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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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"THE DANGEROUS BRASSIERE" AND THE NEVUS ASSOCIATED POLYPOID MELANOMA: CONNECTION SEEMS PLAUSIBLE?

Kordeva S[1], Tchernev G[1,2], Ivanov L[2], Broshtilova V[3].

[1]*Onkoderma- Clinic for Dermatology, Venereology and Dermatologic Surgery, General Skobelev 26, 1606 Sofia, Bulgaria.*

[2]*Department of Dermatology and Venereology, Medical Institute of Ministry of Interior, General Skobelev 79, 1606, Sofia, Bulgaria.*

[3]*Department of Dermatology and Venereology, Military Medical Academy, 1606, Sofia, Bulgaria.*

Abstract.

The development of cutaneous melanoma of the skin based on dysplastic nevus is not uncommon. The causes of the progression of nevi to melanomas are numerous and not well understood at present. Certain genetic and epigenetic factors have a major influence on this evolution. We describe a 46-year-old female patient with multiple dermal melanocytic nevi who developed a polypoid melanoma in one of them. After a carefully performed anamnesis, the mole that developed into melanoma was found to be localized in the dorsal area adjacent to the brassiere and underwent permanent and daily mechanical irradiation during the last 6-7 years. Around this mole there were 5 other moles with similar clinical and dermatoscopic morphology, which did not transform into melanomas and were not subjected to mechanical irritation.

The patient had a dermatological examination 6 years ago and it was suggested that this lesion has to be surgically removed, which she declined.

The patient was treated surgically and the lesion suspicious for cutaneous melanoma was removed in two stages according to the generally accepted AJCC/EJC recommendations.

In parallel, 5 additional melanocytic nevi were removed, which histologically had features of dysplastic dermal melanocytic nevi but no signs of progression to melanoma.

This article discusses the causes of nevus -associated melanomas and emphasizes the thesis of potential malignant transformation through mechanical irritation - in this case that of the brassiere. The moles localized in this area, although clinically and dermatoscopically inapparent, should be treated surgically. This painless, short-term manipulation has a preventive effect on the future development of cutaneous melanomas.

Key words. Nevus associated melanoma, irritated nevus, polypoid melanoma, surgery, brassiere.

Introduction.

Melanocytes are pigment-producing cells, derived from the neural crest, which can be found in the skin, eyes, bones, inner ears and leptomeninges [1]. From pathogenetical point of view, cutaneous melanoma (a malignant skin cancer), melanocytic nevi (benign skin formations) and dysplastic nevi (a form between the nevi and melanoma) have a common ancestor – the melanocyte [1].

Atypical moles, Clark nevi, B-K moles are all synonyms found in the literature for dysplastic nevi [2]. However, only a few of the atypical moles have a "microscopic appearance" of a dysplastic nevus [2]. On a clinical examination, the dysplastic nevi share visual similarity to the melanoma lesions, often even described with the ABCDE morphological characteristics for melanoma [2].

Genetic alterations are the probable main cause for the development of both benign and malignant melanocytic tumors [3].

Acquired nevi are a result from several mutations in the melanocytes, which have already extended to the epidermis, and are often associated with a mutation in the BRAF gene [3]. Although BRAF mutations were found to be prevalent (with 66% estimated rate) in cutaneous melanoma [4], Uribe et al. [4] suggests that some mutations alone are not enough to induce a malignant transformation of a benign lesion.

Over the last four decades with a constant increase in incidence rates, cutaneous melanoma is presented as one of the fastest developing malignancies worldwide [5]. Being on the lower part of the Fitzpatrick scale (type 1&2), having different lifestyle factors cooperated in your everyday life such as the use of indoor tanning beds, excessive sun exposure, not wearing enough or any sun protection and etc. are all very well-known risk factors for developing melanoma [5].

