ICI therapy and specialized medical care. Early detection and management of side effects can help ensure the continued benefit of immunotherapy in cancer treatment while minimizing discomfort, complications and preserving patients' health status and quality of life.

UPDATE ON UVEAL MELANOMA TREATMENT

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Uveal melanoma, a rare and aggressive form of melanoma that arises in the uveal tract primarily metastasizes to the liver. There were limited systemic treatment options available for metastatic uveal melanoma, and the prognosis for patients with metastatic disease was generally poor. There is no universally standardized approach to the management of uveal melanoma. Chemotherapy and immunotherapy, have historically shown limited effectiveness in uveal melanoma. The reasons for this include the unique biology of uveal melanoma and the relative resistance of these tumors to conventional systemic therapies. Management in non-metastatic disease include surgery, laser therapy, photodynamic therapy and radiation therapy. Liver directed therapies like chemoembolization, radioembolization, regional isolation perfusion and immunoembolization are preferred options in case of "liver only disease". Effective therapy options for cutaneous melanoma like immunotherapy have limited efficacy in uveal melanoma. Pooled analysis for anti CTLA-4 inhibitors showed overall response rate (ORR) ~5–10%, median progression free survival (PFS) ~3 months and median overall survival (OS) ~6.5–10 months. Disappointing results for anti PD-1 inhibitors with ORR 3.6%, median PFS 2.6 months and median OS 7.6 months. Combined immunotherapy, anti CTLA-4 plus anti PD-1 showed modest ORR 11.6-18%, median PFS 2.7-5.5 months and median OS 15-19.1 months. Tebentafusp, is a novel bispecific T-cell engager that redirects the immune system to target and kill gp100 expressing uveal melanoma cells. One year OS with tebentafusp was 73% compared to 59% in control arm on single agent: Dacarbazine, Ipilimumab, or Pembrolizumab making this therapy a promising agent in uveal melanoma treatment. Recent publication showed at a minimum follow-up of 36 months, median overall survival was 21.6 months in the tebentafusp group and 16.9 months in the control group (hazard ratio for death, 0.68; 95% confidence interval, 0.54 to 0.87). The estimated percentage of patients surviving at 3 years was 27% in the tebentafusp group and 18% in the control group. Results support a continued long-term benefit of tebentafusp for overall survival among adult HLA-A*02:01–positive patients with previously untreated metastatic uveal melanoma. Unfortunately, uveal melanoma is still a rare disease with a clear unmet need in improving patient prognosis.

Keywords: uveal melanoma, systemic treatment, immunotherapy, tebentafusp, targeted therapies

EUROMELANOMA - PREVENTION CAMPAIGN IN BOSNA AND HERZEGOVINA

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Introduction: Euromelanoma is pan-European association, under the auspices of the European Academy of Dermatovenerology (EADV), which deals with the prevention of skin cancer. It started in Belgium in 1999.

Euromelanoma was created as part of this preventative strategy, with the initial aim of encouraging all European countries to start skin cancer screening campaigns to help raise awareness and educate the general public on the prevention, early diagnosis, and treatment of skin cancer. In this regard, the goal of this pan-European campaign has been to have a public, scientific, and political impact on skin cancer awareness and prevention.

Since 2011, Bosnia and Herzegovina has been an equal member of the Euromelanoma association. Two mail goals of campaign are : primary prevention (provide information about skin cancer – *awareness*) and secondary prevention (offer free skin examinations – dermoscopic *early detection)*

With the initiative from Sarajevo, the campaign was spreading to the entire territory of Bosnia and Herzegovina. Total: 4 main clinical centers and 32 health facilities in 30 cities.

Methods: We will present all the activities we did during the 13 years of the Euromelanoma campaign in Bosnia and Herzegovina. Euromelanoma questionnaires were used . Also the most illustrative examples of melanoma in situ found during the campaign. We will also go through some static data at the campaign in the level of Europe as well as in Bosnia and Herzegovina.

Results: Activities, raising awareness about skin cancers, providing free dermoscopic examinations through persistent work for 13 years, resulted in many saved lives. Our results for B&H shows by reactions of skin of subjects to summer sun, the largest number of them belonged to type 'initially, skin burns, and then tans'. Of the total number 19.6% had severe sunburns before the age of 18 years. Despite the fact that a large number of subjects had university degree, use of adequate and correct UV protection is insufficient.

Conclusion: We achieved many positive results in the field of skin cancer through political impact as well as scientific work, the implementation of dermoscopy as the most important method of early detection of skin cancer. The importance of prevention and self-examination as well as the negative impact of UV radiation. The campaign, Euromelanoma, spread out quickly over the Europe and is now one of the largest, simultaneous preventive actions in the world, in 33 countries.

CAMPAIGNS FOR PREVENTING SKIN CANCER IN MONTENEGRO

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The Euromelanoma campaign, spearheaded by esteemed dermatologists, is dedicated to conducting free screenings with a twofold objective: early detection of malignant skin tumors for potential cure, and most importantly, raising awareness about the imperative need for protection against harmful UV radiation.

The highly impactful Euromelanoma campaign from last year, titled "It's not the Years, It's the UV mileage," garnered significant visibility throughout Montenegro. The campaign sought to shed light on how lifestyle choices, occupations, and past experiences contribute to the risk of developing melanoma. To effectively communicate with the public, we enlisted the support of renowned personalities from the realms of film, music, sports, fashion, and science. Through a promotional video, these influential figures conveyed vital messages about the importance of preventive screenings. Billboards adorned the entire landscape of Montenegro, while dermatologists actively engaged with electronic and print media, as well as social media platforms (Instagram and Facebook). The overwhelming number of dermoscopic examinations conducted in May clearly indicated the substantial impact of our outreach efforts. Moreover, medical students delivered lectures on "The Impact of Sun Exposure on the Skin" in various high schools.

This year's campaign carries the slogan "Do You use protection ?" with a strong emphasis on the significance of adopting preventive measures to reduce the risk of photoaging and skin cancer. Special attention has been given to improving UV radiation protection among adolescents, as research shows an 18% higher risk of developing melanoma in patients who experienced sunburns before the age of 18. Euromelanoma Day was observed on May 25, 2023, in eleven municipalities across Montenegro. For the first time, dermatologists from numerous private healthcare institutions joined forces in support of the campaign. Furthermore, municipalities without resident dermatologists were not overlooked, as screenings were conducted at the respective Health Centers to reach citizens in those areas. A promotional video was produced and broadcasted on the national public broadcaster, Radio Television of Montenegro, throughout the month of May. Additionally, the video was shared on social media platforms during the summer months. Inspired by successful Euromelanoma campaigns in other countries, the promotional video features a dance couple delivering an educational performance to underscore the importance of skin self-examination. Medical students from the University of Montenegro organized educational sessions on proper sun protection in preschools and schools across the country as part of this year's campaign. Specialized dermatology trainees and medical students engaged with citizens in Podgorica's central square, providing advice and educational materials. Billboards displaying the slogan of this year's campaign, "Are You Protecting Yourself from the Sun?" were strategically placed in prominent locations in Podgorica, Budva, Cetinje, Nikšić, and Herceg Novi.

Emphasizing the prevention of melanoma is of utmost importance. Although Montenegro has made progress in detecting melanoma at earlier stages compared to five years ago, there is still a significant number of cases diagnosed in advanced stages. Thus, it is imperative to prioritize educational activities for the population. Sustained campaigns spanning over a decade are necessary to instill lasting changes in the habits of the population.

Keywords: euromelanoma, dermoscopy, melanoma

SQUAMOUS CELL CARCINOMA ON SPECIAL LOCATIONS

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Squamous cell carcinoma (SCC) is the most common skin cancer with metastatic potential. At the same time, SCC is a great imitator, primarily if it is localized in specific sites.

One of the specific sites of SCC is the nail apparatus. There is often a substantial delay in diagnosing SCC in the nail unit because it is often misdiagnosed as chronic paronychia, onychomycosis, pyogenic granuloma, subungual warts, subungual exostosis, keratoacanthoma, or amelanotic melanoma. Due to that, there is often a significant delay between the onset of nail SCC and the diagnosis.

Lip and external ear SCC are among the most frequent locations of SCC when we talk about specific sites, although they can be relatively common in clinical practice. Erythroplasia of Queyrat (EQ) is an in situ squamous cell carcinoma of the penis, usually presenting as one or more bright red, shiny patches/plaques of the penile mucosae of uncircumcised middle-aged to elderly males. Correct and prompt recognition of EQ is of utmost importance to properly treat such a condition and avoid genital amputations.

In this lecture, other specific site locations of SCC will be described to present their most common clinical and dermoscopic presentations, all to diagnose this malignant skin tumour that gives metastases early.

In this regard, dermoscopy has been shown to play a helpful role in assisting the early recognition of cutaneous SCC , with consequent reduction of its morbidity and mortality. This is not the case when it comes to SCC located on so-called special sites or when there is not much data in the literature on dermoscopic characteristics of SCC in specific sites. Therefore, in this lecture, previously published papers will be cited, as well as presented cases of SCC in particular sites, all to demonstrate clues for early diagnosis of SCC that occur less frequently but are still present in our clinical practice and hints that will help us in the dermoscopic evaluation and early detection.

SKIN CANCER PREVENTION CAMPAIGNS IN CROATIA

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For two decades, Croatian Dermatovenerological Society of the Croatian Medical Association, and Referral Center of the Croatian Ministry of Health for Melanoma are conducting the most popular public health campaign for early detection of malignant skin tumors, with a special focus on melanoma. This campaign involves a series of multi-month activities that imply a medical, humanitarian and advisory aspect throughout the Republic of Croatia, and are directed towards three different groups of people- general population, dermatologists and other healthcare workers and the state institutions. High importance is given to educating and informing citizens about the harm of unreasonable exposure to UV radiation and recognizing symptoms suggesting the development of malignant skin tumors that each individual can notice during self-examination. Education is provided through lectures to medical personnel and kindergarten teachers, elementary school pupils, teachers and professors in primary and secondary schools, on public forums, through pamphlets and posters, and through all mass media. Croatian dermatovenerologists succeeded to incorporate the subject of the effects of UV radiation on the skin and the importance of photoprotective behavior in Croatian national school curriculum and to provide teaching aids and materials for teachers. For years, the education of doctors of family medicine, pediatricians, school medicine specialists and surgeons of various professions is also being conducted. Apart from education, dermatovenerologists organize free-of charge skin screenings for the public that are being held in dermatovenerologist and other other physicians' offices, nursing homes, and public areas such as squares and beaches throughout the Republic of Croatia. In these activities, special attention is paid to the most vulnerable groups of citizens , such as children, persons over the age of 50, and all those who are professionally exposed to UV radiation or live in areas with a large number of sunny days such as Croatian islands and coastal areas. Fifteen ago the Republic of Croatia joined the pan - European prevention campaign against melanoma and skin cancer entitled Euromelanoma. The Euromelanoma is implemented throughout the Republic of Croatia in partnership with the Ministry of Health of the Republic of Croatia, the Ministry of Environment and Energy and the Ministry of Tourism of the Republic of Croatia, the Croatian Dermatovenerology Society and Croatian Association for dermatooncology of the Croatian Medical Association and the Croatian Melanoma Referral Center, and is associated with all the activities mentioned. We need to point out that public health preventive activities related to early detection of melanoma and other malignant skin tumors are the most recognized of all conducted in Croatia, and that positive long-term results in this area may be measured by the increasing number of detected melanoma at a prognostically preferred stage. Throughout the above mentioned activities, over the past years, more than 60.000 Croatian citizens have been examined and more than 20 000 children, teachers and professors have been educated.

CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF BASAL CELL CARCINOMA

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Basal cell carcinoma (BCC) is the most common malignant tumor in white populations. The most recent European guidelines containing recommendations with regard to the diagnosis, therapy and follow-up of patients with BCC will be presented. BCCs were categorized according to the new EADO clinical classification into 'easy-to-treat' (most common BCCs) and 'difficult-to- treat' BCCs (all locally advanced BCCs and common BCCs which, for any reason, pose specific management problems due to patient or tumor characteristics). BCC can also be classified according to the risk of recurrence into high risk and low risk. Diagnosis is based on clinico-dermatoscopic features, although histopathological confirmation is mandatory in equivocal lesions and in the presence of features of aggressive forms. Other non-invasive imaging techniques (reflectance confocal microscopy and/or optical coherence tomography) shall be used, when available, to improve the diagnostic accuracy in difficult to recognize BCCs. A treatment algorithm was proposed according to the different clinical stages. The first-line treatment of BCC is complete surgery. In low-risk BCCs, a safety margin of 3–4 mm is recommended for standard excision with 2D histology while high-risk BCCs should be excised with a safety margin of at least 5 mm, if anatomically feasible. Topical or destructive (blind) treatments can be considered for low-risk superficial and nodular BCC in patients declining surgery or not amenable to surgery. Photodynamic therapy using 5-ALA or MAL in combination with red light is an effective treatment for superficial and low-risk nodular BCCs. Management of 'difficult-to-treat' BCCs should be discussed by a multidisciplinary tumor board. Micrographically controlled surgery shall be offered in high-risk and recurrent BCC, and BCC located on critical anatomical sites. Radiotherapy represents a valid alternative in patients who are not candidates for or decline surgery, especially elderly patients. Hedgehog inhibitors (HHIs), vismodegib or sonidegib, should be offered to patients with locally advanced and metastatic BCC. Immunotherapy with anti-PD1 antibodies (cemiplimab) is a second-line treatment in patients with progression of disease, contraindication, or intolerance to HHI therapy. Electrochemotherapy may be offered when surgery or radiotherapy is contraindicated. An early involvement of the interdisciplinary best supportive care team is recommended for symptomatic patients with locally advanced and metastatic BCC. The diagnosis of Gorlin syndrome is based on clinical criteria. In Gorlin patients, regular skin examinations are required to diagnose and treat BCCs at an early stage. Long-term follow-up is recommended in patients with high-risk BCC, multiple BCCs, and Gorlin syndrome.

ACTINIC KERATOSIS DIAGNOSIS AND TREATMENT GUIDELINES

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Actinic keratoses (AK) are potential precursors of cutaneous squamous cell carcinoma (cSCC). They can develop into cSSC *in situ* and become invasive in a low percentage of cases. AK is the most frequent neoplasia in white populations, frequently occurring within a cancerous field induced by UV radiation. AKs and field cancer should be treated to avoid transition to invasive cSSC. A collaboration of multidisciplinary experts from the European Association of Dermato-Oncology, the European Dermatology Forum, the European Union of Medical Specialists, and the European Organization of Research and Treatment of Cancer, was formed to develop European recommendations on AK diagnosis and treatment, based on current literature and expert consensus. This guideline addresses epidemiology, diagnostics, risk stratification, and treatments in immunocompetent as well as immunosuppressed patients. The diagnosis of actinic keratosis and field cancerization is made by clinical examination. Dermatoscopy, confocal microscopy, OCT, LC-OCT can help in the differential diagnosis of actinic keratosis and other skin neoplasms and biopsy is indicated in clinically and/or dermatoscopically suspicious and/or treatment refractory lesions. The choice of treatment depends on the patient's and lesion characteristics. For single non-hyperkeratotic lesions, the treatment can be started upon patients' request with destructive treatments or topical treatments, although monitoring and self-examination can also be advised. For multiple lesions, field cancerisation treatment is advised with topical treatments and photodynamic therapy. Preventive measures (sun-protection, self-examination and repeated field cancerisation treatments of previously affected skin areas in high-risk patients) are advised.

CLINICAL PRACTICE GUIDELINES FOR THE MANAGEMENT OF SQUAMOUS CELL CARCINOMA

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Cutaneous squamous cell carcinoma (cSCC) is the second most common skin cancer. The updated European guidelines (version 2023) issued recommendations on the diagnosis, classification and staging of invasive cSCC.

The vast majority of cSCCs are common primary, typically indolent cSCCs, with five-year cure rates of greater than 90%. Common primary cSCCs are localized cSCCs, classified as low-risk or high-risk according to the presence of high-risk features. In cSCCs overall, the proportion of local recurrence is approximately 3%-5% and the proportion of nodal metastasis is approximately 3%-5%. However, in cSCCs with high-risk features, the frequency of local recurrence may increase up to 30% and the frequency of metastasis may increase up to 35%. Advanced cSCC is classified as locally advanced (lacSCC), or as metastatic (mcSCC) with locoregional and/or distant metastasis. Diagnosis is based on clinical and dermoscopic examination and is confirmed with biopsy and histology, followed by staging with, when indicated, imaging studies.

For common primary cSCC, first-line treatment is surgical excision with post-operative margin assessment or micrographically controlled surgery. Achieving clear surgical margins is the most important treatment consideration for cSCCs amenable to surgery. Further recommendations include radiotherapy as primary treatment for non-surgical candidates/tumors, and systemic anti-PD-1 agents for patients with metastatic or locally advanced cSCC who are not candidates for curative surgery or radiotherapy. All patients with advanced cSCC should be evaluated in multidisciplinary board meetings, in order to address the risks of treatment toxicity as well as the age, frailty, co-morbidities and preferences of patients, and to decide optimal management.

DERMATOLOŠKE MANIFESTACIJE HEPATITIS C INFEKCIJE

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Infekcija hepatitis C virusom (HCV) pored oštećenja jetre dovodi do različitih kliničkih manifestacija na drugim organima i organskim sistemima. Među ekstrahepatičnim manifestacijama kutane manifestacije su česte, a ponekad i prvi znak postojeće infekcije.

Različiti faktori vezani za sam virus, genetske i faktore okoline mogu da budu odgovorni za nastanak lezija na koži. U najvećem broju slučajeva tačan mehanizam putem koga virus izaziva ili pogoršava oboljenje kože nije u potpunosti razjašnjen.

U oboljenja kože koja su često udružena sa HCV infekcijom spadaju Lichen planus, mešovita krioglobulinemija i Porphyria cutanea tarda dok se ređe javljaju Erythema nodosum, Erythema multiforme, Pyoderma gangrenosum, Urticaria chronica, Vitiligo, Alopecia areata... Promene na koži mogu biti deo kliničke slike drugih ekstrahepatičnih poremećaja i maligniteta udruženih sa HCV infekcijom kao što je oboljenje tireoidee i HCV udružena trombocitopenija, non-Hodgin lymphom, hepatocelularni karcinom. Takođe infekcija HCV može pogoršati postojeće kožno oboljenje, a i sama terapija osnovnog oboljenja dovodi do određenih promena na koži.

HCV infekcija zahteva multidisciplinarni pristup a uloga dermatologa u timu je da učestvuje u ranom postavljanju dijagnoze kao i lečenju dermatoza koje se pogoršavaju ili se javljaju tokom kliničkog toka i lečenja infekcije.

DISEMINOVANA KUTANA HERPES SIMPLEX VIRUSNA INFEKCIJA

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Herpes simplex virusi (HSV) su ubikvitarni patogeni koji pripadaju grupi humanih herpes virusa (HHV). Zajednička karakteristika infekcija uzrokovanim ovim virusima je odsustvo virusne eliminacije nakon primoinfekcije. Uprkos razoju celularnog i humoralnog imunskog odgovora, HHV trajno ostaju u latentnom stanju u različitim ćelijama domaćina. Pod određenjim okolnostima, naročito u stanjima imunosupresije, dolazi do njihove reaktivacije i nastanka kliničkih manifestacija.

Infekcije HSV su veoma česte u čitavom svetu. Procenjuje se da je 72% stanovništva Srbije inficirano HSV tip 1 (HSV-1), dok je 10% inficirano tipom 2 HHV (HSV-2). Oba tipa virusa se prenose direktnim kontaktom sa lezijama, kao i kontaminiranim sekretom. Manifestnu primarnu infekciju karakterišu bolne, mukokutane vezikulozne promene, koje mogu biti praćene i konstitucionalnim simptomima. HSV-1 obično uzrokuje lezije u orofacijalnom regionu, dok je HSV-2 najčešće dovodi do genitalne infekcije. Znatno ređe se sreće primarna infekcija na drugim lokalizacijama. Nakon primoinfekcije, virus se iz zahvaćenih zona aksonskim putem transportuje retrogradno do neurona senzornih gangliona u kojima uspostavlja latenciju. Reaktivacija HSV nastaje ili spontano ili usled pada otpornosti organizma, lokalne traume, delovanja UV zraka, temperature, u stanjima emocionalnog stresa i hormonskih promena. HSV se tada preko aksona anterogradno transportuje do odgovarajućih regiona kože i sluzokože, gde se dolazi do njegove replikacije. Recidivi bolesti se klinički manifestuju grupisanim vezikulama ograničenim na manja područja u odnosu na primarnu infekciju, obično bez pridruzenih konstitucionalnih simptoma.

Kod pacijenata sa narušenom epidermalnom barijerom ova uobičajena sekvencija interakcija HSV sa ljudskim organizmom moze biti poremećena. Diseminovana kutana HSV infekcija se odlikuje širenjem virusa “per continuitatem”, odnosno putem obolele kože. Prvenstveno se javlja kod pacijenata sa atopijskim dermatitisom, ali se sreće i u drugim dermatološkim bolestima gde je epidermalna barijera narušena. Diseminovana kutana HSV infekcija se karakteriše iznenadnom pojavom monomorfnih, grupisanih, umbilikovanih vezikula u regionima prethodno zahvaćenim osnovnom bolešću. Često je praćena povišenom temperaturom i limfadenopatijom. Iako je klinička prezentacija karakteristična, često je uzrok pogrešne dijagnoze. Smatra se jednim od malobrojih urgentnih stanja u dermatologiji. Blagovremena dijagnoza i adekvatna terapija značajno smanjuju rizik od nastanka komplikacija i smrtnog ishoda.