However, even with the genetic understanding of the disease and the above-mentioned risk factors, there are still a few missing pieces from the puzzle called "melanoma". After a thorough search of the literature, we found scarce information about one of the most commonly seen but poorly described triggering risk factors – chronic mechanical irritation.

We present a case with a 46-year-old female with a history of chronic mechanical irritation due to the use of a brassiere (a piece of woman's underwear), which developed in our observation a nevus associated polypoid melanoma alongside multiple dysplastic nevi. The dermatosurgical approach was demonstrated once again as the most efficient method when dealing with skin malignancies. A short review of the existing literature will be done regarding the relationship between dysplastic nevi and melanoma, contributing risk factors of cutaneous melanoma.

Case report.

A 46-year-old female came to the dermatology department with primary complaints of multiple pigmented lesions located on the back and the waist areas both dating from 20 years (1a-1c). Six years ago, the patient reported three nevi being removed in the abdominal area, with a recommendation for the removal of another pigmented lesions located on the back, which she refused. The patient came to the department 6 years later with a request for physical examination of the lesions on the back and further therapeutic approach to be established if necessary.

The patient reported no comorbidities or skin malignancies in any family member. The routine blood tests showed slight abnormalities in the Gran% - 77.8%, squamous cell – 41.0/uL, LDL – 3.6 mmol/l and urea 2.6 mmol/l. CT scan of the thorax, abdomen and pelvis was ordered. An abnormal finding in the uterus was found – it had a CT characteristic of a myoma nodule, an inhomogeneous hyperdense oval lesion was visualized in the uterine wall in the left lateral area with axial dimensions - 2.58/3.91 cm.

The dermatological examination showed six very distinguishable pigmented lesions located on the back, clinically and dermatoscopically suspected for dysplastic/ irritated melanocytic nevi (Figures 1a-1c) One of them has been suspected of nevus associated cutaneous melanoma- the number 1 on picture 1b (Figures 1a-1c).

The patient was recommended surgery for the suspected lesions.

After disinfection, under local anesthesia with lidocaine, the melanoma-suspicious tumor formation as well as the five pigmented lesions suspicious for dysplastic nevi were removed by elliptical excision with resection margins of surgical security of approximately 0.3 cm in all directions. The remaining defects were closed by single interrupted sutures. Daily dressings with povidone iodine were performed. The histopathology results (Figures 1d-f) came positive for five dysplastic nevi and the histology for lesion 1 (polypoid lesion) was represented by atrophic epidermis, compact melanocytic proliferation of large, epithelioid an isomorphic cells with marked pleomorphism, centrally located large nuclei with scattered chromatin and 1-2 large nucleoli, abundant cytoplasm forming a dense conglomerate in a richly vascularized stroma. Lympho-vascular and perineural invasion were absent; clear resection lines, Breslow 4.3mm. The histological picture corresponded to a nevus associated polypoid melanoma (Figures 2-4).

The patient was referred to the oncology department for a SPECT/CT. Sentinel lymphoscintigraphy was performed in planar and SPECT/CT mode after intradermal application of 99mTc-Nanocol at four sites around the operative cicatrix on the skin on the back, scintigraphic SPECT/CT data of lymphatic drainage to both axillary regions with delineation of one sentinel lymph node in each (with greater intensity on the right), their projection site is marked on the patient's skin. Lymphatic drainage to inguinal areas is not established. The patient was recommended a re-excision for the melanoma lesion with a surgical safety margin of 2 cm in all directions and removing of the sentinel lymph nodes. She agreed and a second surgical intervention was planned with: a re-exsicion of the primary cicatrix (Figure 5a), and the detection and performance of the sentinel lymph node – one in the left (Figure 5b) and one in the right (Figure 5c) axillar regions. A 2 cm resection of the cicatrix from the primary tumor was performed in the lumbar region (Figure 5a). A layered suture with one drain was placed. Histology was not indicative for the availability of tumour cells. Melanoma was staged as : stage 2C (pT4bN0M0).

Discussion.