BACTERIAL SKIN INFECTIONS - A DIAGNOSTIC AND THERAPEUTIC CHALLENGE

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Bacterial infections represent one of the most common dermatological conditions that account for ~20% of dermatology visits.

Providing a mechanical barrier from which contaminating organisms are constantly being removed by desquamation and producing antimicrobial peptides skin enables the maintenance of an internal environment of homeostasis. Disruption of the delicate balance between host and microorganisms can result in skin infections that involve interrelated adaptive and innate immune systems.

The normal skin microbiota is composed of huge numbers of bacteria like aerobic cocci, aerobic and anaerobic coryneform bacteria, and Gram-negative bacteria, that live as commensals on its surface and within its follicles. Overgrowth of some of these resident organisms may cause different types of skin infections. Likewise, bacteria not normally found there may colonize the epidermis and lead to infection. Staphylococci and streptococci cause most bacterial skin conditions, which range from common infections such as impetigo and cellulitis to severe multisystem disorders. Also, other Gram-positive and Gram-negative bacterial infections have a wide variety of localized and widespread cutaneous manifestations that could represent signs of a systemic bacterial infection or underlying immunodeficiency.

The nomenclature of cutaneous bacterial infections reflects the site, depth, and extent of the infection as well as the organism involved. Timely recognition, adequate diagnosis, and treatment of bacterial infections as very common and transmissible dermatological conditions are of great importance for general national health. This lecture reviews several different clinical presentations of skin infections, treatment, and potential prevention.

Keywords: bacterial infections, clinical presentation, therapy

UPDATE ON NONTUBERCULOUS MYCOBACTERIAL SKIN INFECTIONS

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Non-tuberculous mycobacteria (NTM) are ubiquitous microorganisms in the natural environment, mainly present in water and soil. They can cause a wide spectrum of skin and soft tissue infections as well as bone, pulmonary and disseminated disease. The incidence of NTM skin infections has increased dramatically during the past several years which has been contributed to climate changes as well as improved disease recognition and improved diagnostic tests.

The epidemiology of NTM skin infections depends on geography-based environmental exposure. Skin infections most commonly follow inoculation through contact of damaged skin. Predisposing factors include skin trauma, immunosuppression, diabetes, genetic or acquired defect of IFN-γ pathway, treatment with biological drugs (TNF-α inhibitors), surgical or cosmetic procedures.

NTM skin infections are most commonly caused by *M. marinum*, *M. ulcerans* and *M. fortuitum* complex (*M. fortuitum*, *M. chelonae*, *M. abscessus*). Rarely, *M. haemophilum*, *M. avium* complex, *M. scrofulaceum* and *M. szulgai* are diagnosed. Rapidly growing mycobacteria, *M. abscessus*, *M. chelonei* and *M. fortuitum* have increasingly been reported in association with plastic surgery and cosmetic procedures, following tattooing, liposuction and mesotherapy. Post-injection abscesses, injections in alternative medicine, acupuncture, catheter use, and hemodialysis have also been recognized as risk factor.

NTM can cause a wide spectrum of clinical lesions, including erythematous papules and plaques, painful abscesses, ulcers and nodules, sporotrichoid nodular lesions, verrucous plaques, chronic granulomatous or necrotic skin lesions, panniculitis, cellulitis and regional lymphadenitis. Clinical lesions are not specific to the causative mycobacteria species. In immunocompetent patients, lesions are usually more localised, while in immunosuppression they tend to be widespread and disseminated. NTM skin infections can also induce reactive dermatosis such as Sweet syndrome, pustular eruptions or erythema nodosum.

Incubation period can take many months, leading to delay in diagnosis. The prognosis depends on early and accurate diagnosis. Examination of the bioptic skin specimen for acid-fast staining bacilli and identification of the causative pathogen by cultivation are the cornerstone of diagnosis. Susceptibility testing is recommended since drug resistance varies in different species. Histopathological examination is nonspecific but can help in correlation with clinical picture and microbiological findings. Molecular methods using PCR may be useful in some cases. New diagnostic tools, such as antigen detection assays, measurement of other biomarkers and improved amplification tests are under investigation to provide more sensitive diagnostic tests.

Treatment of mycobacterial infections is challenging and depends on the causative pathogen and its antimicrobial sensitivity. Ciprofloxacin, clarithromycin, trimethoprim-sulfamethoxazole, doxycycline and some other antibiotics should be used according to treatment recommendations. A combined treatment approach, including surgical debridement and prolonged antibiotic treatment has been used in some chronic and resistant infections.

ONYCHOMYCOSIS: DIAGNOSIS AND TREATMENT IN PRACTICE

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Onychomycosis is still the most common nail disorder seen in clinical practice and may occur at any age. The majority of onychomycosis cases are due to dermatophytes (60–90%), most commonly anthropophilic dermatophytes. Yeast infections account for up to 10–20% of cases, with the most common pathogen being *Candida* spp.

There are multiple techniques available for diagnosing onychomycosis, but the most performed are potassium hydroxide (KOH) and fungal culture. Molecular detection by PCR is much more sensitive and is recommended as a supplementary detection method in combination with microscopic preparation and fungal culture.

Onychomycosis is challenging to treat and is associated with high recurrence rates and treatment failure. There are several treatment options available for onychomycosis, including oral and topical antifungals, device-based therapies (ie, lasers), surgical nail avulsion, nail debridement, and combination therapies.

Oral therapy is considered the gold standard for onychomycosis both in children and adults and is recommended for all types of onychomycosis especially when ≥ 50% of the nail is affected andmultiple nails are infected. Currently, terbinafine, itraconazole, and griseofulvin are US FDA-approved for onychomycosis treatment. Fluconazole is not US FDA-approved for onychomycosis treatment but is frequently used off-label.

New oral antifungal agents, posaconazole, posravuconazole L-lysine ethanolate, otesesconazole, voriconazole and albaconazole, show promising results in the treatment of onychomycosis. However, none of these drugs are yet approved for the treatment of onychomycosis, although many are approved for the treatment of invasive fungal infections.

Topical antifungal therapy is a therapeutic option when oral antifungal agents are contraindicated or cannot be tolerated. Most commonly used are ciclopirox 8% nail lacquer, efinaconazole 10% solution, tavaborole 5% solution, and amorolfine 5% nail lacquer.

Novel broad-spectrum topical antifungal agents that have shown promising results in the treatment of onychomycosis include topical terbinafine, ciclopirox hydrolacquer, tazarotene, lanoconazole, and luliconazole. Complete and mycologic cure rates were higher than with other topical antifungals. However, further studies are needed to evaluate their efficacy andsecurity profile.

CARBON DIOXIDE FRACTIONAL LASER IN SKIN RESURFACING

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Introduction: Fractional carbon dioxide laser in past few years has been used in the treatment of many dermatological diseases and aesthetic procedures.

Main objectives of the study are: to confirm the efficiency and safety of the fractional CO_2 laser in skin renewal, and to check the possibility of having a synergistic effect in patients who besides carbon dioxide laser are treated with PRP /platelet-rich plasma/ too.

Material and methods: The study was prospective, case control study and carried out at the Department of Dermatovenerology, with total number of 232 patients included in the study. The patients were divided into three groups. The first group (Examined Group 1) included 107 patients treated with fractional CO_2 laser on monthly basis. The second group /Control Group/ covered 100 patients treated with neither laser nor plasma in the same period but subjected to local therapy with drugs or other noninvasive procedures under the existing protocols for treatment of certain diseases. The third group /Examined Group 2/ treated 25 patients with combined therapy of CO_2 laser and PRP in the treatment of facial rejuvenation or treatment of acne scars. Inclusive criteria for entering the study are patients who have one of the following clinical conditions: acne scars, scars from different backgrounds, stretches, photodamaged skin, hyperpigmentation's. Exclusionary criterion in the study is the use of: oral retinoids in period of 6 months prior to the laser treatment, use of anticoagulation therapy, age under 18, presence of systemic diseases in the patient, using artificial light sources, sauna, during the treatment, use of fillers, pregnancy and herpes viral skin infections. Patients in the second group (CG) undergone therapeutic modalities depending on the diagnosis of the disease, and according to the existing protocols for certain diseases. For patients with acne scars and patients who undergone rejuvenation, the comparison was made with retinoids, topically applied to the skin.

The results and conclusion: fractional CO_2 laser used in treatment of acne scars, is an effective and safe method. with significant better effect from the therapy, greater patients' satisfaction, minimal side effects. In the treatment of skin rejuvenation, the laser treatment is effective and safe, causing statistically significant higher satisfaction in relation to the control group of patients. Satisfaction with the treatment in patients undergoing rejuvenation is greater than in any of the examined groups. In all three indicative subgroups of the laser examined group (acnes, rejuvenation, skin imperfections) there are no statistically significant mutual differences in relation to the laser treatment, i.e. it is equally efficient. The combined laser treatment using platelet-rich plasma versus laser monotherapy shows greater cumulative assessment of the effect of applied treatment, but without statistical significance. At the same time, the combined laser therapy with PRP is associated with greater patients satisfaction by the treatment and with significantly greater satisfaction with the appearance of regarding pigmentations after the treatment versus laser monotherapy.

SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS: AN UPDATE

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Lupus erythematosus (LE) is a chronic inflammatory connective tissue disorder characterized by loss of immune tolerance with pathogenic autoantibody production, immune complex deposition, and tissue damage. LE encompasses a broad spectrum of subtypes, which include systemic lupus erythematosus (SLE) and cutaneous lupus erythematosus (CLE). Whereas SLE generally involves various organs and systems, CLE mainly affects skin and mucosa and can be further classified into acute, subacute, and chronic CLE.

The lesions of subacute CLE (SCLE) are typically non-scaring, annular and/or papulo-squamous, symmetrically distributed over the photo exposed areas. Also, some atypical forms have been described: erythrodermic, annulare centrifugum-like, toxic epidermal necrolysis-like, etc. Even though SCLE patients commonly meet criteria for SLE (based on mucocutaneous, immunological and serological findings), both the ACR and SLICC criteria for SLE identify patients with relatively mild systemic disease.

De novo idiopathic SCLE in the elderly, wide spread lesions out of sun-exposed areas, recalcitrant course of the disease and presence of B symptoms should prompt the search for underlying malignancy. On the other hand, with new and emerging drugs, there are many new drug-induced cases of SCLE.

With many new drugs on the horizon, vigorous photoprotection and antimalarials are still the first therapeutic options in this group of patients.

KAPILAROSKOPIJA U DIJAGNOZI AUTOIMUNIH BOLESTI

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Uvod: Postavljanje precizne dijagnoze u autoimunim bolestima je izazovan deo reumatologije, zbog velikih preklapanja u simptomatologiji i razlika u kliničkom toku, komorbiditetima i prognozi. Kapilaroskopija je neinvazivan metod za dijagnostiku izmena u mikrocirkulaciji kože u regiji proksimalnog nabora nokta, gde su petlje položene paralelno površini kože, što ih čini lako dostupnim pregledu.

Metode: Tehnički uslovi za izvođenje kapilaroskopije su jednostavni; pregled se može raditi specijalizovanim instrumentima, ili videomikroskopom, sa uveličanjem x50 do x200. Polarizovano svetlo ima manji značaj nego u dermatoskopiji, koristi se kontaktni medijum koji smanjuje refleksiju svetlosti sa površine kože. Memorisanje digitalnih fotografija kapilaroskopije u elektronskom kartonu pacijenta olakšava praćenje mikrocirkulatornih izmena, i praćenja progresije ka patološkom nalazu. Pregledaju se svi prsti šaka osim palčeva, i analiziraju parametri: broj petlji/mm, palisadni raspored, postojanje kapilarnih isključenja (avaskularnih zona), morfologija petlji i postojanje patoloških oblika (megakapilara, kapilarnih ektazija, mikroaneurizmi, bizarnih oblika), znakova neoangiogeneze, krvavljenja, vidljivost subpapilarnog pleksusa, prisustvo edema.

Rezultati: Pri interpretaciji nalaza kapilaroskopije koriste se internacionalno prihvaćene preporuke. Skleroderma obrazac karakterišu megakapilari, hemoragije, avaskularne zone, neoangiogeneza. Rana skleroderma ima očuvan palisadni raspored i gustinu, sa malim brojem dilatiraih petlji ili megakapilara. U aktivnoj fazi skleroderma obrasca postoje brojne dilatirane petlje, i hemoragije, umereno smanjenje gustine petlji i edem papilarnog tkiva. U kasnom obrascu skleroderme gustina pelji je niska, postoje avaskularne zone i znaci angoineogeneze.

Zaključak: Kapilaroskopija je prepoznata kao značajan element u diferencijalnoj dijagnozi brojnih autoimunih bolesti, i jedan od dijagnostičkih kriterijuma sistemske skleroze koji može biti uočljiv u ranoj fazi bolesti. S obzirom da se orjentacija o obrascu kapilaroskopije može uraditi ručnim dermatoskopom, poznavanje tehnika pregleda, metoda interpretacije nalaza, postaje neophodan deo dermatološke prakse.

Ključne reči: kapilaroskopija, autoimune bolesti, sistemska skleroza

METHOTREXATE IN PSORIASIS TREATMENT

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Despite significant advancements in psoriasis therapy over the past ten years, methotrexate and other traditional antipsoriatic drugs remain the primary treatment approach for many patients. While some of these drugs have been on the market for decades, there is limited evidence regarding their optimal use. Dermatologists often struggle with issues such as the appropriate starting dose, the best dosing regimen, the need to add folic acid (and the recommended amount and frequency), and the appropriate approach to treating children or elderly patients when using methotrexate. The aim of this presentation is to provide a comprehensive review of the existing evidence and answer some of these challenging questions, providing the audience with up-to-date knowledge on the use of methotrexate in psoriasis.

JAK-STAT PATHWAY INHIBITORS IN TREATMENT OF PSORIASIS

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The JAK-STAT signaling pathway mediates key cellular processes including immune response, cell differentiation, division and death. Medications that interfere with different JAK-STAT signaling patterns have potential indications for various medical conditions, including. inflammatory or immune mediated diseases such as psoriasis, vitiligo, atopic dermatitis and alopecia areata.

Inflammation in psoriasis is mainly promoted by IL-23, which induces the differentiation of naïve T-cells into Th17 lymphocytes and their clonal expansion. IL-23 signal transduction is mediated by TYK2. IL-22, produced by Th22 cells, is mediated by the JAK-STAT pathway and induces keratinocyte proliferation. The release of IL-22, in association with IL-15, is signaled by JAK1 and JAK3; therefore, JAK/TYK inhibition is a potential target for its treatment.

Tofacitinib, solcitinib, baricitinib and deucravacitinib showed a PASI75 response superior to that of placebo at both week 8 and week 12 in RCTs on moderate to severe plaque psoriasis. In meta-analysis, tofacitinib (15 and 10 mg, BID) and deucravacitinib (6 mg BID and 12 mg/d) had the best Physician Global Assessment (PGA) and PASI75 responses (at weeks 8 and 12) among JAKi. Drugs under study are deucravacitinib, brepocitinib, and ropsacitinib, all TKY2 inhibitors. Tofacitinib 5 mg BID may be effective in treating nail psoriasis in 33% of patients achieved NAPSI50 at week 16. The only topical JAKi under study is an JAK1/JAK2 inhibitor brepocitinib.

JAK2/TYK2 inhibitors are promising, more immunologically selective, restricting the possibility of side effects and leading to replace classic immunosuppressants.

Keywords: psoriasis, JAK STAT inhibitors

NAIL PSORIASIS: A TREATMENT CHALLENGE

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Psoriasis is a chronic, immune-mediated disease that affects skin, scalp and nails. Nail involvement is seen in 50% of patients with skin lesions and in 80% of patients with psoriatic arthritis. Clinical features of involved nails are pitting, red lunular spots and crumbling in a case of nail matrix affection and onycholysis, subungual hyperkeratosis, leukonychia, oil spots, and splinter hemorrhages in a case of nail bed psoriasis. Treatment of nail psoriasis is extremely challenging. Topical therapies with corticosteroids, vitamin D derivates and immunomodulators are used in a mild nail psoriasis. However, these methods are barely effective due to a limited penetration of topically applied substances and therefore a relapses are common. Intralesionally applied corticosteroids or intralesional methotrexate therapies are more effective however the way of administration of these drugs is painful and patient compliance is low. In more severe nail psoriasis or in a case of three and more nail involvement, conventional systemic therapy with methotrexate, cyclosporin and acitretin is effective but with a great caution of organ toxicities in the long term use. The efficacy of PD-4 inhibitor apremilast and biologic drugs such as TNF inhibitors, IL-17 and IL-23 inhibitors are well proved in series of clinical investigations and they have best long term efficacy in the treatment of nail psoriasis.

HIDRADENITIS SUPPURATIVA: CURRENT DEVELOPMENTS AND FUTURE ASPECTS IN PATHOPHYSIOLOGY AND TREATMENT

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Hidradenitis suppurativa/acne inversa (HS/AI) is a chronic, relapsing, inflammatory, potentially mutilating skin disease of the terminal pilosebaceous glands that manifests with painful, inflammatory lesions in the apocrine glandular regions of the body, particularly the axillary, inguinal, and anogenital regions. Intensive clinical and experimental research and the review of new therapeutic approaches have almost completely renewed knowledge in the field of HS/AI since the publication of the old german guideline in 2012. A point prevalence of active disease of 0.3% was observed in Germany, rising to 3.0% taking into account the scars typical of HS/AI. Pillars of HS/AI pathogenesis are abnormal differentiation of the keratinocytes of the pilosebaceous gland and massive accompanying inflammation. The primary lesions of HS/AI are inflammatory nodules, abscesses, and draining tunnels predominantly at predilection sites (axillary, submammary, inguinal, genital, and perineal). Recurrences in the last 6 months with at least 2 lesions at the sites of predilection indicate HS/AI. Although these criteria can be used to make a clinical diagnosis with a high accuracy of 97%, the disease is still little known, as the delay in diagnosis in Germany of 10.0±9.6 years proves. Patients with HS/AI suffer from a significant reduction in quality of life, especially when there is a high degree of morbidity. In daily practice, HS/AI should be classified and its activity assessed using a validated instrument, primarily using the International Hidradenitis Suppurativa Severity Scoring System (IHS4), in order to be able to make correct treatment decisions. HS/AI is divided into two forms related to the severity of the always detectable inflammation, namely the active, inflammatory and the inactive, predominantly non-inflammatory forms. While the intensity of the inflammatory form is divided into mild, moderate and severe HS/AI using the IHS4 classification and treated accordingly with medications, the predominantly non-inflammatory form is treated surgically according to the Hurley grade of the affected location, namely Hurley-Grade I, II and III. The new S2k guideline on the therapy of HS/AI will provide an accepted decision-making aid for the selection and implementation of a suitable/sufficient therapy for patients with HS/AI. Oral tetracyclines or 5-day intravenous clindamycin therapy are equivalent to the effectiveness of the oral systemic combination of clindamycin and rifampicin. Subcutaneously administered adalimumab and secukinumab are approved for the treatment of HS/AI. Various surgical procedures are available for the predominantly non-inflammatory form of the disease. The combination of drug therapy to reduce inflammation with a surgical procedure to eliminate irreversible tissue damage is currently considered a holistic therapy procedure for HS/AI. Several new therapeutic compounds are currently studied in phase II and III trials. Regular monitoring and, if necessary, adjustment of the therapy with regard to a changing degree of disease severity is recommended.

UPDATE ON VITILIGO TREATMENT 2023

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Narrowband (NB) UVB phototherapy has been established as an effective treatment for vitiligo. The previously released British Association of Dermatology (BAD) guidelines on PUVA stated that NB UVB is at least as effective as PUVA; the match of repigmentation to normal skin color is better with NB UVB than with PUVA and NB UVB is more effective in inducing repigmentation in unstable vitiligo than PUVA.

In the last couple of years BAD published the guidelines on vitiligo (2021) and NB UVB phototherapy (2022), respectively. Both documents agreed that NB UVB (whole body or localized) should be offered as first-line phototherapy to people with vitiligo who have an inadequate response to topical therapy and/or who have extensive or progressive disease. This may be combined with topical calcineurin inhibitor (more evidence for tacrolimus) or potent topical corticosteroid, for localized sites.

Janus kinase inhibitors (JAKi) represent a new class of targeted immunotherapy. Since the publication of the above guidelines, ruxolitinib, first topical JAKi for the treatment of vitiligo, has been licensed. In addition, there have been a number of reports of effectiveness of systemic JAKi, already licensed for other skin conditions, in vitiligo. Recent research demonstrated the notable improvement in recalcitrant vitiligo patients treated with oral upadacitinib. The clinical trial has shown that oral ritlecitinib was effective and well tolerated in patients with active non-segmental vitiligo.

The introduction of JAKi is the biggest advance in the vitiligo treatment since NB UVB phototherapy in the late 1990s.

DERMATOLOGIC DISORDERS IN TRANSGENDER PATIENTS

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Transgender persons face a multitude of dermatologic conditions related to the cutaneous effects of gender-affirming hormone therapy and procedures; many are often underdiagnosed and underrecognized. For transmasculine persons, common conditions include acne vulgaris and male pattern hair loss. For transfeminine persons, hirsutism, pseudofolliculitis barbae, and melasma are most common. Gender affirming surgery may result in keloids and other surgery-related complications. Specific aspects of skin health in transgender persons should be addressed when providing multidisciplinary gender-affirming care.

SYPHILIS TREATMENT - A MODERN CHALLENGE

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Syphilis treatment seems to be stuck in time. For more than 80 years the first line medication for treating syphilis is Penicillin. Deposit penicillin formulations improved over time to be easier to use and not so painful: smaller, elongated crystals of a median size of less than 12.5 µm contribute to a fluent deployment from the syringe, and dilution in normal saline alleviates the pain at the injection site. *Treponema pallidum* shows no resistance to this treatment but there are challenges for the treatment of β-lactams allergic patients, pregnant women, congenital syphilis and neurosyphilis. Neurosyphilis and neonatal syphilis requires a prolonged and intensive administration of intravenous aqueous crystalline penicillin G. The patient needs to be admitted in a dermatological department. Allergy to penicillin must be documented as there is a trend in exaggeratedly consider all adverse reaction as a severe allergic reaction.

Doxycycline is the second line treatment and new evidence suggests a potential use of this drug for Pre-Exposure Prophylaxis (PrEP) and Post-Exposure Prophylaxis (PEP). It is not yet known if the large-scale use of those methods will not select resistant *T. pallidum* strains. At this stage doxycycline can be used only as PEP for STI prevention. No relevant data is available for using tetracycline and minocycline instead of doxycycline.

Ceftriaxone proved to be useful in the treatment for neurosyphilis and cefixime in the treatment for early syphilis. Linezolid used as oral treatment demonstrated excellent therapeutic properties for syphilis, including neurosyphilis (it penetrates the central nervous system). A point mutation that may cause resistance in *T. pallidum* was described. Other tested drugs are Amoxicillin, zoliflodacin, and spectinomycin. Those antibiotics treatments represents only a small part of the whole strategy to defeat syphilis. Communities must be involved, not only for the screening but for a strategy to notify the contacts.

DERMATOLOGIC MANIFESTATIONS OF HIV INFECTION

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Through the United Nations, the world committed to end AIDS by 2030 by reducing new HIV infections as well as annual AIDS related deaths and by eliminating all forms of HIV-related stigma (Political Declaration on HIV and AIDS. Ending Inequalities and Getting on Track to End AIDS by 2030. United Nations General Assembly, 2021). HIV can nowadays be fully controlled by potent and safe antiretroviral therapy. Transmission to others and progression to AIDS are then completely stopped. HIV can remain undiagnosed for years despite the presence of clear indicator conditions diagnosed in patients that require treating physicians to test for HIV. Patients with HIV indicator conditions have a substantial risk of an underlying HIV infection but remain frequently untested or not identified for possible preventive care. This causes significant delays in diagnosing HIV with unwanted health sequelae and missed opportunities to interrupt transmission networks. A key strategy to end AIDS is to diagnose HIV earlier by unbiased HIV testing of all people with HIV indicator conditions and to guarantee access to adequate HIV prevention in at risk individuals. Many opportunities to test for HIV and protect at risk individuals remain unused.

Human Immunodeficiency Virus (HIV) is a retrovirus infection which causes an acquired immunodeficiency of the host via reduction in the number of CD4 T cells. Without appropriate treatment, a person with HIV will eventually progress to the advanced stage of infection, Acquired Immunodeficiency Syndrome (AIDS).

Dermatological conditions are extremely common during HIV infection and will affect approximately 90% of all people living with HIV. These conditions can be both specific to HIV, as well as common skin problems found in general population. Cutaneous manifestations will generally increase in incidence with advancing HIV disease and declining immune function, causing significant morbidity. Hence, early recognition and testing in patients presenting with such conditions may allow HIV infection to be diagnosed and treated earlier. Antiretroviral medications used for treatment of HIV can also be implicated.

Increased susceptibility to bacterial, viral, fungal and parasitic infections is common and these can appear at different stages of the disease. People living with HIV have an increased risk of developing cutaneous malignancies due to their impaired immune response. Prior to widespread treatment with HAART, the AIDS-defining Kaposi sarcoma was the most prevalent malignancy in the HIV population due to infection by human herpesvirus 8. Cutaneous T- and B-cell lymphomas are also more prevalent with HIV infection.

People with undiagnosed HIV may potentially present to any hospital, clinic or primary care/general practice setting. HIV testing should be considered during any clinical contact when a person presents with an indicator condition. Regarding primary prevention, the envisioned standard for all healthcare professionals is that they link their patients at risk for HIV to appropriate HIV preventive care.

HPV ON THE CUTTING EDGE OF DERMATOLOGY, VENEREOLOGY AND MEDICINE IN GENERAL

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Anogenital warts (condylomata acuminata) are the most common HPV lesions presented in men, however, during the last decade the other HPV-associated exaggerated lesions such as condylomata plana, penile, scrotal, and anal intraepithelial neoplasias, as well as the penile, tonsillar and oropharyngeal cancer have been studied a little bit more extensively. Consistent studies are still sparse for male population. More than 35 types of HPV infect the genital tract; types 16 and 18 inducing about 70% of high-grade intraepithelial genital neoplasias and HPV 6 and 11 causing 90% of anogenital warts. However, the "banality" of anogenital warts should not be underestimated providing that the high risk HPV DNA 16 and 18 can be isolated (PCR) from "benign" HPV-associated genital lesions in 10-20% of patients, i.e. more than it is usually expected. On the other hand, the presence and the recalcitrant course of HPV DNA 6 and 11 associated diseases represent a significant physical and psychological problem for both men and women.

A prophylactic vaccine that targets these types should thus substantially reduce the burden of HPV-associated clinical diseases. Ultimately, within the spectrum of therapeutic options for condylomata, no method is really superior to others; recurrences occurred in 30-70% of cases. However, the proactive sequential treatment representing the combination of the ablative and immunomodulatory treatment (imiquimod, sinecatechins) might be considered as treatment of choice today. We definitely need the HPV vaccination programme to get rid of one of the oldest and up to now unsolved problems of humankind. Managing both partners is necessary in order to eliminate the virus in the population. Approaches to this include prophylactic vaccines such as nonavalent (9-v) HPV vaccine for both men and women. This should be the only way to significantly decrease the numbers of infected persons. Besides, a proper dermatological training is required as the clinical criterion is still very important and the HPV-induced lesions are quite often misdiagnosed unless managed by the skilled professional. It can be thus concluded that the HPV-genital infections represent a significant dermato-venereological issue, and the dermatovenereologists should definitely be the part of the HPV vaccine programme team.

LICHEN SCLEROSUS OF THE ANOGENITAL REGION

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Lichen sclerosus is a chronic inflammatory disease that most commonly affects the anogenital region. The prevalence ranges from 0.1% to 0.3% in dermatological institutions and 1.7% in gynecological institutions. It occurs 3 to 10 times more frequently in women than in men. The traditional belief suggests that there are two peaks in women: prepubertal and postmenopausal, but recent research indicates that this condition often develops during the reproductive period before and after childbirth. In men, there are two peaks: in childhood (children up to 7 years old and adolescents) and in adulthood (30-50 years old), while the frequency of this disease decreases in older age. The disease is multifactorial and involves autoimmune, genetic, and hormonal factors, as well as the influence of local external factors. Autoimmune diseases are more common in individuals with lichen sclerosus compared to the general population, including thyroid diseases, vitiligo, alopecia areata, rheumatoid arthritis, primary biliary cirrhosis, pernicious anemia, Crohn's disease, ulcerative colitis, morphea, systemic lupus, and multiple sclerosis. All patients with symptoms and signs of suspected lichen sclerosus should be examined and started on therapy to cure the disease or prevent the formation of scar tissue in specific cases. Some possible complications include urethral stenosis and malignant transformation into squamous cell carcinoma. Diagnosis is mostly clinical in the majority of cases. The gold standard in therapy involves potent and very potent topical corticosteroids.

KOŽNE MANIFESTACIJE HRONIČNE VENSKE BOLESTI STADIJUMA C4 I SMERNICE ZA LEČENJE

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Hronična venska bolest (HVB) predstavlja veoma učestalo oboljenje koje u svom toku prolazi kroz 6 kliničkih stadijuma. Dok su simptomi u prva tri stadijuma obično blagi, od 4. stadijuma počinju veće tegobe bolesnika. U ovom stadijumu koji se dalje može podeliti na dva podstadijuma (a i b), javljaju se brojne promene na koži. Najznačajnije su: hiperpigmentacije, rđasta purpura i hipostazni dermatitis, koje se javljaju u podstadijumu a, kao i lipodermatoskleroza u podstadijumu b. Takođe u ovoj fazi bolesti veoma je čest i kontaktni alergijski dermatitis. Velika je disproporcija između intenziteta kožnih promena i simptomatologije koju pacijenti imaju.
Osim brojnosti različitih promena na koži koje se javljaju u ovom stadijumu HVB, one su često veoma slične kliničke slike i međusobno se preklapaju. Stoga su greške u postavljanju dijagnoze lako moguće i veoma česte. Njihovo lečenje se u znanoj meri razlikuje, tako da je ispravna dijagnoza od suštinskog značaja.
Pravilna dijagnoza i adekvatna terapija su od esencijalne važnosti kako bi se zaustavilo napredovanje bolesti i sprečila progresija u terminalne stadijume bolesti, koje vode otvaranju ulkusa na potkolenicama.

DIAGNOSTIC CHALLENGES OF THE "BLUE SKIN" - OCHRONOSIS

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The term ochronosis is derived from the word "ochre" in Greek language, which refers to yellow discoloration although it is characterized by a clinical appearance of blue-black or gray-blue pigmentation, which reflects the histological finding of yellow-brown deposits in the dermis. There are two types of ochronosis: (1)endogenous that is, alkaptonuric ochronosis and (2) exogenous ochronosis (EO).

Endogenous ochronosis or alkaptonuria is a rare, autosomal recessive disorder that is caused by a deficiency in homogentisic acid oxidase (HGAO). Affected people excrete high levels of homogentisic acid (HGA) in the urine, which then darkens when it is alkalinized or oxidized. Deposits of blackish-brown pigment also occur in connective tissue, and are responsible for the typical skin discoloration together with characteristic disorders in internal organs; these changes usually begin at around the age of 40 years. The disease is also characterized by arthropathy of the large joints. Less common features include cardiovascular abnormalities, and renal, urethral and prostatic calculi.

There is no effective therapy for this disorder, although nitisinone inhibits the enzyme that produces HGA.

EO is an acquired condition with no systemic manifestations as a result from the use of topical hydroquinones phenol, quinine injection, resorcinol, picric acid, mercury, and oral antimalarialsa. It is clinically and histologically similar to alkaptonuria. It presents as asymptomatic bilaterally symmetrical speckled blue-black macules and several gray-brown macules, typically affecting the malar areas, temples, lower cheeks, and neck. Histopathology is a gold standard in the diagnosis of EO with the presence of the ochre-colored, banana-shaped fibers in the dermis being pathognomic histopathological feature. The treatment is often far from gratifying. Sun-protection, topical retinoid acid, glycolic acid, and a topical corticosteroid (low-potency creams), chemical peeling with glycolic acid or tricarboxylic acid or Q-switched Nd: YAG laser showed some improvement in dyschromia.

AUTOIMMUNE BULLOUS DISEASES IN PREGNANCY

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Autoimmune bullous diseases (AIBDs) are rare organ-specific diseases characterized by the appearance of blisters and erosions on the skin and mucous membranes. These dermatoses are marked by the development of autoantibodies targeting the autoantigens located in intercellular junctions, *i.e.*, between keratinocytes or in the basement membrane area. Therefore, the fundamental division of AIBDs into the pemphigus and pemphigoid groups exists. Although AIBDs are uncommon in the general population, their overall incidence is somewhat higher in women of all ages, for which a pregnant women can be likely affected too. While the pemphigoid gestations is exclusive bullous dermatosis of pregnancy, the other AIBDs can also start or worsen during this period. The appearance of AIBDs in childbearing women is a particularly sensitive situation requiring exceptional clinicians' caution due to the possibility of pregnancy complications with adverse effects and risks to the mother and the child. Also, there are numerous management difficulties in the period of pregnancy and lactation related to the drugs' choice and safety.

TREATMENT OF A PATIENT WITH SKIN CANCER - PROFESSIONAL, ETHICAL AND RATIONAL ASPECT - WHAT IS BEST FOR THE PATIENT?

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The incidence of skin cancers has been increasing steadily over the last decades. Although there have been significant breakthroughs in the management of skin cancers with the introduction of novel diagnostic tools and innovative therapies, skin cancer mortality, morbidity and costs heavily burden the society. Several questions are to speak about them in the modern dermato-oncology according skin carcinoma patients.

Does professionalism really always mean that the patient will be treated professionally, and does following professional guidelines really always mean the best for the patient? Do we always make human decisions /humanely, ethically/, or are we sometimes guided by other inclinations: concern for our own safety, fear of a professional mistake, of a lawsuit, or are decisions sometimes made due to a lack of knowledge and, above all, experience? Is what the professional guidelines dictate always rational and reasonable - the example of re-excision of keratinocyte cancer? What all should in daily practice influence our decisions: age of the patient, general condition of the patient, region of change, type of malignant process, stage of disease progression?

Several types of treatment, not only surgery, can be used to remove or destroy skin cancers. The options depend on factors such as the tumor size and location, and a person's age, general health, and preferences. These cancers very rarely spread to other parts of the body, although they can grow into nearby tissues if not treated.

All of the treatments listed here can be effective when used in appropriate situations. The chance of the cancer coming back (recurring) ranges from less than 5% after Mohs surgery to up to 15% or higher after some of the others, but this depends on the size of the tumor. Small tumors are less likely to recur than larger ones. Even if a tumor does recur, it can often still be treated effectively and patient life is not in danger.

Each patient with skin cancer is a story in itself. The treatment must be individual, and important part of individuality is getting into the soul of the patient. Professional treatment must include the expertise but also rational judgment and be based on ethical principles and humanity. Only someone with extensive personal experience can provide sovereign and professional advice for the benefit of the patient. To choose the optimal treatment, doctor must have knowledge, experience and courage. Only a good person who loves people can be a good practitioner what is all the more truth when treating a cancer patient.

ADVERSE SKIN REACTIONS TO DRUGS

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Introduction: The skin is the organ most often affected by drug reactions. Most of these reactions are mild and resolve without consequences, however, in 2-6.7% of patients, they can develop into potentially life-threatening conditions (1).

Goal: By analyzing recent literature data, determine the frequency and type of the most common adverse drug reactions on the skin.

Discussion: Adverse skin reactions to drugs represent a heterogeneous field of cutaneous manifestations that can mimic any dermatosis. About 30 different skin reactions ranging from mild dermatitis to severe conditions with systemic manifestations have been described. They occur in about 10% of hospitalized patients, and in 1-3% of people who take a lot of drugs at the same time. There is a lack of comprehensive data on the occurrence of adverse drug reactions in outpatient settings, but their frequency is considered to be 1-3% in developed countries, 2-5% in developing countries, and 2.6-15.1% in dermatological practice (2, 3). The most frequently reported adverse reactions are exanthema (maculopapular rash), urticaria/angioedema, fixed drug eruption and a minor form of erythema multiforme. Most of these eruptions are mild, self-limiting, and usually resolve after discontinuation of the drug and a short course of therapy. Exfoliative dermatitis (erythroderma), hypersensitivity syndrome, bullous erythema multiforme, Stevens Johnson syndrome (SJS) / Toxic epidermal necrolysis (TEN) occur less frequently (3). The most severe, life-threatening drug reactions are SJS/TEN, which today are considered as a variants of the same condition. They differ according to the area of skin involvement (<10% SJS, >30% TEN, between 10% and 30% SJS-TEN overlapping syndrome). SJS has a mortality rate of less than 5% while in TEN it is 20-30%, when most patients die of sepsis. Medicines that most often cause adverse skin reactions are beta-lactam antibiotics, sulfonamides, NAIL, antiepileptics, allopurinol (3, 4). Predisposing factors for the occurrence of these reactions to the drug are: female gender, older age, previous medicinal eruption, positive family history, existence of acute viral infections (especially acute Epstein Barr virus and human herpes viruses 6 and 7), simultaneous intake a lot of drugs, as well as a cross-reaction associated with previous hypersensitivity to various drugs, sunscreens, cosmetics, food, or insect bites (2). Drug reactions can be immunological and non-immunological. Most (75-80%) are caused by predictable, non-immunological mechanisms, 20-25% by unpredictable factors that may or may not be immunologically mediated. Immune-mediated reactions make up 5-10% of all reactions (4, 5).

Conclusion: Adverse skin reactions to drugs are common and can be caused by various medicaments. They manifest from barely noticeable and mild reactions to very serious life-threatening reactions. The most serious manifestation is TEN, which can be fatal in 20-30% of patients. It is important that the skin changes are related to the drug in a timely manner and that the suspect drug be excluded from the therapy as soon as possible.

ATOPIC DERMATITIS IN ELDERLY PATIENTS

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Atopic dermatitis affects 0.5-2.6% of elderly population, worldwide. Factors specific for atopic dermatitis in elderly patients include innate physiological changes of aging, decline in skin barrier function, dysregulation of innate immune cells, and skewing of adaptive immunity to Th2 response. Diagnostic and treatment approach in the elderly may be challenging. In differential diagnosis, scabies, pemphigoid, mycosis fungoides, contact dermatitis and dermatitis due to air pollution, must be excluded. Furthermore, comorbidities such as diabetes mellitus, dyslipidemia, congestive heart failure, osteoporosis, hypertension, gastroesophageal reflux, etc. are frequent and may affect treatment options. Also, elderly patients usually need complex polypharmacy to manage their chronic health conditions. Alongside with that, the elderly are at risk of age-associated physiological, functional, and cognitive changes. These changes as a segment of vicious circle increase the risk of adverse drug effects in this age group. All mentioned above suggest that atopic dermatitis in elderly population may be puzzling, so different clinical aspects of this disease will be discussed.

TREATMENT OF CHRONIC URTICARIA

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Urticaria is a condition characterized by the development of wheals (hives), angioedema or both. The lifetime prevalence of acute urticaria is approximately 20%. The duration of chronic spontaneous urticaria (CSU) is usually longer than one year. Based on the duration urticaria is classified to acute and chronic. Chronic urticaria can be spontaneous and inducible.

Diagnostic work up in chronic urticaria is to exclude differential diagnosis diagnoses, assess disease activity, impact and control and to identify triggers of exacerbation or, where indicated, any underlying causes.

The treatment of choice for CSU are 2nd generation of antihistamines. If patients do not respond to mono dose, the dose is elevated to fourfold.

Patients with chronic spontaneous urticaria that have failed to respond to maximum-dose 2ndgeneration oral antihistamines taken for 4 weeks should be referred to a dermatologist, immunologist or medical allergy specialist to prescribe omalizumab. Omalizumab is a humanized monoclonal antibody that binds to circulating immunoglobulin E (IgE) and reduces the release of inflammatory mediators from mast cells and basophils. If omalizumab does not help, patients can be treated with cyclosporine, methotrexate, leukotriene receptor antagonists (eg, montelukast), dapsone, H2-antagonists, mycophenolate, plasmapheresis, phototherapy, intravenous immunoglobulin, etc.

ETIOLOGIJA PRURITUSA I EVALUACIJA PACIJENTA SA PRURITUSOM

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Pruritus je čest simptom u svakodnevnoj dermatološkoj praksi. Smatra se da patogenetski mehanizmi koji dovode do osećaja svraba uključuju prenos signala od perifernih C-nervnih vlakana do neurona u kičmenoj moždini i mozgu. U ovaj proces mogu biti uključeni različiti medijatori svraba.

Pruritus se može klasifikovati prema dužini trajanja, kliničkim manifestacijama, etiološkom faktoru i lokalizaciji. Prema dužini trajanja, pruritus može biti akutan (pruritus koji traje manje od 6 nedelja)i hroničan (koji traje 6 nedelja ili više), dok po kliničkim manifestacijama može biti: pruritus sa prisutnim kožnim eflorescencama (u sklopu dermatoloških oboljenja različite etiologije), pruritus bez vidljivih promena na koži (koji često prati oboljenja bubrega, žučne kese, jetre, neuropatije i dr.) i pruritus sa brojnim sekundarnim eflorescencama na koži koje se javljaju kao posledica češanja (u sklopu sistemskih bolesti). Prema etiološkom faktoru, pruritus se deli na dermatološki (pruritus koji se javlja kao prateći simptom brojnih kožnih oboljenja, kao što su različite forme dermatitisa, psorijaza, infekcije i infestacije kože i dr), sistemski pruritus (kod oboljenja različitih sistema organa, kao na primer hronična bubrežna insuficijencija, oboljenja jetre, hematološka i limfoproliferativna oboljenja, maligniteti, lekom izazvan pruritus i dr), neurološki pruritus koji se javlja kod oboljenja perifernog i centralnog nervnog sistema (brahioradijalni pruritus, notalgia parestetica, multipla skleroza i dr), psihogeni pruritus (udružen sa depresijom, psihogenim ekskorijacijama, deluzionim parazitozama, i dr) i mešoviti tip pruritusa kada postoji kombinacija uzroka iz prethodno navedenih grupa, koji udruženo mogu biti praćeni svrabom. Prema lokalizaciji, pruritus može biti lokalizovani (sa ili bez promena na koži) i generalizovani (sa ili bez promena na koži).