Melanocytes are pigment-producing cells located mainly in the skin [6]. Their main function is to protect the epidermal layer of

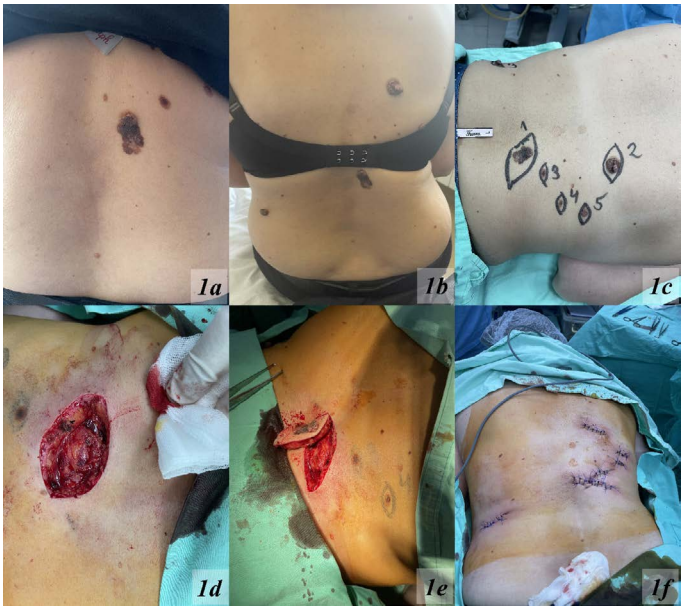

Figure 1. 1a: *Nevus-associated polypoid melanoma localized lateral to the posterior sweat trough.* ***1b:*** *Nevus-associated polypoid melanoma localized adjacent to/under the brassiere.* ***1c:*** *Preoperative resection field marking in a patient with nevus-associated polypoid melanoma and multiple dysplastic nevi in the back area.* ***1d,e:*** *Deep surgical excision to the musculature in the form of an ellipse.* ***1f:*** *Postoperative finding after surgical removal of 6 melanocytic lesions in the dorsal area.*

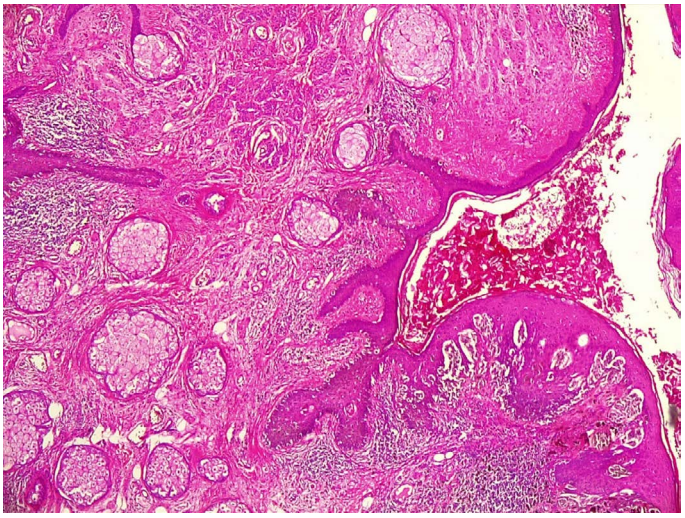

Figure 2. *Dermal nests of melanocytes, adjacent to pagetoid spread of atypical melanocytes.*

the skin by producing a pigment (melanin), which absorbs the UV radiation and thus protecting the layers below from further DNA damage [6].

Melanocytic lesions can be simply divided into several categories: benign nevi , dysplastic nevi, and malignant melanoma [7]. The benign lesions are symmetrical, evenly pigmented and the edges of the nevus are usually well-defined [7].