Posebna kategorija pruritusa je idiopatski pruritus, kod koga svrab kao simptom postoji i perzistira, ali i sprovođenjem detaljnog ispitivanja se ne nalazi uzrok svraba. Iako protokoli za reevaluaciju ovih pacijenata nisu jasno definisani, u dostupnoj literaturi je preporuka da reevaluacija stanja u prvim godinama bude na četiri do šest meseci, a kasnije ređe.

Pacijenti koji pate od svraba često imaju poremećen kvalitet života zbog čega im je otežano normalno fizičko i psihološko funkcionisanje. Pošto je prisustvo pruritusa udruženo sa mnogim različitim bolestima, dijagnostika i lečenje pruritusa su izazov za lekare. U cilju evaluacije pacijenta sa pruritusom potrebno je uzeti detaljnu medicinsku anamezu, sprovoditi potrebne i individualizovane dijagnostičke procedure i primeniti adekvatnu terapiju u skladu sa kliničkom slikom i opštem stanju pacijenta.

USMENE PREZENTACIJE
ORAL PRESENTATIONS

KLINIČKE I HISTOPATOLOŠKE KARAKTERISTIKE SKVAMOCELULARNOG KARCINOMA KOŽE-ISKUSTVO REFERENTNE TERCIJARNE USTANOVE

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Uvod: Pacijenti sa skvamocelularnim karcinomom kože (SCC) operisani u ranim stadijumima bolesti imaju dobru prognozu, dok kod neblagovremeno lečenih pacijenata može doći do pojave metastaza ili letalnog ishoda. Cilj sprovedenog istraživanja bio je ispitivanje histopatoloških karakteristika SCC u populaciji pacijenata operisanih u referentnoj tercijarnoj ustanovi.

Metode: U retrospektivnu studiju uključeno je ukupno 597 pacijenata operisanih zbog SCC na Klinici za opekotine, plastičnu i rekonstruktivnu hirurgiju UKCS u periodu od marta 2019. do decembra 2022. godine. Analizirane su demografske karakteristike pacijenata, kliničke i histopatološke karakteristike tumora.

Rezultati: Prosečna starost pacijenata iznosila je 75.9 ± 10.2 godina i većina je imala prebivalište na teritoriji Beograda (82.0% vs 18.0%). SCC se češće javljao kod muškaraca nego kod žena (61.1% vs 38.9%). Kod 26.0% pacijenata radilo se o multiplim lezijama. Invazivne forme SCC bile su zastupljenije u odnosu na Mb Bowen (71.8% vs 28.2%) i učestalije su se javljale u regiji glave i vrata u odnosu na druge delove tela (73.7% vs 26.3%). Skoro polovina pacijenata (46.5%) je imala histološki verifikovan G1 tumora, 37.6% je imalo G2 , 9.8% G3, dok je najmanje bio zastupljen G4 (6.1%). Retikularni dermis bio je invadiran u 40.2% slučajeva, masno tkivo u 12.6%, mišić u 9.4%, dok su površniji tumori koji zahvataju samo papilarni sloj bili najmanje zastupljeni, u 8.5% slučajeva.

Zaključak: Imajući u vidu značajno veću zastupljenost invazivnih formi SCC koje u najvećem broju slučajeva infiltrišu retikularni sloj kože, potkožno masno tkivo i mišić čime se povećava rizik za metastatsku bolest, potrebno je promovisati značaj redovnih dermatoloških pregleda pacijenata u cilju otkrivanja i lečenja in situ formi SCC.

Ključne reči: Tumori kože, Skvamocelularni karcinom kože, Mb Bowen

UTICAJ VREMENSKOG INTERVALA OD EKSCIZIONE BIOPSIJE PRIMARNOG MELANOMA DO BIOPSIJE LIMFNOG ČVORA STRAŽARA NA STATUS LIMFNOG ČVORA

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Uvod: Biopsija limfnog čvora stražara (SLNB) danas je standardna procedura u dijagnostici melanoma, koja nam služi za rano otkrivanje metastaza u limfnim čvorovima (LČ), određivanje stadijuma bolesti, a samim tim i dalje lečenje. Indikacije za SLNB zavise od debljine primarnog melanoma po Breslow-u. Trenutno ne postoji jedinstvena preporuka o optimalnom intervalu. Holandske nacionalne smernice za melanom zagovaraju strogi maksimalni vremenski interval od šest nedelja. Važno je razmotriti vreme SLNB u lečenju melanoma, jer bi moglo imati uticaj na ranu detekciju metastaza u LČ, a samim tim i dalji tok bolesti.

Cilj naše studije je da se ispita da li je vremenski interval između primarne dijagnoze i SLNB povezan sa pojavom metastaza u SLN.

Metode: U studiju je uključeno 406 pacijenata kojima je između 2010. i 2017. godine u VMA dijagnostikovan melanom, a potom učinjena SLNB radi detekcije metastaza. Ispitivana je korelacija intervala (do 6 nedelja/duže od 12 nedelja) od ekscizije do SLNB, zatim korelacija između lokalizacije limfnih basena (vrat, aksila, ingvinum) i broja ektirpiranih LČ (1 i više od 1), kao i statusa SLN (pozitivan ili negativan).

Rezultati: Od ukupnog broja pacijenata (n=406) kod njih 20,7% (n=84) je detektovana metastaza u SLN. Istraživanjem tri različita intervala, nije pokazana statistička značajnost. Statistička značajnost je pokazana kod pacijenata kod kojih je ekstirpirano više SLN u odnosu na pacijente sa jednim ekstirpiranim SLN ($p<0,005$).

Zaključak: U našoj studiji je pokazano da interval od ekscizije primarnog tumora do SLNB nema uticaja na pozitivnost SLN. Nije bilo značajne statističke razlike u detekciji metastaza u limfnom čvoru stražaru u odnosu na vreme (manje od 6 nedelja/duže od 12 nedelja) od ekscizione biopsije primarnog melanoma do biopsije limfnog čvora stražara.

Ključne reči: Melanom; SLNB; Interval; Detekcija; Metastaza;

ZNAČAJ ODNOSA NEUTROFILA I LIMFOCITA I MELRISK KOEFICIJENTA ZA PREDIKCIJU METASTATSKOG MELANOMA U SENTINEL LIMFNOM NODUSU

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Uvod: U dosadašnjoj literaturi pokazana je povezanost odnosa broja neutrofila i limfocita sa patohistološkim nalazom dijagnostičke biopsije limfnog nodusa stražara kod pacijenata nakon ekscizije melanoma. Na osnovu navedenog koeficijenta i patohistoloških parametara melanoma pri primarnoj eksciziji predložen je MELRISK koeficijent za predikciju postojanja metastaza melanoma u limfnom nodusu stražaru.

Cilj rada je ispitati povezanost odnosa neutrofila i limfocita i MELRISK koeficijenta sa pozitivnim nalazom metastaza u limfnom nodusu stražaru u studiji serije slučajeva iz naše ustanove.

Metode: U studiji su analizirani podaci ukupno 39 pacijenata starosti od 36 do 87 godina kod kojih je učinjena biopsija limfnog nodusa stražara. Korelirani su podaci odnosa neutrofila i limfocita, izračunatih MELRISK procenata za svakog pacijenta i patohistološkog nalaza biopsije sentinel limfnog nodusa.

Rezultati: Statističkom obradom podataka kvalitativnih i kvantitativnih varijabli u IBM SPSS 21 uz pomoć testova korelacije i regresije uočava se slaba povezanost odnosa neutrofila i limfocita sa MELRISK koeficijentom. Uočava se slaba negativna korelacija odnosa neutrofila i limfocita i slaba pozitivna korelacija MELRISK koeficijenta sa patohistološkim statusom biopsije sentinel limfnog nodusa. Ipak, u svim sprovedenim testovima, bez obzira na jačinu korelacije, nije uočena statistički značajna povezanost ispitivanih parametara.

Zaključak: U analiziranim podacima naše studije slučaja ne pokazuje se povezanost prediktivnog procenta MELRISK koeficijenta sa patohistološkim nalazima biopsije sentinel limfnog nodusa. Takođe, ne uočava se uticaj odnosa neutrofila i limfocita sa MELRISK prediktivnim koeficijentom.

Ključne reči: MELRISK, melanom, sentinel limfni nodus

PRIKAZ SLUČAJA – KOMPLETNI ODGOVOR NA IMUNOTERAPIJU PEMBROLIZUMABOM U PACIJENTA S METASTATSKIM MELANOMOM

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Uvod: U relativno kratkom vremenskom razdoblju, strategije liječenja metastatskog melanoma korištenjem imunoterapije s inhibitorima imunoloških kontrolnih točaka su se značajno promijenile i rezultirale nevjerojatnim poboljšanjem preživljavanja pacijenata. Prikazujemo učinak pembrolizumaba u slučaju pacijenta s metastatskim melanomom.

Metode: 63-godišnji muškarac primijetio je ubrzan rast madeža na desnoj sljepoočnici krajem 2017. Nakon dijagnostičke obrade i kirurškog tretmana, potvrđen je nodularni melanom stadija IIC (T4b N0 M0). Nakon ekstirpacije sumnjivog limfnog čvora na vratu desno u 8/2018, otkrivena je metastaza melanoma u limfnom čvoru. PET CT u 10/2018 potvrdio je metastaze u submandibularnom limfnom čvoru i velikoj hepatalnoj leziji što je potvrđeno i patohistološki nakon ekstirpacije submandibularne žlijezde desno (2 od 5 limfnih čvorova pozitivna) i biopsije jetre. BRAF mutacija nije bila prisutna. Pacijent je započeo liječenje imunoterapijom pembrolizumabom u 1/2019 (početno ocijenjen ECOG PS ½).

Rezultati: Nakon samo 4 ciklusa imunoterapije, stanje pacijenta se poboljšalo (ECOG PS 0). Kontrolne dijagnostičke obrade svaka 3 mjeseca pokazivale su kontinuiranu regresiju jetrene metastaze.

Nakon ukupno 42 ciklusa pembrolizumaba, postignuta je kompletna regresija jetrene metastaze inicijalne veličine 72x106x115 mm (potvrđeno na MRI jetre i PET CT-u). Nastavljeno je daljnje intenzivno praćenje pacijenta. Pacijent je i dalje bez znakova bolesti i dobrog je zdravstvenog stanja.

Zaključak: Ovaj slučaj ističe važnost pravovremenog pristupa navedenoj terapiji kako bi pacijentima s metastatskim melanomom, koji je nekada imao lošu prognozu, pružili mogućnost izlječenja. Takav je slučaj u našeg pacijenta koji je nakon 2 godine i 5 mjeseci liječenja pembrolizumabom postigao potpuni odgovor na terapiju.

Ključne reči: metastatski melanom; imunoterapija; pembrolizumab

PRIMENA NIVOLUMABA KOD PACIJENATA SA UZNAPREDOVALIM MELANOMOM - ISKUSTVO KLINIKE ZA ONKOLOGIJU UKC NIŠ

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Uvod: Inhibitori kontrolnih tačaka (ICI) kod pacijenata sa uznapredovalim melanomom su značajno su unapredili ishod lečenja, u poređenju sa konvecionalnom hemioterapijom. Nivolumab spada u grupu ICI i može se primeniti kao monoterapija, ili u kombinaciji sa Ipilimumabom, kod pacijenata sa uznapredovalim melanomom, bez obzira na BRAF mutacioni status.

Metode: Na klinici za onkologiju, univerzitetskog kliničkog centra Niš smo u periodu od jula 2020. do oktobra 2023.g. sproveli retrospektivnu analizu koja je uključila 49 pacijenta sa uznapredovalim melanomom lečenih Nivolumabom. Isključujući kriterijum bio je ECOG performans status ≤ 2. Efikasnost Nivolumaba procenjivana je ispitivanjem perioda bez progresije (PFS) i ukupnog preživljavanja (OS), korišćenjem Kaplan Meierove metode.

Rezultati: U grupi pacijenata lečenih Nivolumabom zabeležena je neznatno veća zastupljenost ženskog pola (51%), a prosečna starost je iznosila 67±12,8 godina. Veći broj pacijenata (63.2%) nije imao detektovanu mutaciju u BRAF genu i 87.8% njih je terapiju primalo u prvoj liniji. Distribucija po stadijumima bila je sledeća; M1c (32.6%), M1a (20.4%), CSIII (20.4%), M1d (16.3%) i M1b (10.2%). Vrednost laktat dehidrogenaze je u trenutku uvođenja terapije bila elevirana povišena kod više od trećine pacijenata (38.7%), dok je prosečan broj datih ciklusa terapije po pacijentu bio 8. Medijana PFS iznosila je 7.03 meseci, dok je OS iznosio 9.43 meseci. Neželjeni efekti zabeleženi su kod 26% pacijenata, a najzastupljenija je bila kožna toksičnost (69%). Većina neželjenih efekata bila je gradusa 1-2 (92%), i nije zahtevala obustavu terapije.

Zaključak: ICI predstavljaju terapiju izbora kod pacijenata sa uznapredovalim melanomom, ali faktori poput povišenih vrednosti LDH, broja i veličine metastaza predstavljaju prognostički loše parameter ishoda imunoterapije. Značajno kraće preživljavanje kod naših pacijenata, u poređenju sa podacima iz realne kliničke prakse, mogu se pripisati kasnijem otkrivanju uznapredovalog melanoma.

Ključne reči: melanom, imunoterapija, iskustvo centra

IMUNOTERAPIJSKI RECHALLENGE: DVA KLINIČKA PRIMJERA

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Uvod: Metastatski melanom donedavno je bio neizlječiva bolest, što uporabom novih načina liječenja promijenilo, prije svega primjenom imunoterapije. Imunoterapija je pojam koji obuhvaća različite modalitete liječenja, uključujući primjenu inhibitora kontrolnih točaka (ICI). ICI su vrlo potentno sredstvo u liječenju metastatskog melanoma, no kod određenog broja pacijenata dolazi do progresije bolesti i/ili razvitka imunosno posredovanih nuspojava (irAE), što neminovno dovodi do prestanka primjene ICI. Međutim, u ponekih pacijenata može se pokušati ponovno primjeniti imunoterapija (rechallenge) u svrhu kontrole bolesti, a ponekad i izlječenja. U ovom radu prikazati će se dvoje pacijenata kod kojih smo se odlučili za ponovnu primjenu ICI nakon razvitka nuspojava na incijalnu terapiju.

Metode: Prikaz toka liječenja dvoje pacijenata oboljelih od metastatskog melanoma.

Rezultati: Riječ je o dvoje pacijenata kod kojih se na inicijalnu primjenu ICI prati kompletna remisija uz pojavu irAE u vidu autoimunog hepatitisa, odnosno artritisa. Nakon provedenog imunosupresivnog liječenja i prekida u primjeni ICI kod oba slučaja prati se regresija irAE, no istovremeno i povrat osnovne bolesti. Posljedično se ponovno uvede u terapiju ICI, što rezultira kompletnom remisijom, odnosno parcijalnom remisijom, uz izostanak ponovne pojave autoimunog hepatitisa kod prve pacijentice i ponovnu pojavu artritisa u drugog pacijenta.

Zaključak: Iako je imunoterapija promijenila paradigmu liječenja velikog broja onkoloških pacijenata, mjesto ponovnog uvođenja imunoterapije u toku liječenja nakon incijalne primjene nije sasvim jasno. Za odgovoriti na pitanja poput kod kojih pacijenata primijeniti rechallenge, kojim lijekovima i u kojem trenutku liječenja biti će potrebne daljnje studije.

Ključne reči: melanom, imunoterapija, nuspojave, rechallenge

INFLAMMATORY BIOMARKERS AS A PREDICTIVE PARAMETER FOR THE FIRST-LINE ANTI-PD1 IMMUNOTHERAPY IN METASTATIC MELANOMA: MULTICENTRE RETROSPECTIVE STUDY

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Background: Immune system plays an important role in the pathogenesis of all cancers, including melanoma. Biomarkers derived from complete blood count, considered to bean indirect measure of the immune inflammatory response, have been recognized as the useful prognostic factor in some tumours, but the evidence is limited in relation to melanoma. We have analyzed these biomarkers in patients with metastatic melanoma treated with first-line anti-PD1 immunotherapy.

Methods: In this multicenter retrospective study blood samples of 69 melanoma patients (26 females and 43 males),older than 18 years, treated with first-line anti-PD1 therapy were collected up to one month before the start of the treatment. The baseline LDH (bLDH) and inflammatory biomarkers[neutrophil to lymphocyte ratio (bNLR), monocyte to lymphocyte ratio (bMLR), lymphocyte to monocyte ratio (bLMR), platelet to lymphocyte ratio (bPLR) and pan-immune inflammation value (bPIV)] were analyzed, as well as their correlation with duration of treatment and progression-free survival.

Results: The mean age of the patients is 66.6 years (29 to 96). Most patients have the pathological subtype of nodular melanoma, and the most common location of the primary tumor is on the trunk. The mean Breslow thickness is 4.86mm (0.7 to 27), and the most of patients has ulceration (46% present, 19% absent and 35% unknown). In most patients, the BRAF mutation is negative (64% negative and 36% positive). Most of them have 1-3 metastatic site at the beginning of therapy (83% 1-3 and 17% >3). Mean value of bNLR, bPLR, bMLR and bPIV in analyzed samples were 3.97, 187.39, 0.38 and 571.74, respectively. Mean age is 66.55, and median is 70 (min 29, max 96). Patients with elevated bLDH had significantly higher mean bNLR (4.76 vs 3.45; $p<0.05$), bPLR (222.75 vs 164.33; $p<0.05$) and bPIV (906.17 vs 335.17; $p<0.05$) than patients with normal bLDH. Patients with PFS of more than 12 months had significantly lower mean bNLR (3.85 vs 4.54; $p<0.05$), bMLR (0.29 vs 0.44; $p<0.05$) and bPIV (341.72 vs 719.55; $p<0.05$) when compared to patients with a PFS<12 months. Also, lower bNLR and bMLR was found in patients with PFS > 24 months ($p<0.05$). Patients with bNLR and bMLR below cut-off values were associated with duration of therapy > 12 months ($p<0.05$).

Conclusions: This study showed the association between of bNLR, bPLR, bMLR and bPIV values and elevated bLDH, previously recognized as a poor prognostic/predictive marker in patients with metastatic melanoma. A significant correlation between the values of these inflammatory biomarkers was shown in relation to the duration of therapy, as well as to the 12-month PFS rate. Further studies are needed to confirm possible prognostic/predictive value of inflammatory biomarkers.

KLINIČKE KARAKTERISTIKE KARCINOMA KOŽE KOD PACIJENATA ZRAČENIH ZBOG TINEE CAPITIS U DETINJSTVU

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Uvod: Tokom 50-tih godina 20. veka iradijacija poglavine X zracima bila je zvanično prihvaćena metoda za lečenje tinee capitis kod dece. Posledice ovakvog načina lečenja postale su vidljive godinama kasnije u vidu pojave agresivnih formi tumora glave i vrata, karcinoma štitaste žlezde kao i meningeoma kod zračenih pacijenata.

Metode: U retrospektivnu studiju uključeni su pacijenti operisani zbog karcinoma kože ili defekta na koži poglavine na Klinici za opekotine, plastičnu i rekonstruktivnu hirurgiju, UKCS, a koji su u detinjstvu bili zračeni zbog tinee capitis. Analizirane su demografske karakteristike pacijenata, kliničke i histopatološke karakteristike tumora kože, kao i pojava komplikacija nakon operativnog lečenja.

Rezultati: U studiju je bilo uključeno 37 pacijenata prosečne starosti 60.6±7.8 godina. Kod 86.5% pacijenata bili su prisutni tumori kože, a kod 43.2% je registrovan recidiv. Oko 64.9% pacijenata imalo je multiple lezije na prvom pregledu. 32.43% imalo je agresivne, uznapredovale forme BCC, ulcus rodens ili ulcus terebrans. U 18.9% slučajeva bila je prisutna aseptična nekroza kosti, a u 72.9% pacijenata registrovana je umerena ili teška atrofija kože poglavine. Hirurške komplikacije su se javile u 43.2% slučajeva i bile su povezane sa prisustvom aseptične nekroze kosti ($p=0.001$) i teške atrofije kože ($p<0.05$) bez obzira na regiju na poglavini.

Zaključak: Lečenje ovih pacijenata je veliki izazov zbog pojave agresivnih, rekurentnih formi tumora i često je praćeno komplikacijama. Ova studija otkriva populaciju pacijenata potencijalno pod većim rizikom za nastanak teških formi BCC, ulcus rodens ili ulcus terebrans i zahteva učestale kontrole od strane dermatologa i plastičnog hirurga.