Moles with atypical clinical features (atypical moles, dysplastic nevi), such as variation in size, irregular borders and in homogenous pigmentation, were described for the first time as B-K mole syndrome (“B” and “K” being the families acknowledged) [8] and as FAMMM (familial atypical multiple

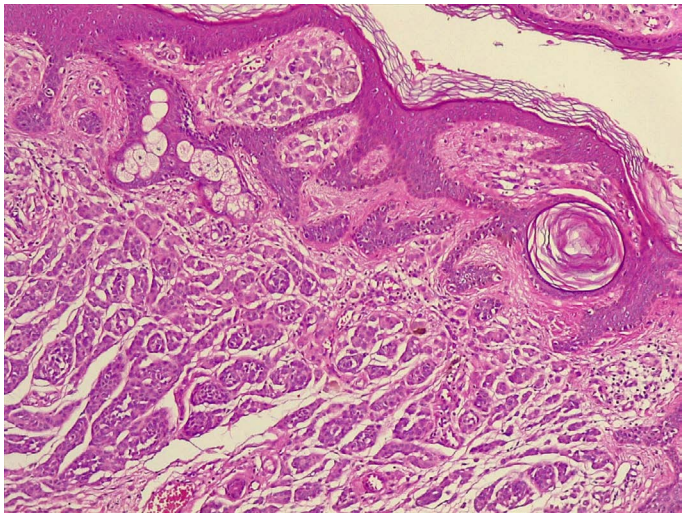

Figure 3. *Dermal nevus and melanoma in the deep part of the lesion – multiple tumour complexes in the papillar derma confluating between each other.*

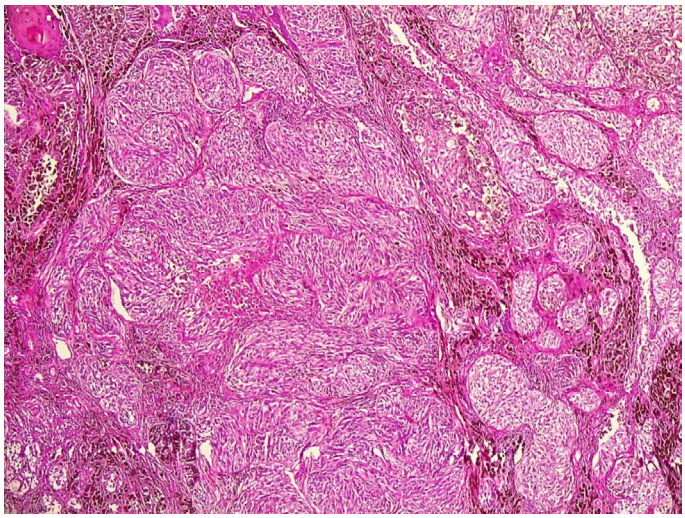

Figure 4. *Severely atypical fusiform melanocytes in desmoplastic stroma HE x 40.*

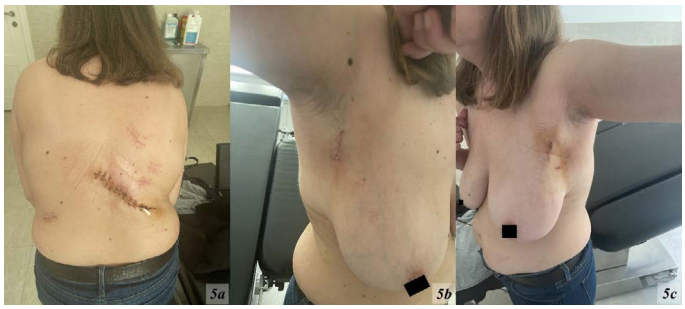

Figure 5. 5a: *Condition after re-excision of the primary tumor with an additional margin of safety of 2 cm. Placement of a glove drain (second surgical session).* ***5b:*** *Removal of a draining lymph node in the right axilla during the second surgical session.* ***5c:*** *Fig. 5b: Removal of a draining lymph node in the left axilla under intubation anesthesia and within the second surgical session.*

mole melanoma syndrome) [9] in families with an unusual increased incidence rate of melanoma [10].