Ključne reči: BCC, SCC, Tinea capitis, ulcus terebrans, ulcus rodens

POSLEDICE COVID-19 PANDEMIJE NA PACIJENTE SA SKVAMOCELULARNIM KARCINOMOM KOŽE

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Uvod: U cilju obezbeđivanja kapaciteta za lečenje COVID-19 pozitivnih pacijenata, došlo je do reorganizacije zdravstvenog sistema širom sveta uključujući i odlaganja elektivnih procedura, preventivnih i redovnih kontrolnih pregleda pacijenata. Razlika u dostupnosti tercijarnim zdravstvenim ustanovama tokom pandemije postala je izraženija, a posledice se još uvek sagledavaju. Cilj istraživanja bio je ispitivanje dostupnosti zdravstvene zaštite pacijentima sa skvamocelularnim karcinomom kože (SCC) tokom COVID-19 pandemije.

Metode: Retrospektivno su analizirane demografske karakteristike pacijenata i histopatološke karakteristike SCC operisanih u periodu 15.3.2019.-31.12.2022.godine u Klinici za opekotine, plastičnu i rekonstruktivnu hirurgiju UKCS. Analiziran je ukupno 701 uzorak i ispitivane su razlike između pacijenata sa prebivalištem van Beograda i pacijenata sa prebivalištem u Beogradu u prepandemijskom, pandemijskom i postpandemijskom periodu.

Rezultati: U postpandemijskom periodu pacijenti sa prebivalištem van Beograda bili su mlađi u odnosu na pacijente iz Beograda (70.55 vs. 76.66; p=0.005) i imali su značajno veću zastupljenost invazivnih formi SCC (90.3% vs 70.3%, p=0.022). Pre pandemije nije bilo značajne razlike u najvećem dijametru tumora između ispitivanih grupa. Tokom pandemije dolazi do porasta najvećeg dijametra u obe grupe ali i dalje bez statističke značajnosti (13.5 mm vs 15 mm; p=0.057), dok posle pandemije tumori pacijenata van Beograda postaju značajno veći (15 mm vs 27 mm; p<0.001). Nije pokazana razlika u debljini tumora između ispitivanih grupa u postpandemijskom periodu.

Zaključak: Imajući u vidu da su pacijenti sa SCC većim od 20mm u dijametru u riziku od pojave metastatske bolesti, značaj ove studije ogleda se u idektifikovanju grupa ugroženih pandemijom, sa posebnim osvrtom na potencijalnu neophodnost reevaluacije dostupnosti zdravstvene zaštite na tercijarnom nivou.

Ključne reči: COVID-19 pandemija, Tumori kože, Skvamocelularni karcinom kože, Dostupnost zdravstvene zaštite

UTICAJ COVID-19 PANDEMIJE NA LEČENJE PACIJENATA SA MELANOMOM

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Uvod: Pacijenti kod kojih je melanom dijagnostikovan u ranom stadijumu imaju bolju prognozu i veću stopu preživljavanja. COVID-19 pandemija uticala je na dostupnost zdravstvene zaštite širom sveta što je za posledicu imalo pojavu progresiju hroničnih i onkoloških bolesti.Cilj sprovedenog istraživanja bio je ispitvanje uticaja COVID-19 pandemije na dijagnozu i lečenje melanoma.

Metode: U retrospektivnu studiju uključeno je 393 pacijenta koji su po protokolu operisani zbog melanoma u Klinici za opekotine, plastičnu i rekonstruktivnu hirurgiju UKCS u periodu od 1.januara 2017. do 31.marta 2022. godine. Pacijenti su podeljeni u prepandemijsku (01.januar 2017-14.mart 2020) i pandemijsku grupu (15.mart 2020-31.mart 2022). Analizirane su demografske karakteristike pacijenata, kliničke i histopatološke karakteristike tumora.

Rezultati: Melanom je dijagnostikovan kod 339 pacijenta u prepandemijskom i kod 54 pacijenta u pandemijskom periodu. Pacijenti iz pandemijske grupe imali su značajno veću medijanu debljine tumora po Breslow-u (1.80 vs 3.00; p = 0.010), veću zastupljenost melanoma debljih od 2mm (37.8% vs 53.7%; p = 0.026), kao i veći broj mitoza po mm2 (2 vs 5; p < 0.001). Dodatno u pandemijskoj grupi pokazana je i veća učestalost Clark IV-V stadijuma u odnosu na prepandemijsku grupu (44.0% vs 63.0%; p = 0.009). Nije pokazana statistički značajna razlika između ispitivanih grupa u odnosu na pol, starost, lokalizaciju tumora na telu, histološki podtip melanoma, prisustvo ulceracije ili mikrosatelita.

Zaključak: Covid-19 pandemija je dovela do odlaganja preventivnih pregeleda i samim tim odlaganja blagovremene dijanoze i tretmana pacijenata sa melanomom. Rezultati ove studije mogu biti od velikog značaja za organizaciju zdravstvene zaštite ukoliko se sličan scenario pojavi u budućnosti.

Ključne reči: Melanom, Covid-19 pandemija, Tumori kože

MERKEL CELL CARCINOMA KOD PACIJENTA SA TRANSPLANTIRANIM BUBREGOM - PRIKAZ SLUČAJA

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Uvod: Merkel cell carcinoma (MCC) je retka forma kutane neoplazme sa lošom histološkom diferencijacijom i agresivnim kliničkim ponašanjem, čestim rekurencijama i visokom stopom smrtnosti. Postoje brojni faktori rizika među kojima je imunokompromitovanost jedan od najznačajnijih. Pacijenti kod kojih je izvršeno presađivanje bubrega spadaju u grupu onih koji su u većem riziku za razvoj ovog retkog i agresivnog neuroendokrinog tumora kože usled dugotrajne imunosupresivne terapije koja ima ulogu u sprečavanju odbacivanja organa. Poslednjih godina je primećena veća incidenca ovog tumora nakon transplantacije bubrega i sve više radova opisuje ove slučajeve, kako lokalne rekurecije MCC tako i metastaze ovog tumora u limfnim čvorovima, mozgu, kostima, jetri i plućima.

Prikaz bolesnika: U ovom radu opisan je slučaj šezdesetsedmogodišnjeg muškarca kome je transplantiran bubreg 2001. godine i koji je uzimao imunosupresivnu terapiju. Na pregled se javio zbog brzorastućeg crvenog čvora na desnoj podlaktici za koji je učinjena ekscizija. PH nalaz je pokazao da se radi o Merkel cell karcinomu i da se tumor nalazi na bazalnom i bočnim rubovima resekcije. PH nalaz učinjene reekscizije pokazao je da nema tumora na resekcionim rubovima. Nakon dobijanja urednih nalaza radiološke dijagnostike indikovana je adjuvantna radioterapija. Nakon 6 meseci došlo je do pojave limfonodopatije desne aksile. PH nalaz ekstirpiranih limfnih čvorova je pokazao da se radi o metastazama Merkel cell carcinoma (2/16). Na osnovu postojećih vodiča, pacijentu su savetovane redovne kontrole svaka 3 meseca uz UZ preglede limfnih nodusa vrata, aksila, ingvinuma, abdomena i male karlice, a svakih 6 meseci i PET-CT/MSCT endokranijuma, grudnog koša, abdomena i male karlice.

Zaključak: Merkel cell karcinom iako se retko dijagnostikuje, ovaj neuroendokrini tumor predstavlja drugi najčešći uzrok smrti od karcinoma kože, posle melanoma. Razlog leži u njegovoj agresivnosti i rapidnoj progresiji. Zato bi kliničari morali biti na oprezu i u vidu imati i ovaj tumor kada se pacijent pojavi sa solitarnom brzorastućom eritematoznom nodularnom promenom a da u ličnoj anamnezi ima podatak o transplantaciji organa i uzimanje imunosupresiva. Takođe bi bilo preporučljivo objasniti svim pacijentima koji su bili podvrguti transplantaciji značaj primarne prevencije i redovnih dermatoloških pregleda.

Ključne reči: Merkel cell carcinoma, transplantacija bubrega, imunosupresija

BEYOND THE ABCD, A CASE SERIES OF MELANOMAS LACKING THE CLASSICAL CRITERIA

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Introduction: Many thick, life-threatening melanomas do not have classic ABCD (asymmetry, border irregularity, color variegation, diameter of 6mm).Here, we report a case series of melanomas with atypical presentations.

Objective: To demonstrate the limitations of the ABCD mnemonic.

In the first case, we present a completely benign ABCD + lesion, right next to a flat symmetrical, uniform in color, with regular borders, <6mm, invasive melanoma. Nodular melanomas are by default symmetrical and with regular borders(case 2), often non-pigmented, resembling a benign lesion(case 4). Micromelanomas, with less than 6mm diameter, can be easily detected bydermoscopy(case 3),long before they show clinical signs. Sometimes patients report lesions that they have been observing for more than a year and did not ask for help, since it was ABCD negative(case 5). Therefore, the ABCD rule alone may not be sufficient for the diagnosis of pre-invasive melanoma.

Many suggestions have been made to improve this mnemonic. The Ugly duckling sign is by far the simplest yet most effective rule for clinical evaluation. Three CCC(color, contour, change), 'Do UC (different, uneven, changing), G for Geometric shape, replacing D with dark, E with EFG, and adding Feel, because many cases excised only at the request of the patient's "feeling" turn out to be malignant. The ABCD rule for pediatric patients already has been altered.

Conclusion: Relying on the ABCD mnemonic alone could lead to overlooking early melanomas. Further research is needed to introduce new rules to improve early melanoma detection and overall patient outcomes.

Keywords: ABCD rule, melanoma, early detection, nodular melanoma.

LICHEN SCLEROSIS TREATMENT WITH ERBIUM YAG LASER OUR EXPERIENCE

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Introduction: Lichen sclerosus (LS) is an inflammatory skin disease that usually involves the anogenital area where it causes itching and soreness, sexual dysfunction, urinary dysfunction in men and is associated with genital cancer. The course of LS can be chronic.

Treatment remains unsatisfactory, in particular in women as disabling scar formation is common despite treatment. The Er:YAG laser with specific non ablative modality, which causes shrinkage of collagen fibers and consequently triggers neocollagenesis, might be another therapeutic option for lichen sclerosus,where an alteration in the distribution of collagen is very important.

Methods: In this study, 12 women between the ages of 35 and 65 years were included, diagnosed for the first time with vulvar LS, confirmed with biopsy without any treatment before. The study was carried out over the period from March 2020 till December 2021.

In the first session, the Er:YAG laser (SP Dynamis, Fotona, Slovenia) was applied with a PS03x handpiece with fluence of 7 J/cm2, 2 Hz, and spot of 7 mm in continuous application.

Then Er:YAG treatment modality (Fotona SMOOTH mode) that causes gentle coagulative heating of the skin was used. The modality delivers laser energy onto the skin in a fast sequence of low-fluence laser pulses inside an overall super-long pulse of 200 ms to 350 ms. every so often when the area whitened, it was cleaned with gauze soaked in physiologic fluid.

The objective was to achieve uniform whitening and an increase in local heat until erythema of the area or whitening was observed after 10 minutes of application. Three sessions were applied in monthly intervals.

Results: From 12 patents 3 of them stop the procedure after 1 treatment and after follow up no symptoms and signs from LS and they confirmed satisfaction with one treatment. After the treatment, we advise the application (Centella asiatica (Cicabio Bioderma) and Neomycin) was recommended for 7 days, twice a day, together with an intimate moisturizing cream Cicaplast (La rosh posey). After the procedure the patients reported only small sensation that last only 2 days and erythema after the laser procedure. Satisfaction was measured by asking simple question regarding the improvement of the symptoms and also after procedure no one from the patients used corticosteroid as a topical treatment.

Conclusion: Laser treatment with Erbium Yag laser was well tolerated by patients and significantly reduced the impact of lichen sclerosis on patients' lives

Keywords: laser, erbium yag, lichen sclerosus

COMORBIDITIES IN PATIENTS WITH SEVERE ALOPECIA AREATA

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Introduction: Alopecia areata (AA) is an autoimmune disease characterized by chronic and relapsing course, especially in its severe forms. AA frequently co-occurs with other autoimmune and inflammatory diseases.

Aim: To evaluate the demographic characteristics and frequency of comorbidities in patients with severe AA.

Methods: A cross-sectional study was conducted on 168 hospitalized patients with severe AA (SALT>30). The medical records were reviewed for demographic data and the presence of comorbidities. The patients were divided into two groups: children (<18 years) and adults (≥18 years).

Results: Out of 168 patients, 78 were (43.4%) children and 90 adults (56.6%). The median age was 18 years (range 2-74). In children, the male-to-female ratio was 1.1:1. In adults, the female-to-male ratio was 2.5:1. Most common comorbidities in both groups were atopic diathesis (children 15.4%, adults 14.4%) and Hashimoto's thyroiditis (children 12.8%, adults 16.7%). Only 4 patients had vitiligo, 3 of whom were adults (3.3%). Comparing adult and pediatric patients, metabolic syndrome and psychiatric disorders were more frequent in adults, 20.0% vs 2.5% (p=0.01) and 14.4% vs 2.5% (p=0.007), respectively.

Conclusion: Our study shows a high frequency of autoimmune and inflammatory diseases in adult and pediatric patients with AA, with atopic diathesis and Hashimoto's thyroiditis in every seventh patient. Our findings also show a significantly higher frequency of metabolic syndrome and psychiatric disorders occurring in adult AA patients compared to children. We concur that screening for specific comorbidities in AA patients is necessary; therefore, future studies need to evaluate the potential impact of comorbidities on AA prognosis.

Keywords: Alopecia areata, Comorbidities, Children, Adults

PREVALENCIJA SUPURATIVNOG HIDRADENITISA U BEOGRADU

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Uvod: Hidradenitis supurativa (HS) je hronična inflamatorna bolest koju karakterišu bolni čvorovi i apscesi koji pucaju, izazivajući sinusne tunele i ožiljke najčešće u aksilarnoj, ingvinalnoj, perianalnoj i submamarnoj regiji. Prevalencija u svetu se značajno razlikuje i iznosi od 0,00033% do 4,1%. U Srbiji do sada nisu sprovođene epidemioloske studije HS.

Metode: Ovo istraživanje predstavlja monocentričnu studiju sprovedenu u Vojnomedicinskoj akademiji u Beogradu i deo je projekta Global Hidradenitis suppurativa Atlas. U istraživanje su uključene zdrave pratnje pacijenata koje su popunjavali upitnik u kome su se izjašnjavale o polu, starosti, težini, visini, konzumiranju cigareta i o postojanju bolnih čvorova na koži. Pregledane su sve osobe koje su se izjasnile da imaju promene definisane u upitniku i svaka deseta osoba koja se izjasnila da nema promene.

Rezultati: Studija je uključivala 490 ispitanika. Klinički smo pregledali 64 osobe nasumično i 7 osoba koje su prijavile simptome. HS je pronađen kod 2 nasumična ispitanika i 2 koja su prijavile simptome. Prevalencija je bila 0,82%. Nije bilo statistički značajne razlike između polova (2 vs 2, p=1), starosti (40.5 vs 47, p=0.3), indeksa telesne mase (25.7 vs 25.3, p=0.35) između grupe pacijenata sa HS i kontrolnom grupom. Skrining upitnik je imao osetljivost 0,5 (2/4), specifičnost 1 (62/62), pozitivnu prediktivnu vrednost 1,00 (2/2) i negativnu prediktivnu vrednost 0,97 (62/64).

Zaključak: Prevalenca HS u Beogradu iznosi 0,82%. Oboljenje se javlja sa podjednakom učestalošću kod oba pola, dok su za uticaj pušenja i indeksa telesne mase potrebna opsežnija ispitivanja na većem broju ljudi.

Ključne reči: hidradenitis suppurativa, prevalencija

MANAGEMENT OF REFRACTORY CHRONIC SPONTANEOUS URTICARIA: A 10-YEAR RETROSPECTIVE ANALYSIS OF CLINICAL-EPIDEMIOLOGICAL CHARACTERISTICSAND THERAPEUTIC OUTCOMES

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Introduction and Objectives: Chronic spontaneous urticaria (CSU) is a condition characterized by daily or near-daily hives and/or angioedema lasting at least six weeks, primarily affecting individuals aged 40-60, with a higher incidence in women. Primary treatment with second-generation H1 antihistamines is effective in 50-70% of patients, highlighting the need for alternative treatment options. Our research aims to assess the safety and efficacy of treatment options for refractory CSU patients, with a focus on different modalities.

Materials and Methods: We collected clinical data from 43 patients diagnosed with refractory CSU, resistant to maximum doses of H1 antihistamines and short-term systemic corticosteroid therapy, treated at the Clinic of Dermatovenereology from January 2013 to October 2023. Data included patient demographics, disease duration, clinical characteristics, disease severity, comorbidities, and laboratory parameters (CRP, C3, C4, IgE, ANA and autologous serum skin test results). Disease severity and treatment outcomes were evaluated using UAS7 and AAS7 scores. Statistical analysis was performed with significance set at $p < 0.05$.

Results: Among the 43 patients, 72.1% were women, median disease duration was 15 months, and angioedema was present in 60.5%. Treatment modalities included dapsone (67.4%), cyclosporine (37.2%), and omalizumab (23.3%). Dapsone therapy was successful in 50% of patients, cyclosporine in 75%, and omalizumab in all patients. Some patients experienced disease relapse after discontinuing therapy, with variations depending on treatment approach. Adverse events were observed, particularly with dapsone and cyclosporine. Laboratory parameters showed no significant correlation with disease severity or treatment outcomes.

Conclusion: Our research reaffirms existing findings on gender distribution, disease characteristics, and associations with comorbidities in CSU patients. The success of dapsone, cyclosporine, and omalizumab treatments aligns with previously published data. The absence of significant correlation between laboratory parameters and disease severity or treatment outcomes underscores the need for further research to identify specific CSU biomarkers.

OMALIZUMAB U TERAPIJI HRONIČNE URTIKARIJE- NAŠE ISKUSTVO

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Uvod: Omalizumab je biološki lek koji sadrži humana monoklonska anti IgE antitela i od 2014. godine koristi se u lečenju pacijenata sa hroničnom urtikarijom koji nemaju terapijski odgovor na maksimalne doze antihistaminika.

Metode: Retrospektivno smo analizirali pacijente sa hroničnom spontanom urtikarijom lečene u Klinici za kožne i polne bolesti VMA biološkom terapijom- omalizumabom u periodu od 2021-novembra 2023. godine. Analizirani su pacijenti odrasle životne dobi >18 godina života, a period praćenja iznosio je 2 godine. Analizirane su karakteristike pacijenata, efekat terapije, dužina trajanja i doza terapije, kao i neželjeni efekti lečenja.

Rezultati: Ukupno je analizirano 10 pacijenata sa dijagnozom spontane hronične urtikarije, 7 muškaraca i 3 žene. Prosečna životna dob pacijenata iznosila je 46,7 godina (min. 19- max. 66 godina). Prosečna dužina trajanja bolesti do uvođenja biološke terapije je iznosila 27,4 meseci (min.3-max.140 meseci). Svi pacijenti 10/10 su, pre uvođenja omalizumaba, lečeni kontinuiranom četvorostrukom dozom antihistaminika i sistemskom kortikosteroidnom terapijom, 2/10 pacijenta lečeno je i ciklosporinom A, a 1/10 pacijenta Dapson om. Udruže alergijske bolesti imao je 1 pacijent (alergijski rinitis i bronhijalnu astmu). Angioedem manifestovao se kod 7/ 10 pacijenata. Svim pacijentima ordiniran je omalizumab u dozi od 300 mg s.c. jedanput mesečno. Ni kod jednog pacijenta nije bilo skraćivanja intervala terapije. Kod 5/10 pacijenata nakon prve doze leka došlo je do remisije bolesti, kod 4/ 10 pacijenta nakon prve 3 doze, a kod 1/ 10 pacijenata nakon 4. doze leka. Dužina trajanja terapije bila je 9,3± 2 meseca. Kod 4 pacijenta je terapija obustavljena nakon 12 meseci, kod 2 od 4 pacijenta nakon 2 meseca došlo je do ponovne pojave urtike radi čega je omalizumab vraćen u terapiju. Svi pacijenti (10/10) dobro su podneli terapiju, nisu evidentirani neželjeni efekti.

Zaključak: Kod naših analiziranih pacijenata omalizumab se pokazao kao bezbedan i efikasan lek u terapiji hronične spontane urtikarije.

Ključne reči: hronična urtikarija, terapija, omalizumab

FISH TANK GRANULOM

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Uvod: Fish tank granuloma predstavlja retku infekciju kože čiji je uzročnik Mycobacterium marinum. Mikobakterium marinum je bakterija koja se često nalazi u slatkoj i morskoj vodi širom sveta. Često je infekcija kod osoba koje su u kontaktu sa vodom iz akvarijuma, ali i osobama koje su u kontaktu sa zivim školjkama ili ribom. Granulom se obično javlja na koži gornjeg ekstremiteta, a u nekim slučajevima i na licu.

Prikaz slučaja: U ovom radu opisujemo slučaj infekcije M. marinum koja se manifestovala kao promena na kozi desnog kažiprsta. U pitanju je pacijent u dobi od 26 godina koji navodi da je bio u kontaktu sa vodom iz akvarijuma nakon čega je doslo do pojave promene na kažiprstu u vidu erozije i eritema koja nije prolazila. Učinjena je biopsija za PH analizu i analiza na bakteriju micobacterijum marinium koja je bila pozitivna, a PH nalaz odgovarao Fish tank granulomu. Započeta je terapija sa sistemskim antibioticima prvo Dovicin tbl u periodu od 14 dana potom Rifampicin i Clindamicin u trajanju od 6 nedelja. Za mesec dana je došlo do regresije promena.