Acquired atypical mole syndrome (or FAMMM syndrome) is a rare cutaneous disease characterized by a development of numerous dysplastic nevi and melanoma on the skin [11].

Some studies suggest that patients with the FAMMM syndrome have an estimated risk of nearly 100% for melanoma development by the age of 70 [10,12,13].

Melanoma development is also possible in patients with the so called "sporadic" dysplastic nevus syndrome [14].

Dysplastic nevi (DN) are often referred to as an intermediate form between common benign lesions and melanomas [15]. It should be noted that patients with dysplastic nevi might have insufficient DNA repair or overexpression of pheomelanin which may result in further DNA damage and tumor progression [15]. In the literature they are often described as potential precursors for melanoma or as markers for an increased risk for developing one [15] and thus should be kept in mind when examining atypical moles. An increased 10-fold risk for melanoma development was found in patients with more than five dysplastic nevi [16].

Despite DN being classified as "mild, "moderate" and "severe", other collectives have linked the melanoma risk only with the dysplastic nevi showing high grade histological atypia [17].

A consensus seems to be impossible because the only way to identify if the melanocytic nevus is indeed dysplastic, we would have to perform a biopsy and further observation on the evolution of the lesion would be impossible [18].

Cutaneous melanoma is the most aggressive type of skin cancer responsible for about 90% of skin cancer-related deaths [19]. With a worldwide increase in incidence rate over the years for melanoma – 25 new cases per 100,000 population in Europe and 60 new cases per 100,000 in Australia [20], as clinicians we must inform our patients about the importance of regular skin examinations and frequent follow-ups in terms of lowering these numbers in the future.

Phototypes (types1&2), a high number of acquired melanocytic nevi, UV radiation and damage, painful sunburns in childhood and excessive sun exposure in adulthood contribute to the melanoma formation [20]. These are all very well-known risk factors among the population.

However, different risk factors contribute differently to melanoma development. For example, the melanin found in the melanocytes, is considered a protective agent from UV light and that explains why some phototypes on the Fitzpatrick's scale (types1&2) have an increased risk for developing skin cancer [20].

Mechanical injuries are linked with the development of acral melanoma and melanoma located on the extremities [21]. A retrospective study with 369 melanoma patients performed by Kaskel et al. [21] concluded that 32 of the patients considered an association between the melanoma and past trauma, 22 patients reported single traumatic event, 10 a persisting irritation and two reported an irritation to a pre-existing melanocytic nevus (later on confirmed as melanoma on acquired or congenital

nevus) [21]. Since most of the patients with melanoma on the extremities were also reporting a traumatic event, we should consider more often a history of trauma in these anatomical locations [21].

According to Holm et al. [22] the human dermis can undergo malignant transformation due to several risk factors, including chronic injury [22].

Chronic irritation as a potential risk in terms of skin cancer development has been discussed since 1828 [23].

A case report presented by Nakai et al. [24] showed a patient with chronic irritation due to sewing resulting in hyperpigmentation on the thumb which clinically resembled a malignant melanoma. The patient had no history of systemic, inherited disease or exposure to chemicals thus leaving mechanical irritation as the only explanation for the hyperpigmentation [24].

According to a paper by Morales Suarez-Varela et al. [25], 73% of the patients had no family history of malignancy and thus concluded that the malignancy was a result from rather environmental than genetic factors.

In the case presented by our team, the patient's malignant lesion was under a lot of irritation due to a constant wear of a brassiere in her everyday life (patients anamnestic data).

Keeping in mind that she denied having skin malignancies in the family or comorbidities, we can conclude that the mechanical irritation during the years could have been one of the main risk factors for developing nevus associated polypoid melanoma.

A systemic meta-analysis by Gandini et al. [26] have found that one of the most important risk factors for melanoma development are the number of the common and/or atypical nevi with an estimated relative risk (RR) = 6.89;95% [26].

The relationship melanocytic nevi-melanoma isn't one sided and should be further investigated [27]. A systemic review by Dessinioti et al. [27] stated that the presence of nevi in histological correlation with melanoma (also called nevus-associated melanoma or NAM) is an interesting side to the theory on malignant transformation of nevi to a nevus-associated melanoma.

Evidence provided from different collectives on the matter has stated the different nature, in terms of genetics, histology and etc. of the NAM and the de novo occurring cutaneous melanomas [28,29].

Clinicopathological differences were found between the de novo developing melanomas and the nevus-associated melanomas, proving the possibility of different origin of both type of lesions [29].

"Dermatoscopic clues" for NAM such as negative pigment network, tan areas without structure and areas without identifiable structures were provided by Reiter et al. [30].

The carcinogenic evolution proposed by Clark et al. [8] in 1978 suggests that in patients with history of melanoma, the dysplastic nevi is the precursor for melanoma.

A systematic review by Dessinioti et al. [27] suggests that 65% of the nevus-associated melanomas develop within a dysplastic nevus.

In the cohort study by Bosch-Amate [28] with 2,227 patients, the nevus-associated melanomas were 22.86% and the patients which developed them were younger, with a fairer phototype, had higher nevus count and the tumors were located on the trunk in comparison with the de novo melanomas.

A retrospective study performed by Lin et al. [31] showed no prognostic implication on the overall survival rate of patients with de novo versus nevus-associated melanoma. Despite this, we should acknowledge these two lesions as different subtypes in the melanoma family [28].

Polypoid melanoma is a rare type of nodular cutaneous melanoma in which the tumor is directly connected to the skin by a pedicle [32]. It has young onset development (20-39 years), with predisposition sites such as the back area and a survival rate of 5 years [32]. Clinically, it is presented with exophytic growth and ulceration [32]. This type of melanoma has a poor prognosis due to thickness and ulceration and a possible risk of vascular embolization [33].

Although cutaneous melanoma is an aggressive disease with a high mortality rate, if diagnosed early it is curable [34].

When examining the skin lesions, we must consider the relationship between clinical findings, risk factors and family history as a whole [34].

Cutaneous melanoma is diagnosed based on a physical examination of the skin [35].

The ABCDE (asymmetry, border, color, diameter, evolution) and "ugly duckling" sign (moles that doesn't look normal or stand out from the rest on the body) are used in the daily practice as diagnostic criteria [35].

Dermoscopy remains the classical method used in the everyday clinicians practice [35]. New horizons may be set with the current technological development in the medical field, such as artificial intelligence-driven image analysis, 3D body imaging, reflectance confocal microscopy (RCM), optical coherence tomography (OCT) and much more, providing more precision in the diagnostic world [35,36].

Surgical management is currently the best option for localized, invasive melanoma with approximately 5-year survival rate [37,38]. The standard procedure for localized cutaneous melanoma is the wide local excision [37].

After the initial staging, the evaluation for sentinel lymph node biopsy remains very important [36]. Lymph node metastasis impacts the prognosis of the disease and the further treatment [39]. A less invasive alternative than traditional dissection is the sentinel lymph node biopsy [38]. This step provides further information about the following treatment options [38].

Conclusions.

Early detection, prevention and eradication of malignancies seem to be a never-ending topic in the dermatology field.

With the current innovations in the diagnostic area, the diagnosis of skin cancer seems faster, more precise, and less time-consuming.

In the early stages of melanoma development, the survival rate is much higher than those in the later stages. Therefore, the patients must realize the importance of regular physical examinations, and we as clinicians should improve our skills and knowledge.

We present a case with a 46-year-old female with a history of chronic mechanical irritation due to the use of a brassiere (a piece of woman's underwear), which developed on the back

a nevus associated polypoid melanoma alongside multiple dysplastic nevi. Dermatosurgery was once again proved as the most efficient way of eradication of skin malignancies.

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