Zaključak: Rana dijagnoza infekcije i odgovarajuća antimikrobna terapija su glavni za uspešno lečenje. Incidenca M. Marinum u Francuskoj je 0.09/100000 ljudi i 0.05-0.27 u Americi. Urađena je i studija u Italiji gde je izolovana u 4.5% bazena i ivica bazena.

Ključne reči: fish tank granuloma; mycobacterium marinum; terapija;

TEŽAK OBLIK SUPURATIVNOG HIDRADENITISA- PRIKAZ SLUČAJA

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Uvod: Supurativni hidradenitis (SH) je hronično inflamatorno oboljenje koje se karakteriše rekurentnim bolnim apscesima, nodusima, sinusnim traktovima i ožiljavanjem, pretežno u intertriginoznim regijama. U zavisnosti od težine bolesti, značajno utiče na mentalno zdravlje i kvalitet života. U lečenju se kombinuju medikamentozni i hirurški pristup. Biološki lekovi, anti-TNF u odobrenoj dozi za SH se preporučuju kod pacijenata sa umerenom do teškom kliničkom slikom. Takođe u upotrebi su i IL12/23 inhibitori (ustekinumab), IL-1 inhibitori (anakinra), IL-17 inhibitori (sekukinumab).

Prikaz slučaja: muškarac u dobi 40 godina, sa uznapredovalim oblikom HS. U dvadesetim godinama dolazi do pojave pilonidalnog sinusa glutealno, a potom i gnojnih čireva intertriginozno sa opsežnim zahvatanjem kože. Inicijalno je lečen hirurški i sistemskim antibioticima, sa delimičnim poboljšanjem. U periodu 2012.-2017. godine lečen je adalimumabom sa dobrim terapijskim odgovorom prve dve godine lečenja, a potom se gubi efikasnost. U februaru 2023. godine lečen izotretinoinom (80 mg/dn), bez terapijskog odgovora. Jula 2023. godine učinjena je ekscizija izmenjene kože obe aksile i započeta je dvojna antibiotska terapija Klindamicin i Rifampicin u standardnim dozama tokom 9 nedelja, a nakon toga je u planu započinjanje terapije acitretinom.

Zaključak: Lečenje SH je često složeno i zahteva balansiranje između medicinskih i hirurških opcija lečenja, pored rešavanja terapije bola i komorbiditeta koji mogu biti u vezi sa bolešću. Dostupni tretmani su ograničeni, uglavnom off-label, a često su potrebne hirurške intervencije za postizanje remisije. Savremena biološka terapija nam pruža nove mogućnosti u lečenju SH, ali su potrebna dodatna klinička iskustva da bi se procenila njihova efikasnost.

Ključne reči: hidradenitis; apsces; sinusni trakt; biološka terapija;

POIKILODERMIČNI MYCOSIS FUNGOIDES USPEŠNO LEČEN BRENTUXIMAB VEDOTINOM

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Uvod: Primarni kutani ćelijski limfomi predstavljaju heterogenu grupu non-Hodgkin limfoma (T ili B limfocita, NK ćelija) sa različitim spektrom kliničkih formi, fenotipskih i histopatoloških karakteristika. Mycosis fungoides (MF) predstavlja najčešću formu primarnog kutanog T ćelijskog limfoma (CTCL). Terapijski protokol zavisi od stadijuma bolesti, sa ciljem da se smanji morbiditet i ograniči progresija bolesti.

Metode: Predstavljamo slučaj 67-ogodišnje pacijentkinje hospitalizovane na KDV aprila 2022, sa promenama u vidu jasno ograničenih eritematoznih plakova i pojedinačnih egzulcerisanih tumora promera do 5x5cm na koži trupa i esktremiteta, praćenih izraženim pruritusom u ukupnom trajanju od 3 godine.

Rezultati: Urađene su 3 biopsije kože, histopatološki nalaz je odgovarao CD30-pozitivnom MF. Nakon kompletne evaluacije laboratorijskih parametara (laktat dehidorgenaza 829 U/L, beta-2-mikroglobulin 3.73 mg/L) i dijagnostičkih procedura (ehosonografija mekih tkiva vrata, aksila i ingvinuma na kome je uočena obostrana aksilarna i ingvinalna limfadenopatija), kod pacijentkinje je utvrđen IIb stadijum, kada je konzilijarno odobrena primena sistemske terapije (methotrexate uz acitretin). Prvi ciklus terapije brentuximab vedotin-om započet je decembra 2022, a zatim nastavljen na 3 nedelje, do ukupno 14 ciklusa. Sve vreme trajanja terapije, pacijentkinja je redovno klinički i laboratorijski praćena. Postignuta je kompletna regresija svih kožnih promena, uključujući i tumorske promene, sa mestimičnim perzistiranjem poikilodermije, uz odsustvo limfadenopatije.

Zaključak: Ekspresija CD30 molekula je od velikog značaja u izboru terapije CTCL, zbog čega je neophodno praćenje tokom svih stadijuma bolesti. Brentuximab vendotin je CD30 antitelo-lek konjugat, koji je pokazao odličan odgovor u lečenju CD30-pozitivog MF, bez toksičnosti povezane sa konvencionalnom terapijom.

Ključne reči: mycosis fungoides, CD30, brentuximab vedotin, lečenje

TRASFORMISANI CD30+ MYCOSIS FUNGOIDES

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Uvod: Mycosis fungoides (MF) predstavlja najčešći tip kožnog T-ćelijskog limfoma, koji obično prati indolentni tok. Međutim, kod manjeg broja pacijenata klinički tok može biti agresivniji sa transformacijom neoplastičnih limfocita u klonski identičan fenotip krupnih ćelija.

Prikaz slučaja: Muškarac starosti 39 godina kome je dijagnostikovan MF u šesnaestoj godini. U prvih nekoliko godina bolesti lečen PUVA (psoralen + UVA) terapijom sa acitretinom (Re-PUVA), interferonom alfa sa dobrim terapijskim efektom. Od aprila 2019. godine dolazi do progresije bolesti i razvoja tumoroznih lezija kada je započeta radioterapija nakon koje dolazi do povlačenja promena na koži. Sa progresijom bolesti u januaru 2021. godine patohistološki je potvrđena transformacija bolesti u krupnoćelijski CD30+ MF. Od juna 2021. godine do juna 2022. sprovedena sistemska terapija brentuksimab vedotinom, sa dobrim terapijskim odgovorom, ali 3 meseca po završetku terapije dolazi do ponovne pojave tumora na koži lica, trupa i ekstremiteta. Trenutno je na terapiji metotreksatom 20 mg nedeljno uz nbUVB fototerapiju 3x nedeljno i intralezionu primenu triamcinolon acetonida.

Zaključak: Transformacija MF u krupnoćelijski CD30+ oblik predstavlja agresivnu formu bolesti i značajan klinički izazov. Brentuksimab vedotin kao terapijska mogućnost u ovoj agresivnijoj varijanti, pokazala je dobre rezultate.

Ključne reči: Mycosis fungoides, transformisani oblik, CD30+, brentuksimab vedotin, kutani limfom

LEUKEMIJA KOŽE - RETKA MANIFESTACIJA HRONIČNE MIJELOMONOCITNE LEUKEMIJE

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Uvod: Hronična mijelomonocitna leukemija (CMML) je mijeloidna neoplazma sa karakteristikama mijelodisplastičnog sindroma i mijeloproliferativnih maligniteta, sa tendencijom transformacije u akutnu mijeloidnu leukemiju (AML). Leukemija kože (LC), retka je ekstramedularna manifestacija leukemija, kod CMML je u literaturi opisano 89 slučajeva LC.

Metode: Prikazujemo pacijenta starosti 71 godina koji unazad dve nedelje ima lividne noduluse i papule na prednjoj strani trupa i grudnog koša.

Rezultati: Oktobra 2021. pacijentu je dijagnostikovana CMML-2. U laboratorijskim analizama registrovana je leukocitza (19.6x109) i monocitoza (45%). Flow citometrijom periferne krvi utvrđena je povećana frakcija monocita (53%) i mijeloblasta (0.1%). U aspiratu kostne srži predominatno je bila prisutna populacija monocita, 16% displastičnih monocita i 14% monoblasta. Zbog progresije bolesti (Le 152x109, Mo 49%), anemije i trombocitopenije, u januaru 2023. započeta je terapija merkaptopurinom, nakon čega dolazi do pada broj leukocita (Le 30x109). Na dermatološkom pregledu marta 2023, postavljena je sumnja na LC. Urađena je biopsija, patohistološki se uočava gust dermalni infiltrat atipičnih ćelija. Imunohistohemijki ćelije su CD45+, CD68+, CD13+, HLA-DR+, CD14+, CD3-, CD20-, MPO-, CD117-, CD115-, čime je potvrđena dijagnoza LC u sklopu CMML. Nakon 10 dana od našeg pregleda, pacijent je preminuo, stoga dalje eksploracija nije bila moguća.

Zaključak: LC se izuzetno retko javlja kod pacijenata sa CMML, kada je povezana sa blastnom transformacijom i lošom prognozom. Kod pacijenata sa CMML, leukemija kože je prediktivni faktor progresije u AML. Rano postavljanje dijagnoze je imperativ kako bi dalja hematološka intervencija bila moguća. Patohistologija sa imunohistohemijom neophodna je za potvrdu dijagnoze, s obzirom da su kliničke manifestacije heterogene i mogu imitirati druge dermatoze.

Ključne reči: leukemija kože, CMML, prognostički faktor

KUTANI ERITEMSKI LUPUS SLIČAN ROZACEI – PRIKAZ SLUČAJA

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Uvod: Kutani eritemski lupus se prema dizeldorfskoj klasifikaciji kategoriše kao akutni, subakutni, hronični i intermitentni. Najčešći oblik hroničnog eritemskog lupusa je diskoidni lupus koji se obično manifestuje na licu u vidu jasno ograničenih, eritematoznih, induriranih plakova sa skvamom, atrofijom, promenom pigmenta i ožiljavanjem, dok je rozacei slična klinička prezentacija retka forma eritemskog lupusa.

Metode: Prikazujemo bolesnicu starosti 56 godina koja je pod dijagnozom rozacee unazad 5 godina lečena lokalnom i sistemskom terapijom uključujući i produžene kure antibiotika i izotretinoinom, ali sa inkompletnom regresijom promena na koži lica i recidivima. Na fotoagraviranim predilekcionim mestima lica su registrovane kožne promene u vidu difuznog svetloružičastog eritema sa pojedinačnim sitnim eritematoznim papulama u frontalnoj i malarnoj regiji. Diferencijalno dijagnostički smo razmišljali o fotodermatitisu, Morbus Morbihan, sarkoidozi kože i kutanom lupusu. Laboratorijski nalazi uključujući i komponente komplementa, ANA, anti dsDNA, ACE i antigen Helicobacter pylori u stolici su bili u granicama referentnih vrednosti ili negativni, RTG pluća i srca uredan a patohistološki nalaz biopsije je išao u prilog eritemskog lupusa.

Rezultati: Primenjena je sistemska terapija antimalarikom uz savet o zaštiti od sunca i fotoprotektivne kreme na koju je došlo do kompletne regresije kožnih promena i održavanja remisije.

Zaključak: Autori žele da podsete na ovu retku kliničku formu kutanog lupusa, podstaknu preispitivanje dijagnoze rozacee kod slučajeva rezistentnih na različite modalitete terapije i ukažu na značaj biopsije kože pre empirijskog ordiniranja terapije kod bolesnika sa rozaceiformnim lezijama i fotosenzitivnošću.

Ključne reči: diskoidni eritemski lupus; rozacea; antimalarik; diferencijalna dijagnoza

SCABIES NORVEGICA

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Uvod: Scabies Norvegica, ili krustozni scabijes, je redak i veoma zarazan oblik bolesti. Karakteriše ga ogromna infestacija parazita što rezultira pojavu promena na koži u vidu infiltrovanih plakova sa skvamom. Uglavnom se javlja kod imunokompromitovanih osoba.

Prikaz slučaja: Žena u dobi od 66 godina, koja unazad dve godine ima prisutne promene na koži trupa i ekstremiteta u vidu eritematoznih plakova prekrivenih skvamom praćenih intenzivnim svrabom. U više navrata sprovedena antiskabijesna teraija 5% permetrinom bez terapijskog odgovora. U poslednja 2 meseca dolazi do pogoršanja promena na koži u vidu eritrodermije sa izraženom deskvamacijom. Učinjen je test strugotine kože na sarcoptes scabiei koji je bio pozitivan. Patohistološki nalaz biopsije izmenjene kože, je ukazao na hroničnu spongiotičnu dermatozu sa prisutnim delovima parazita Sarcoptes scabiei. Daljim ispitivanjem nije dokazano prisustvo sekundarne imunodeficijencije. Započeta je terapija ivermektin kapsulama 16 mg u ukupno 5 doza na 1. 2. 8. 9. i 15. dan uz lokalnu terapiju permetrinom. Na navedenu terapiju je došlo do povlačenja promena.

Zaključak: Scabies norvegica je veoma redak oblik bolesti koja se najčešće javlja kod imunokompromitovanih osoba, ređe kod imunokompetentnih osoba, kao što je bio slučaj kod naše bolesnice. Sistemski ivermektina je efikasan u lečenju ovog oblika bolesti

Ključne reči: scabies, norvegica, ivermektin, permetrin, antiparazitska terapija.

PARADOKSALNA (PALMOPLANTARNA) PSORIJAZA KAO NEŽELJENI EFEKAT PRIMENE ADALIMUMABA U LEČENJU MB. CROHN I MB. BECHTEREW – PRIKAZ SLUČAJA

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Uvod: Inhibitori TNFa (adalimumab) koriste se kao monoterapija ili često u kombinaciji sa metotreksatom u lečenju mnogih autoimunskih bolesti među kojima su Mb. Crohn i Mb. Bechterew. Ovi lekovi predstavljaju i jedan od mogućih modaliteta lečenja psorijaze, ali nekada njihova primena može dovesti do pojave neželjenih efekata u smislu pogoršanje postojeće forme psorijaze ili pojave palmoplantarne psorijaze de novo.

Rezultati: Slučaj 1: Muškarac, 52 godine, započeo je lečenje Mb. Bechterew 2017. godine primenom metotreksata u kombinaciji sa adalimumabom, koju je dobro podnosio sve do februara 2023. godine kada dolazi do pojave pustula na eritematoznoj osnovi najpre na koži šaka i stopala, a zatim narednih nekoliko dana i pojave eritematoznih plakova na koži natkolenica, potkolenica, aksila i interglutealno. Na RTG kičmenog stuba i stopala uočene su degenerativne promene u vidu rubnih osteofita, najizraženije u regiji Th1, koje odgovaraju osnovnoj bolesti. Na PH nalazu bioptata izmenjene kože sa šake i potkolenice dokazana je pustulozna psorijaza. Pacijentu je obustavljena dalja terapija adalimumabom i indikovana primena secukinumaba u daljem lečenju i psorijaze uz lokalnu kortikosteroidnu terapiju sa zadovoljavajućim efektom. Slučaj 2: Žena, 31 godina, kod koje je nakon ordiniranja IV ciklusa adalimumaba u sklopu lečenja Mb. Crohn došlo do pojave pustula na šakama i stopalima, a tokom narednih par dana i pojave eritematoznih plakova difuzno po koži trupa i donjih ekstremiteta. Na PH nalazu bioptata izmenjene kože šaka i stopala dokazana je psorijaza. Iz terapije je isključen adalimumab i započeta terapija Ciklosporinom A 5 mg / kg TM uz lokalnu kortikosteroidnu terapiju sa adekvatnim terapijskim efektom.

Zaključak: Pojava paradoksalne psorijaze usled primene adalimumaba predstavlja kontraindikaciju za dalji nastavak lečenja navedenim lekom. U zavisnosti od preostalih modaliteta lečenja osnovne bolesti, dalje lečenje novonastale psorijaze može se tretirati primenom drugih bioloških lekova uz lokalnu kortikosteroidnu terapiju ili primenom sistemske i lokalne terapije prema protokolu lečenja psorijaze.

Ključne reči: adalimumab, paradoksalna psorijaza, lečenje

PRIMENA VIZMODEGIBA U LEČENJU UZNAPREDOVALIH ILI INOPERABILNIH BAZOCELULARNIH KARCINOMA KOŽE – PRIKAZ SLUČAJA

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Uvod: Bazocelularni karcinom kože (BCC) je jedan od najčešćih malignih tumora kože čija se incidenca povećava sa godinama života. Češće se javlja kod muškaraca, a predilekciona mesta su fotoeksponirani delovi kože. U osnovi razvoja ove bolesti je oštećenje DNK bazalnih ćelija kože koje može biti posredovano jonizujućim zračenjem, upotrebom nekih lekova ili kod genetski predisponiranih osoba (Gorling sy). Glavni modaliteti lečenja uznapredovalih ili metastatskih BCC su hirurška ekscizija, radioterapija i ciljana (target) terapija. Vizmodegib predstavlja ciljanu terapiju BCC inhibicijom Hedgehog signalnog puta koji je odgovoran za proliferaciju i diferencijaciju bazalnih keratinocita kao i usklađivanje ova dva procesa.

Prikaz slučaja: Muškarac, 71 godina života, prva promena pojavila se 1996.godine, na koži lica, u vidu ranice koja ne zarasta, kada je dijagnostikovan BCC i učinjena hirurška ekscizija promene. Do recidiva dolazi 2000. godine, kada je pacijent operisan, da bi 2019. godine zbog recidivantnih promena u regiji čela, gornje usne, nosa i leve polovine lica bio ponovo hirurški lečen. U junu 2023. godine pojava novih promena na licu kao i recidiva prethodnih lezija sa infiltracijom tumorske mase u kožu i potkožno tkivo infraorbitalne i zigomatične regije sa destrukcijom poda orbite i infiltracijom u kožu očnog kapka levo. Zbog nemogućnosti nastavka operativnog lečenja, obzirom da se radi o pacijentu sa uznapredovalim metastatskim BCC kome je onemogućena primena radioterapije, u septembru 2023. godine započeto je lečenje Vizmodegibom u dozi od 150 mg dnevno. Na kontroli u oktobru 2023. godine pacijent ne navodi pojavu neželjenih efekata terapije, a promene na koži su u značajnoj regresiji.

Zaključak: Primena Vizmodegiba predstavlja efikasan i bezbedan vid lečenja inoperabilnih bazocelularnih karcinoma kože.

Ključne reči: metastatski bazocelularni karcinom, vizmodegib, lečenje

STEČENA REATIVNA PERFORIRAJUĆA KOLAGENOZA - PRIKAZ SLUČAJA

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Uvod: Stečena reaktivna perforirajuća kolagenoza je retka dermatoza sa još uvek nerazjašnjenom etiologijom i patogenezom. Oboljenje može biti povezano sa različitim sistemskim oboljenjima, najčešće sa dijabetes melitusom i hroničnom bubrežnom insuficijencijom. Transepidermalna eliminacija izmenjenog kolagena smatra se ključnom za stečenu reaktivnu perforirajuću kolagenozu.

Metode: Prikazujemo slučaj pacijenta koji je došao na pregled zbog promena na koži koje su se prvi put pojavile pre tri godine. Nakon pojave prvih promena pacijentu je dijagnostikovan skvamocelularni karcinom pluća kliničkog stadijuma T4N3M0. Promene su bile difuzno raspoređene, u vidu eritematoznih papula i nodusa sa eleviranim ivicama i centralnim keratotičnim čepovima.

Rezultati: Kod našeg pacijenta laboratorijski rezlutati kompletne krvne slike, šećera u krvi, hepatograma i bubrežne funkcije su bili u granicama referentnih vrednosti.

Konačna dijagnoza stečene reaktivne perforirajuće kolagenoze je postavljena na osnovu kliničke slike i patohistološke analize.

Zaključak: Dijabetes i hronična bubrežna insuficijencija se smatraju čestim komorbiditetima udruženim sa stečenom reaktivnom perforirajućom kolagenozom. U poslednje vreme sve više se prijavljuju slučajevi kod kojih je oboljenje povezano sa različitim malignitetima , kao što je bio slučaj i sa našim pacijentom.

Ključne reči: stečena reaktivna perforirajuća kolagenoza, malignitet, perforirajuća kolagenoza

BULOZNI PEMFIGOID IZAZVAN LEKOM PEMBROLIZUMAB

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Uvod: Bulozni pemfigoid (BP) je najčešće autoimuno bulozno oboljenje kože kod starijih osoba.

BP može biti izazvan lekom. Pembrolizumab je anti-PD-1 inhibitor i predstavlja prvu terapijsku liniju za lečenje brojnih maligniteta. Kod BP izazvanog pemrolizumabom period inkubacije je obično duži (20-80 nedelja) a oboljenje može trajati nekoliko meseci nakon prekida terapije.

Metode: Predstavljamo slučaj 71-ogodišnje pacijentkinje sa adenokarcinomom pluća (ekspresija PD-L1 u 80% tumorskih ćelija) kod koje je nakon 26 ciklusa (78 nedelja) pembrolizumaba u dozi od 200 mg došlo do pojave kožnih promena nakon povećanja doze na 400 mg.

Rezultati: Na kliničkom pregledu diseminovane bule na eritematoznoj osnovi ispunjene seroznim i hemoragičnim sadržajem kao i erozije prekrivene hemoragičnim krustama uz izražen pruritus. Dijagnoza BP potvrđena je histopatološkim nalazom, direktnim imunofluorescentnim testom i nalazom anti-BP180 i anti-BP230 IgG autoantitela u serumu (ELISA). Pacijentkinja je lečena je prednizonom (0,5 mg/kg/dan) sa postepenim snižavanjem doze, dapsonom (1,5 mg/kg/dan) i lokalnom primenom 0.05% klobetasol propionata. Potpuna regresija kožnih lezija postignuta je nakon 3 nedelje. Pembrolizumab nije isključen, već je sledeći ciklus odložen. Zbog neželjenih efekata, dapson je isključen nakon 3 meseca terapije. U periodu od narednih 6 meseci zabeležena su dva blaža recidiva BP.

Zaključak: BP je redak neželjeni efekat lečenja pembrolizumabom i u većini slučajeva ne zahteva prekid terapije, kao u našem slučaju. Kod težih slučajeva preporučuje se prekid imunoterapije, a terapija se nastavlja nakon postizanja kontrole BP.

Ključne reči: bulozni pemfigoid, pembrolizumab, neželjeni efekti, lečenje

XANTHOMA DISSEMINATUM-PRIKAZ BOLESNIKA

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Uvod: Xanthoma disseminatum (XD) je veoma retka bolest, koju karakteriše proliferacija histiocita sa deponovanim lipida. Bolest najčešće zahvata kožu i sluznice, ali i druge organe. Uglavnom se javlja kod mlađih od 25 godina života, ali može da nastupi u bilo kom uzrastu. Karakteriše se pojavom žuto-braon papula i nodusa, simetrično raspoređenih na koži lica, trupa i pregiba.

Prikaz bolesnika: Muškarac, u dobi od 62 godine, hospitalizovan je zbog pojave diseminovanih žuto mrkih papula, plakova i nodusa na licu, gornjem delu trupa i nadlakticama. Prve promene su nastale pre pet godina bez subjektivnih tegoba. Na prijemu urađene su laboratorijske analize (hemoglobin 102 g/L, eritrociti 3.64 x 10^{12}/L, sedimentacija eritrocita 59 mm/h, kreatinin 163 μmol/L, lipidni status je bio u granicama referentnih vrednosti jer je bolesnik već bio na terapiji statinima), razmaz periferne krvi (uredan nalaz), ultrazvuk abdomena i male karlice (desni bubreg redukovanog parenhima), kompjuterizovana tomografija grudnog koša, abdomena i male karlice (opisuje se redukovani parenhim desnog bubrega). Osnovnim histopatološkim pregledom izmenjene kože i imunohistohemijskim bojenjem ($CD68^+$ i $CD1a^-$) postavljena je dijagnoza Non-Langerhans histiocitoze. U cilju diferencijalno dijagnostičkog određivanja tipa bolesti kao i proširenosti učinjena je scintigrafija skeleta (sakupljanje radiofarmaka na distalnim okrajcima femura). Konsultativnim pregledima otorinolaringologa i endokrinologa nije utvrđena zahvaćenost sluznica i postojanje dijabetes insipidusa. Uzimajući u obzir kliničku sliku, tok bolesti, patohistološki nalaz i ostale analize postavljena je dijagnoza Xanthoma disseminatum.

Zaključak: Budući da je kod pacijenta bolest lokalizovana na koži, odlučeno je da se nastavi lečenje statinima i učini hirurška ekscizija većih nodusa na licu uz redovne tromesečne kontrole.

POSTER PREZENTACIJE
POSTER PRESENTATIONS

GIGANTSKI PRIMARNI KUTANI APOKRINI KARCINOM - KLINIČKA PREZENTACIJA I HIRURŠKI TRETMAN

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Uvod: Primarni kutani apokrini karcinom (PCAC) predstavlja ekstremno retku maligni neoplazmu. Potvrda dijagnoze kao i razlikovanje i verifikacija od metastaze tumora dojke može biti izuzetno zahtevna čak i nakon patohistološke analize i imunohistohemije. PCAC najčešće nastaje u regijama gde su apokrine žlezde najzastupljenije kao što je aksila, dok se na poglavini izuzetno retko javlja, i u literaturi su opisani samo malobrojni prikazi slučajeva. Nema zvaničnih protokola za tretman i lečenje PCAC.

Metode: Prikaz dijagnostike, lečenja i praćenja pacijenta sa gigantskim PCAC poglavine. Definitivna dijagnoza je postavljena mikroskopski i imunohistohemijskim analizama. Sprovedeno je operativno lečenje - široka ekcizija i rekonstrukcija velikim transpozicionim režnjem i rekonstrukcija sekundarnog defekta autotransplantatom nepotpune debljine.

Rezultati: Naš hirurški tretman obezbedio je potpunu ekciziju tumora, široka ekcizija čiste margine a takodje je dabijen i zadovoljavajući estetskih rezultat i dobar kvalitet života pacijenta kao i adekvatna potvrda dijagnoze. Analizirali smo adekvatan način praćenja pacijenta nakon operacije i set dijagnostičkih procedura i parametara jer protokol za follow up pacijenata sa PCAC ne postoji i stavovi o daljem nastavku lečenja nisu usaglašeni.

Zaključak: PCAC je veoma retka forma tumora, a gigantska forma do sada nije opisana u literaturi. Hirurško lečenje omogućava definitivnu dijagnozu, čiste margine i dobar kvalitet života.

Ključne reči: primarni kutani apokrini karcinom, dijagnoza, hirurški tretman, rekonstrukcija

DA LI SMO ZABORAVILI NA KYRLEOVU BOLEST? PRIKAZ SLUČAJA

M. Mitrović

Opšta bolnica Pančevo

Uvod: Kyrleova bolest (KB) je redak lokalni poremećaj keratinizacije sa formiranjem keratotičnih čepova koji prodiru u dermis. Spada u stečene reaktivne dermatoze udružene sa sistemskim bolestima, naročito hroničnom bolesti bubrega (HBB) i diabetes mellitusom (DM). Karakteriše je hronična, diseminovana ili generalizovana papulozna erupcija sa hiperkeratotičnim konusnim čepovima; promene mogu da konfluišu gradeći hiperkeratotične, verukozne plakove. Predilekciona mesta su ekstenzorne strane ekstremiteta, predeo lopatica i sedalna regija, dok je sluzokoža pošteđena.

Metode: Prikazujemo pacijenta starosti 30 godina koji je prve promene na koži u vidu malih čvorića iz kojih se cedi žućkasti sadržaj, primetio na rukama i trupu pre godinu dana. Promene su praćene svrabom. Zbog navedenih simptoma pacijent je pregledan od strane dermatologa i lečen pod različitim dijagnozama (prurigo nodularis, scabies, folliculitis..). Pacijent boluje od HBB (5. stadijum) i leči se hemodijalizom tri godine. Navodi pozitivnu porodičnu istoriju za bolesti bubrega. Pri pregledu, na trupu, izraženije na lopaticama, prisutne su male papule boje kože, pojedine izdignute, žućkasto-smeđe boje sa keratotičnim vrhom, a poneka sa pukotinom u centru nalik na krater. Subjektivno izražen osećaj svraba.

Rezultati: PH nalaz: epiderm je lokalno hiperkeratotično-diskeratozno izmenjen. U dermalnom delu je prisutan jedan bazofilni čep sastavljen od kolagena i inflamatoma debrisa. Zapaljenska infiltracija i kolagena produkcija je blaga.

Zaključak: Uzimajući u obzir kliničku sliku, osnovnu bolest i nalaz biopsije kože postavljena je dijagnoza KB. Iako je povezanost KB i HBB jasno definisana, često bude zaboravljena. Razmišljati u pravcu KB posebno kod pacijenata u 4. i 5. stadijumu HBB. Diferencijalno-dijagnostički razmotriti druge primarne i sekundarne perforantne dermatoze, prurigo nodularis, folliculitis...

Ključne reči: Kyrleova bolest, hronična

KUTANE ZOSTERIFORMNE METASTAZE KARCINOMA DOJKE

B. Tošić

ZC Knjaževac, Knjaževac

Uvod: Kutane metastaze nastaju kao rezultat progresije primarnih tumora. Javljaju se u 5-10% slučajeva. Retko se vide kao prvi znak maligniteta. Zosteriformne kutane metastaze su metastatske promene na koži sa lokalizacijom u samo jednom dermatomu. Mogu biti u vidu papula, vezikula ili nodusa. Najčešće se javljaju kod karcinoma dojke i malignog melanoma, ali se mogu javiti i kao komplikacija drugih karcinoma.

Prikaz br. 1: Prikazana je pacijentkinja starosti 70 godina sa promenama na koži leve dojke u vidu papula grupisanih u plaže. Dojka je edematozna, a koža zadebljala i infiltrovana. Promene su prisutne unazad 6 meseci. Pacijentkinja je lečena pod dijagnozom Herpes zoster. Ph nalaz nakon biopsije kože: Carcinoma mucinosum glandulae mammae HG2. Tumor vrši invaziju derma sa invazijom dermalnih limfatika. Pacijentkinja navodi postojanje karcinoma iste dojke unazad 2 godine i da joj je po preporuci onkologa uključena hemoterapija.

Prikaz br. 2: Prikazana je pacijentkinja starosti 43 godine sa pojavom eritema, papula i vezikula na koži leve dojke. Dojka edematozna, osetljiva na palpaciju. Promene su prisutne unazad mesec dana. Pacijentkinji je pre 4 godine urađena mastektomija desne dojke. Dg: Ca ductalae mammae invasivum. U momentu pojave promena na koži ultrazvučno nisu detektovane promene koje bi ukazivale na razvoj karcinoma. Kasnije dolazi do pojave metastaza u limfnim žlezdama leve aksile i do pojave promena na koži u predelu ožiljka od mastektomije.

Zaključak: Zosteriformne metastaze su loš prognostički znak i nastaju kao rezultat invazije nerva malignim ćelijama ili kao posledica širenja malignih ćelija duž limfnih sudova u toku progresije bolesti.

Ključne reči: metastaze, karcinom dojke, kutane metastaze

COVID-19 I HIRURGIJA PRIMARNOG MELANOMA KOŽE

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Uvod: Pravovremeno započeto hirurško lečenje predstavlja zlatni standard u terapiji melanoma i održava mortalitet na niskom nivou. Pandemija koju je izazvao virus kovid 19 uticala je na dostupnost zdravstvene zaštite, kako na nacionalnom, tako i na globalnom nivou. Cilj ove studije je da ispita uticaj pandemije kovida 19 na novooperisane bolesnike sa melanomom kože.

Metode: Sproveli smo retrospektivnu studiju koja je uključivala bolesnike sa melanomom kože hirurški lečene u Klinici za plastičnu i rekonstruktivnu hirurgiju Univerzitetskog kliničkog centra Niš u periodu od 1. januara 2017. do 31. avgusta 2023. godine. Upoređivali smo periode pre pandemije (01/01/2017 – 14/03/2023) i tokom pandemije (15/03/2020 – 31/08/2023) procenom starosti bolesnika, pola, zastupljenosti melanoma na određenim delovima tela, debljine po Breslovu, pT stadijuma, stope mitotičkog indeksa, podtipa melanoma i prisustva ulceracije.

Rezultati: Nisu uočene razlike između starosti (p = 0,666), pola (p = 0,720), zastupljenosti melanoma na određenim delovima tela (p = 0,109), debljini po Breslovu (p = 0,172), pT stadijumu (p = 0,274), stopi mitotičkog indeksa (p = 0,257) i prisustva ulceracije (p = 0,787) u dvema ispitivanim grupama. Statistički značajne razlike uočene su kod podtipova melanoma (χ 2 = 9,241; p= 0,026). Distribucija lentigo maligna kod bolesnika sa dijagnozom melanoma tokom pandemije bila je statistički niža.

Zaključak: Do danas, kašnjenje u postavljanju dijagnoze melanoma kože, usled padnemije izazvane kovidom 19, generalno nije dovelo do nepovoljnih karakteristika primarnog melanoma kože. Potrebno je sprovesti dodatne studije u budućnosti kako bi se identifikovali potencijalni uticaj na distribuciju po fazama i dugoročna stopa preživljavanja.

Ključne reči: kovid 19, melanom, hirurško lečenje, debljina po Breslovu, dijagnostičko kašnjenje

PHYTOPHOTODERMATITIS NAKON EKSPOZICIJE LISTOVIMA SMOKVE- PRIKAZ SLUČAJA

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Uvod: Fitofotodermatitis (Phytophotodermatitis) je kliničko stanje kože, koje nastaje nakon ekspozicije kože određenim vrstama biljaka i istovremenim izlaganjem UVA zračenju.

Metode: Prikazujemo pacijenta starosti 62 godine, upućenog na pregled dermatovenerologa pod dijagnozom suspektnog herpes zoster, a zbog opsežnih promena na koži na desnoj strani trupa i desnim ekstremitetima, praćenih osećajem bola i pečenja kože, bez poremećaja opšteg stanja. Lezije na koži su se manifestovale u vidu jasno ograničenog eritema i edematoznih eritematoznih plakova sa pojedinim centralnim vezikulama i bulama, od kojih su neki imali trakast i poligonalan oblik. Promene na koži su odgovarale opekotinama prvog i drugog stepena, sa zahvaćenošću oko 15% površine tela, lokalizovanih jednostrano na prednjoj i bočnoj strani trupa, desnoj podlaktici i šaci, kao i desnom kolenu. Anamnestički je dobijen podatak da je dva dana ranije, tokom sunčanog intervala, pacijent desnom rukom uklanjao mlade stabljike smokve u dvorištu, bez korišenja bilo kakvog vida fotoprotekcije.

Rezultati: Nakon sprovedene lokalne terapije hladnim oblozima, aplikacije topikalnih antibiotskih i kortikosteroidnih kremova tokom dve nedelje, došlo je do regresije aktivnih lezija i epitelizacije kože na mestima prethodnih bula, te pojave rezidualne hiperpigmentacije. Pacijentu je objašnjena priroda privremenih diskoloracija kože i preporučena dalja nega emolijensima i korišćenje protektivne garderobe i fotozaštite pri radu sa biljkama na otvorenom.

Zaključak: Smokva (lat. Ficus carica) pripada vrstama koje u svojim biljnim sokovima sadrže furokumarine koji pod dejstvom UVA zračenja mogu dovesti do nastanka toksične reakcije na eksponiranoj koži. Kod predisponiranih osoba izbegavanjem istovremenog kontakta kože sa delovima drveta i plodovima smokve i UV zračenja, sprečava se pojava fotototoksične reakcije.

Ključne reči: smokva, dermatitis, fotokontakt, UVA zračenje

WOLF ISOTOPIC RESPONSE

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Uvod: Volfov izotopski odgovor pretstavlja fenomen nove dermatološke bolesti koja se javlja na terenu prethodno izlečene dermatološke bolesti. U najvećem broju slučajeva primarna bolest je herpes zoster, druge manje česte dermatoze su varičela i herpes simpleks infekcija. Poremećaji kože koji se mogu razviti na mestima prethodno izlečenog herpes zostera mogu biti granulomatozni (granuloma annulare, uključujući perforantnu varijantu, granulomatozni dermatitis), maligni (karcinom dojke, karcinom bazalnih ćelija i skvamoznih ćelija, leukemija), Kapošijev sarkom, angiosarkom (angiosarkom), urtikarija, papuloskvamozne (psorijaza, lihen planus), sklerozantni (sklerozni lihen, morfea), infiltrativni, ulcerativni, stečeni perforirajuće dermatoze.

Prikazujemo slučaj nastanka granulom annulare perforans na mestu prethodno izlečene herpes zoster virusne infekcije koja je lečena oralnom antiretrovirusnom terapijom.

Prikaz slučaja: Predstavljamo bolesnicu staru 54 godine, kod koje su se promene na desnoj natolenici i potkolenici pojavile nakon izlečenja virusne infekcije izazvane herpes zosterom. Inače, pacijentkinja se leči od dijabetes melitusa tipa II, hipertenzije, reumatoidnog artritisa i epilepsije. Promene su bile u vidu plakova ovalnog oblika, tamnosmeđe boje na periferiji i blago hipopigmentisanih u centru. Histopatološki nalaz je išao u prilog granuloma annulare perforans, koji se karakteriše granulomatoznim dermatitisom sa fokalnom degeneracijom kolagena. Laboratorijske analize: povišen holesterol i trigliceridi, Quantiferon TB-Gold test, HBsAg, anti-HCV, HIV Ag/At: negativan. CDS donjih ekstremiteta: nema znakova arterijske I venske insuficijencije. RTG pulmo et cor: uredan nalaz. EHO abdomena: cista levog bubrega, ostali nalazi normalni. Uzimajući u obzir nalaze kliničkog pregleda i nalaz biopsije, postavljena je dijagnoza granuloma annulare perforans. Pacijentkinja je lečena Pronison tbl. do 0,5 mg/kg nekoliko meseci, bez terapijskog efekta. Methortekate tbl. 10 mg nedeljno je dobijala prethodno od strane reaumatologa koji je prepisao terapiju zbog reumatoidnog artritisa, terapiju je uzima sve vreme tokom lečenja. Potom je u terapiju uveden Keracutan caps. do 0,3 mg/kg, nakon nekoliko meseci dolazi do značajnog poboljšanja. Lokalno je dobijala potentne kortikosteroidne masti, keratolitike i krioterapiju u nekoliko navrata.

Diskusija: Izotopski odgovor vuka pretstavlja pojavu nove dermatološke bolesti koja se javlja na terenu prethodno izlečene dermatološke bolesti. Jedna od najčešćih dermatoza koja se javlja nakon prethodno izlečenog virusa herpes zoster je granuloma annulare, kao i granuloma annulare perforans. Predisponirajući faktor kod našeg pacijenta je dijabetes melitus, koji se javlja kod oko 10% pacijenata sa lokalizovanim granuloma annulare, kao i hiperlipidemija. Mogući predisponirajući faktori za pojavu granuloma annulare uključuju moguću infekciju HIV-om, bolesti štitne žlezde.

Granuloma annulare perforans je retka varijanta granuloma annulare, javlja se u oko 5% slučajeva. S druge strane, to je jedna od čestih varijanti granuloma annulare, koja se javlja na mestu ranije izlečene infekcije virusa herpes zoster.

AKNE VULGARIS- TROGODIŠNJA RETROSPEKTIVNA ANALIZA

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Uvod: Akne vulgaris su hronično inflamatorno oboljenje pilosebacealne jedinice. Javljaju se kod 85% adolescenata i mladih, pogoršavajući im kvalitet života. Nastaju u pubertetu kod genetski predisponiranih osoba. Imaju kompleksnu etiopatogenezu. U svakodnevnoj dermatološkoj praksi poslednjih decenija zapaženo je pomeranje uzrasta, pa se akne vulgaris, u različitim kliničkim formama mogu dijagnostikovati, već kod školske dece (oko 9-10 godine života (komedoni). Komorbiditet akni vulgaris može biti veoma različit, ali je najznačajnija udruženost sa sindromom policističnih jajnika i hiperandrogenim sindromom. Poseban je psihosocijalni efekat akni na adolescente, ne uvek u srazmeri sa težinom kliničke slike. U ovom životnom period, oni se suočavaju sa brojnim promenama, i psihičkim i fizičkim, koje su kompleksne i značajne i bez akni. Sa druge strane i sam period adolescencije je kritično doba za razvoj identiteta, veoma važan u razvoju slike o sebi, vlastitom telu, polnom sazrevanju i socijalizaciji svake individue. Uticaj akni na slici o svome telu je glavni faktor koji se povezuje sa simptomima depresije i suicida. Lečenje akni zavisi od kliničkog oblika akni i uvek je individualno, prilagođeno kliničkom nalazu svakog pacijenta. Kod blažih oblika primenjuje se samo lokalno lečenje (topikalno: retinoidi, benzoil peroksid, antibiotici), dok se kod težih, uz lokalnu, primenjuje i sistemska terapija (oralno: antibiotici, kontraceptivne pilule, izotretinoin). S obzirom da se ovo oboljenje svrstava i u psihodermatologiju, mladim pacijentima treba objasniti njegovu prirodu, terapijske mogućnosti i potrebnu dijagnostiku (naročito kod devojaka zbog sindroma policističnih jajnika), dužina lečenja i neželjene efekte različitih lekova protiv akni (lokalnih i sistemskih i potrebu redovnih kontrolnih pregleda.

Cilj rada: Trogodišnja analiza broja pregledanih i lečenih pacijenata sa aknama, analiza obolelih prema polu, godinama života, kliničkoj slici i terapiji.

Metodologija: Retrospektivna analiza protokola specijalističke dermatovenerološke ambulante Zavoda za zdravstvenu zaštitu u Kosovskoj Mitrovici i statistička obrada dobijenih podataka

Rezultati: U analiziranom periodu (1.1.2017-31.12.2019.godine) ukupno je pregledano 339 pacijenat sa dijagnozom Akne vulgaris, 86.9% devojaka i 13.6% momaka. Pregledani pacijenti su od 19.do 29.godina, prosečno 22.6 godina (devojke 22.7 godina, dok su momci nešto mlađi, 21.7). Kod 36.3% (123) pacijenata primenjena je samo lokalna terapija (topikalni retinoidi noću i azelaična kiselina u toku dana). Kombinovanom peroralnom i lokalnom terapijom, zbog inflamovanih akni lečeno je 61,9% (210) pacijenata, od toga 4.4% (15) Dovicin kapsulama, 7.7% (26) Roaccutane kapsulama, dok su Yaz dražeje ordinirane kod 6.5% (22) pacijentkinja, najčešće uz Inofolic pulvis, nakon obavezne konsultacije ginekologa (9.1%). Dijagnoza sindroma policističnih jajnika postavljena je kod 6.2% (21) studentkinja, koje su praćene i od strane ginekologa i endokrinologa.

Zaključak: U analiziranom trogodišnjem periodu dijagnoza Akne vulgaris češće je postavljena kod devojaka. Svaki treći pacijent lečen je samo lokalnom terapijom, dok je kombinovana peroralna i lokalna terapija, zbog inflamacije primenjena kod dva puta više pacijenata

Ključne reči: acne vulgaris, inflamacija, sindrompolicističnih jajnika, roaccutan kapsule

ERYTHEMA MIGRANS IN PREGNANCY

K. Cvenkel

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Introduction: Lyme disease (LD) primarily manifests as erythema migrans (EM) and can exhibit diverse clinical features, including fever, fatigue. EM in pregnant women can occur equally in all trimesters, with milder severity compared to non-pregnant women.

Methods: A 39-year-old pregnant woman in her third trimester noticed a red, slightly itchy macular lesion measuring 4 x 2 cm on her right upper extremity, appearing three weeks after a tick bite. She was examined by a family doctor who did serological tests using the LIAISON method (IgM and IgG negative), and she received no treatment. The lesion gradually increased but her overall well-being remained good. At the time she was checked in our clinic she had a round erythematous macule, 13x8 mm in size, on the upper right extremity, with a visible peak at its center. No other skin changes were observed. Upon examination in our clinic, she had a round erythematous macule size 13x8 mm with a visible peak on her upper right extremity, and no other skin changes were noted.

Results: Diagnosis of EM relies on clinical assessment. Borrelia burgdorferi can be detected through culture and/or PCR from a skin biopsy. Treatment typically involves antibiotics like amoxicillin, cefuroxime or azithromycin. Doxycycline should be avoided due to potential fetal harm. The typical treatment duration is 14 to 21 days.

Conclusion: EM remains a clinical diagnosis, as serological results can be negative, and regional seropositivity varies. Adequate antibiotic therapy is recommended in any case of gestational LD to prevent spirochaete dissemination and related complications.

Keywords: Lyme disease, erythema migrans, Borrelia burgdorferi, pregnancy

LAŽNO NEGATIVNI LIMFNI ČVOROVI STRAŽARI KOD PACIJENATA SA MELANOMOM KOŽE -NAŠA ISKUSTVA

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Uvod: Lečenje pacijenata sa melanomom kože se promenilo nakon uvođenja biopsije limfnog čvora stražara (SLNB) u rutinsku kliničku praksu. Definisanje statusa drenažnog limfnog basena pruža različite prognostičke informacije. Ipak, još uvek se u potpunosti nije razjasnila tačnost ove procedure u smislu mogućnosti identifikacije lažno-negativnih limfnih čvorova stražara. Nekoliko velikih studija objavilo je podatke o relativno visokoj stopi lažno negativnih SLN(5,6%-21%).

Ciljevi našeg istraživanja su bili da se utvrdi procenat lažno negativnih SLN i da se definiše vremenska grupa recidiva

Metode: U periodu od 2010. do 2017. godine, 410 pacijenata sa melanomom kože je podvrgnuto SLNB proceduri u Klinici za plastičnu hirurgiju i opekotine. Od svih 410 pacijenata kod njih 4 imali smo neuspešnu biopsiju pa je broj koji je ušao u statističku obradu je 406. Studija ispituje proceduru koja se smatra lažno negativnom ako se recidiv razvije u istom drenažnom basenu.

Rezultati: Limfni čvor stražar je bio pozitivan kod 84 (20,5%), a negativan kod 322 (78,5%) pacijenata. Od ukupnog broja pacijenata koji su i nakon biopsije bili u II kliničkom stadijumu kod 17 (5,2%) je došlo do progresije bolesti, odnosno pojave lokalnog recidiva. Kod 5 (29%) od 17 ''lažno negativnih'' limfnih čvorova stražara recidiv se pojavio u prvoj godini nakon izvršene biopsije. Uzroci ovih lažno negativnih procedura mogu se pripisati neuspešnoj proceduri limfoscintigrafije ili patohistološke analize.

Zaključak: Procedura biopsije limfnog čvora stražara u našem istraživanju nije uspela da identifikuje zahvaćenost kod 5,2% pacijenata koji su razvili metastaze u istom drenažnom basenu u roku od jedne ili više godina nakon intervencije.

Ključne reči: sentinel, melanom, limfni čn

SINDROM VENE CAVE SUPERIOR KAO DIFERENCIJALNA DIJAGNOZA KOD ANGIOEDEMA

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Uvod: Sindrom vene cave superior (SVCS) predstavlja skup simptoma i znakova nastalih usled opstrukcije venske i limfne drenaže u gornjem delu grudnog koša, glave, vrata i gornjih ekstremiteta.

Kliničku sliku SVCS je prvi opisao William Hunter 1757. godine, kada je u većini slučajeva predstavljala posledicu tuberkuloznih medijastinitisa i luetične aneurizme ascedentnog dela aorte, a samo 37% je bila uzrokovana malignom bolešću. Savremena istraživanja pokazuju da je u približno 95% slučajeva SVCS odgovoran maligni proces u toraksu, i to u 85-90% bronhogeni karcinom. Sekundarna opstrukcija VCS kod malignih oboljenja rezultat je najčešće direktne invazije od strane tumora (u 68% slučajeva) ili spoljne ili unutrašnje kompresije, ili su u pitanju oba mehanizma. Težina kliničke slike zavisi od brzine njenog nastanka i od anatomskog mesta opstrukcije. Terapija zavisi od uzroka opstrukcije i težine simptoma i zahteva multimodalni pristup sa neizvesnim terapijskim uspehom. Uobičajen tretman izbora u SVCS je radio i/ili hemioterapija.

Metode: Prikazujemo pacijenta sa tegobama unazad dva meseca u vidu gušobolje, crvenila kože vrata i donjeg dela lica, praćenog otokom lica i vrata uz promuklost (povremeno izraženu). Na prijemu izražen tvrd edem u predelu vrata i lica uz edem gornjih ekstremiteta (šaka, predela ručja), ispunjenost jugularnih prostora i naglašenu vaskulaturu venskih krvnih sudova na gornjem delu grudnog koša. Sagledavan ambulantno u više navrata od strane ORL, hematologa, pulmologa pod Dg. Angiedema i lečen ampuliranom antialergijskom terapijom, bez poboljšanja. Rađene su laboratorijske analize, EHO mekih tkiva vrata i tireoideje – nalaz b.o. U ličnoj istoriji: pacijent boluje od psorijaze, PH verifikovane kao psoriasis pustulosa, pre četiri godine i na sitemskoj terapiji metotreksatom, unazad 3 godine u remisiji i na dozi 7,5 mg/nedeljno. Uzima antihipertenzivnu terapiju od 2001.god. U porodičnoj istoriji: otac imao karcinom pluća, brat preminuo od kolorektalnog karcinoma.

Rezultati: Urađene laboratorijske analize: WBC 12,4, RBC 3,96, HGB 117, HCT 0,357, SE 27/h, urea 10,3, d.bilirubin 4,1, HOL 5,26, feritin 309, LDH 1113, CK 250. RTG pluća i srca: transparencija plućnog parenhima obostrano očuvana. Hilusi uredne radiološke prezentacije. Hemidijafragme lučne, jasno konturisane. Desna hemidijafragma elevirana.KF sinusi slobodni. Srce urednog položaja. MSCT grudnog koša: tumorska promena desnog plućnog krila sa stenozom desnog lobarnog bronha, sa hilarnom i medijastinalom propagacijom i infiltracijom. Subokluzivna tromboza VCS i obe brahiocefalične vene. Edem laringealnih struktura u subglotisom delu, bez prikazivanja lumena. Medijastinalna i cervikalna patološka limfonodomegalija. Desnostrana pleuralna efuzija. Nodularne promene u plućima obostrano.Fokalna TSCT lezija desnog lobusa jetre. Fuzija bubrega sa desnostranom prezentacijom. Konsultovan pneumoftiziolog i pacijent prebačen na Kliniku za pneumoftiziologiju radi daljeg dijagnostičkog i terapijskog sagledavanja. Planirana bronhoskopija i zračna terapija.

Zaključak: Uzroci SVCS: medijastinalni maligniteti (primarno mikrocelularni bronhogeni karcinom), Non-Hodgkin limfom, metastaze tumora, benigni procesi, jatrogena tromboza VCS (centralni kateter, dijalizni kateter, pejsmejker, ICD).

Terapija SVCS: kortikosteroidna terapija, diuretici, terapija osnovne bolesti.

Prognoza zavisi od uzroka nastanka SVCS.Benigni procesi – otklanjanjem uzročnika očekuje se potpuno izlečenje.Maligni procesi medijastinuma -u slučaju razvoja cerebralnog ili laringealnog edema moguća je iznenadna smrt. SCVS uzrokovan karcinomom pluća – preživljavanje ispod dve godine, ukoliko ne odgovore na zračnu terapiju – ispod godinu dana.

Ključne reči: sindrom vene cavae superior, angioedem, tumori medijastinuma

BASAL CELL CARCINOMA IN SOLID ORGAN TRANSPLANT RECIPIENTS: CASE REPORT

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Introduction: Solid organ transplant recipients (SOTRs) face an elevated risk of skin cancer compared to the general population, with basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) accounting for 95% of these cases. BCC risk increases tenfold, while SCC incidence rises sixty-five to a hundred times compared to immunocompetent individuals. Photodistributed sites (head, neck, hands) are most vulnerable. UV exposure, older age at transplantation, fair skin, and male gender contribute to this elevated risk.

This case report aims to raise SOTRs skin cancer awareness, emphasizing the significance of a multidisciplinary approach in the treatment.

Methods: A 72-year-old male received a cadaveric kidney transplant in 2010, maintained on Prograf, Cellcept, and Pronison. In 2016, he developed BCC on the left ear and nose, treated with surgical excision and direct closure.

Results:: Subsequent years witnessed recurrent BCC on the nose:

2017 and 2018: Surgical excision and direct closure.

2019: BCC and Morbus Bowen excision with autotransplantation of skin (Wolf) reconstruction and Morbus Bowen on forehead excision and direct closure.

2021 and 2022: Surgical excision and direct closure.

Last excised BCC is infiltrative with unclear margin. New nose lesion emerged.

Conclusion: With a growing SOTR population, this case underscores the importance of skin cancer screening, patient education on sun protection, and early self-diagnosis. Consistent multidisciplinary monitoring is vital, involving dermatologists, transplant clinicians, and surgeons. Early diagnosis, treatment (including surgery), and potential reduction in immunosuppressive medications are crucial to prevent aggressive malignancy behavior.

Keywords: basal cell carcinoma, skin cancer, solid organ transplantation, immunosuppression

CORNU CUTANEUM - LIKE STEČENI FIBROKERATOM NOKTA

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Uvod: Stečeni fibrokeratom nokta (AUFK) je benigni fibrokeratotčni tumor germinalnog matriksa koji nastaje iz proksimalnog nabora nokta ili ponekad iz ležista nokta. Etiologija je nepoznata. Predloženo je traumatsko poreklo tumora, jer se najčešće javlja na prstima ruku i nogu. Chan et al. su predložili termin "stečeni fibrokeratom nokta" jer je ova lezija histološki identična stečenom digitalnom fibrokeratomu, varijanti Steel-ovog fibroma čena belog luka.

Metode: Prikazujemo slučaj stečenog fibrokeratoma nokta, nastalog nakon traume.

Rezultati: Žena starosti 61 godinu sa asimptomatskom izraslinom u predelu nokta drugog prsta desne noge, u trajanju od 4 godine. Promena je nastala nakon traume, tj. "čupanja nokta". Počela je kao mala izdignuta lezija koja izlazi iz ležišta nokta. Tokom perioda od 4 godine, razvila se struktura nalik kožnom rogu. Mogla je da nosi samo otvorene sandale. Dermatološkim pregledom uočena je izrazito hiperkeratotična, tvrda, konična i zakrivljena promena sa potpuno deformisanom nokatnom pločom zahvaćenog prsta. Dermoskopska evaluacija je otkrila belo-žućkaste egzofitne i keratotične strukture. Na rendgenskom snimku uočen je nedostatak terminalne falange 2. prsta desnog stopala. Tumor je hiruški uklonjen, a histopatologija je otkrila papilomatoznu proliferaciju hiperplastičnog, akantotičnog epiderma i fibroznog vezivnog tkiva derma koje sadrži gusta usnopljena kolagena vlakna između kojih su uniformni fibroblasti i oskudan mononuklearni zapaljenski infiltrat sa ekstenzivnom hiperkeratotičnom ortokeratozom na površini epiderma. Nalaz je odgovarao fibrokeratomu. Bez recidiva, 12 meseci nakon ekscizije.

Zaključak: Stečeni fibrokeratom nokta je retka varijanta digitalnog fibrokeratoma. Većina AUFK je lokalizovano u periungvalnom području, u našem slučaju, tumor je nastao iz ležišta nokta. Potpuna hiruška ekscizija tumora se smatra terapijom prve linije za AUFK. Ovaj slučaj je prikazan zbog svoje retkosti.

Ključne reči: Stečeni fibrokeratom nokta, Cornu cutaneum, čen belog luka

NARROWBAND IPL FOR RESISTANT PWS IN ADULTHOOD – CASE REPORT

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Introduction: Port Wine Stains (PWS) are capillary malformations of the skin that are typically present at birth. PWS progressively darken and may become hypertrophic or nodular without treatment. There are several treatment options available for PWS, like pulsed dye laser (PDL) which is the treatment of choice in children.In most of the cases complete clearance cannot be achieved even after multiple PDL treatments, some lesions are resistant to PDL (20 %) even at the higher doses, so narrowband IPL defined by dual filters and sub-millisecond pulse duration could be a better therapeutic choice for adult patients with resistant and non resistant PWS .

Methods: A 42 years old women, on examination presented with unilateral long lasting homogenous two red-bluish patches with purple hue on the face and neck. Not involving mucosa. She reported a huge cosmetic impact through life. She was treated with several laser procedures, including PDL 595 nm laser, but without any therapeutic answer. On a a dermoscopy they were reticular vessels sausage-like vessels, dots or globules vessels. Nonvascular morphology comprised white circles and whitish veil .

Results: After 4 IPL sessions, combining 555 and 530 nm wavelengths, we achived 60 % clearnce, with minimum downtime and no adverse effects.

Resistant PWS cases to PDL may require a combination of treatment methods including narrowband IPL with submilisecond pulse duration.

Conclusion: While much is known about the possible mechanisms of resistance of PWS to PDL treatment, alternative approaches should be developed and subsequently validated. The working basis of the IPL rests on the principle of selective photothermolysis. IPL could be effective alternative to PDL for PWS treatment in adulthood.

Keywords: pls, capillary malformations, ipl, ppl

TREATMENT OF RHINOPHYMA WITH LASER OUR EXPERIENCE

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Introduction: Rhinophyma is characterized by a progressive thickening of nasal skin, which produces a disfiguring soft-tissue hypertrophy of the nose. It is a benign dermatological disease of the nose affecting primarily men in their fifth to seventh decades of life. The main reasons why patients seek help are due to plastic cosmetic and functional impairments such as nasal obstruction.

Methods: We present our results with the application of Erbium:YAG laser in the treatment of Rhinophyma in a 72-year-old male patient. After administering short term IV anesthesia, we performed 2940 nm Erbium:YAG laser therapy (spot size: 3 mm/5 mm, energy: 8 J/cm2, speed 10 Hz) to treat the patient's lesion. We started with laser ablation following the previous markings of the whole nose, while using intra operative local cooling and compression with a local solution of adrenalin the whole time. Immediately after the operation we used a compressive bandage and perioral antibiotics and mild analgesia.

Results: After laser ablation the skin started spontaneous re-epithelization of the surface without scarring. We monitored the patient with photo documentation before and 60 days after the procedure. For at-home therapy we prescribed sun screen protection for the next 3 months and moisturizing lotion.

Conclusion: In our report Rhinophyma of the nose responded well to Erbium: YAG laser treatment comparing to CO2 laser.

Keywords: erbium yag laser, CO_2 laser, ablation, rhinophyma

AMELANOTIČNI MELANOM – PRIKAZ SLUČAJA

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Uvod: Melanom nokta javlja se retko, i najčešće zahvata I i II prst šake ili stopala. Amelanotični melanoma iako izuzetno redak, češće zahvata nokat u odnosu na druge lokalizacije. Karakteriše se odsustvom vidljivog pigmenta pa se često može zameniti skvamocelularnim karcinomom, piogenim granulomom, hroničnom paronihijom. Dermoskopska evaluacija amelanotičnog melanoma predstavlja izazov. Prikazujemo pacijenta sa subungvalnom promenom koja je dermosopski i patohistološki verifikovana kao amelanotični melanoma.

Metode: 77-mo godišnji pacijent upućen dermatologu zbog promene nokatne ploče I prsta leve šake prisutne par meseci unazad sa povremenim krvarenjem. Nastanak promene povezuje sa mehaničkom povredom. Negativna lična i porodična anamneza za melanomske i nemelanomske karcinome kože.

Rezultati: Pri dermatološkom pregledu, uočen je amelanotični nodus prekriven hemoragičnom krustom kao i distrofija većeg dela nokatne ploče I prsta leve šake koju je pacijent povezao sa mehaničkom traumom koja se dogodila par meseci ranije. Dermoskopski nalaz je pokazao ružičastu boju kao i linearne iregularne krvne sudove. Postavljena je sumnja na skavmocelularni karcinom i melanom te je pacijent upućen plastičnom hirurgu radi ekscizije promene sa patohistološkom verifikacijom. Patohistološkim nalazom dokazan je akralni tip melanoma sa nodularnom transformacijom, infiltracijom potkožnog tkiva i kosti.

Zaključak: Amelanotični melanom nokatne ploče predstavlja izazov u dermoskopiji. U slučaju distrofičnog oštećenja nokatne ploče, kao i dermoskopski uočene ružičaste koloracije i prisustvo iregularnih krvnih sudova potrebno je uvek razmišljati o subungvalnom amelanotičnom melanomu.

Ključne reči: Amelanotični melanoma, nokatna ploča, dermoskopija.

PAGETOID RETICULOSIS WORINGER-KOLOPP - RETKA VARIJANTA MYCOSIS FUNGOIDES

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Uvod: Lokalizovana pagetoidna retikuloza, takođe poznata kao Woringer-Koloppova bolest, je retka varijanta mycosis fungoides koja prvenstveno pogađa muškarce srednjih godina. Tipična lezija je solitarni, sporo rastući, jasno ograničeni i hiperkeratotični plak, akralne lokalizacije sa intraepidermalnom proliferacijom neoplastičnih T-ćelija.

Metode: Prikazujemo slučaj lokalizovane pagetoidne retikuloze u predelu leđa, retke anatomske lokalizacije za ovo stanje.

Rezultati: Muškarac star 70 godina sa trogodišnjom istorijom jasno ogranicenog, blago infiltrovanog, ružičasto-smeđeg, keratotičnog plaka, prečnika 10 cm sa papilomatoznom promenom tipa seboroične keratoze, lokalizovanog u donjem delu leđa. U prethodnih 5-6 meseci plak se postepeno povećavao i počeo da svrbi. Klinički i dermoskopski aspekti su ukazivali na Bovenovu bolest. Na drugim mestima nije bilo kožnih promena. Biopsija je pokazala infiltrat od malih atipičnih limfocita sa pagetoidnom invazijom epidermisa, a imunohistohemijska analiza, atipične ćelije koje su bile pozitivne na CD3, CD4, CD8+/-, ali negativne na CD20 i CD79. Nalazi su potvrdili dijagnozu pagetoidne retikuloze. Laboratorijske analize krvi su bile u granicama referetnih vrednosti, Rtg pluća i eho abdomena nisu pokazali sistemsku zahvaćenost.

Lokalna terapija zračenjem pokazuje najveću stopu izlečenja sa najmanjom stopom recidiva. Fotodinamička terapija može biti alternativa zračenju kod mlađih pacijenata. Naš pacijent nije bio zainteresovan za agresivno lečenje. Tri meseca nakon topikalne primene 0,05% klobetasol propionata sa dodatnim emolijensima, primećeno je značajno poboljšanje.

Zaključak: Mnogi aspekti bolesti su i dalje predmet kontroverzi. Za razliku od konvencionalne, kod lokalizovane pagetoidne retikuloze nikada nisu prijavljeni ni ekstrakutana diseminacija ni smrtni slučajevi povezani sa bolešću. Međutim, nakon postavljanja dijagnoze, potrebno je dugotrajno praćenje da bi se isključio njegov diseminovani oblik, koji ima agresivan klinički tok i lošu prognozu.

Ključne reči: Lokalizovana pagetoidna retikuloza, Woringer-Kolopp, Mycosis fungoides