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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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SHARK PEDICLE ISLAND FLAP FOR BASAL CELL CARCINOMA OF THE PERIALAR ZONE OF THE NOSE: PHOTOXICITY AND PHOTOCARCINOGENICITY MEDIATED BY POTENTIALLY NITROSAMINE CONTAMINATED DRUG INTAKE -A NEW EXPLANATION FOR THE SKIN CANCERS PATHOGENESIS?

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Abstract.

Modern skin cancer pathogenesis includes new concepts such as nitroso photocarcinogenesis and nitroso-mediated photosensitivity. The above 2 new concepts are in all likelihood also modeled/determined by photocarcinogens known as nitrosamines and/or NDSRIs available as contaminants in many drugs worldwide.

The phototoxicity of nitrosamines is a known nonspecific property of them, for which evidence exists as far back as 1972.

Current data from 2023/2024 are completely supportive of nitrosamines identified in drugs, with genotoxicity and phototoxicity proven once again.

Regulators' data on polycontamination of a drug with up to several nitrosamines at the same time are of concern. The carcinogens/mutagens in question could also act as bi-/ polycarcinogens depending on whether they are metabolized or not.

Permanent combined intake of potentially/actually nitrosamine-contaminated drugs appears to be key in the subsequent development of multiple cutaneous tumours, according to new findings in the literature. The localization of these tumours in areas exposed to intense solar radiation could also be seen as indirectly pointing to the presence of certain photosensitisers in the human body. Some of these nitrosamines are photocarcinogens and human carcinogens at the same time.

The identification and specification of each of these genotoxic photosensitizers in drugs has yet to be further investigated in detail. The FDA identifies them currently as substances with carcinogenic potency. The clinicopathologic correlations published to date within the intake of potentially contaminated drugs are indicative of 1) the need to redefine skin cancer pathogenesis and 2) the subsequent possible introduction of complete elimination regimens against nitrosamines.

We inform about another polymedication intake in a patient with arterial hypertension and diabetes mellitus, which includes the following medications: gliclazide 60 mg once daily and metformin hydrochloride 850 mg once daily, both since 24 years ; sotalol hydrochloride 80 mg since 2 years; bisoprolol fumarate 5 mg since 17 years; candesartan cilexetil/hydrochlorothiazide 16 mg/ 12.5 mg since 2 years; and lercanidipine hydrochloride 20 mg also since 2 years. Within this intake, it is notable that 1) all 6 of these drugs appear in the databases for possible availability as nitroso compounds, and that 2) this is the seventh consecutive keratinocyte tumor treated surgically (in this period).

In the presented patient, surgical treatment was performed using a shark pedicle island flap for BCC of the nose, which is an ideal option for tumors with location in the alar or periralar area. An optimal postoperative outcome was achieved.

This article focuses on the possible role of drug-mediated photo nitrosogenesis/ carcinogenesis of skin cancer by briefly reviewing and analyzing the available literature to date.

Key words. Shark pedicle island flap, drug related Photocarcinogenesis, Nitroso photocarcinogenesis, candesartan, hydrochlorothiazide, bisoprolol, sotalol, metformin, gliclazide, BCC, skin cancer.

Introduction.

The localization of keratinocytic tumors in areas exposed to solar radiation is a clear indication of its pathogenetic role [1,2]. The heterogeneous mutations identified at the time and after exposure of patients to UV radiation [2] are in all likelihood due to or could be conditioned/explained by other, currently poorly known or not yet definitively identified pathogenetic factors (such as nitrosamines for example).

New, but also old, scientific literature sheds some light on the question: How does photosensitivity arise or what could give rise to it [3-5]? Recently, regulatory authorities in the face of the FDA have identified or provided strong evidence for the presence of contaminants known as nitrosamines/NDSRIs, in about 300 of the most widely distributed drugs worldwide [6]. As early as 52 years ago, it was established that many of these carcinogens/mutagens cause phototoxicity in addition to genotoxicity [3].

There is scant to nonexistent literature data focusing on the nitrosamines identified to date in drug preparations, their bioavailability in peripheral blood as well as in lesional, tumor tissue, in the context of their regular, permanent drug intake.

However, a number of indirect but logically grounded data in the form of clinicopathological correlations are strongly suggestive that any actual/potential/contaminated combined drug intake (of vitamins, antihypertensives, antidiabetics, and/ or antiarrhythmics), could lead to the manifestation of relatively monomorphic, keratinocytic tumors [7-10]. Photocarcinogens, also known as nitrosamines, remain the only logical link between drug intake and subsequent permanent keratinocytic cancer formation [3-5].

Starting from this very hypothesis, we present another patient who developed multiple keratinocytic tumors in the head region against the background of a potentially nitrosamine-contaminated polymedication regimen that included: metformin, gliclazide, sotalol, bisoprolol, candesartan, hydrochlorothiazide, and lercanidipine. New aspects of skin carcinogenesis are discussed in the context of so-called metabolic reprogramming of the tumor cell [7,9,10].

Case report.

An 80-year-old female presented to the dermatology department with primary complaint of a slowly growing tumor formation on the nose, which had been present for approximately 5 years (Figure 1). The patient has a medical history of surgically removed six tumor formations from the head region between 2000 and 2019, with the most recent being an adenoid-cystic type of basal cell carcinoma removed from the forehead in 2019. Her medical history also includes diabetes type 2, arterial hypertension (since more than 25 years), tympanic membrane surgery in 1979, surgery on the right leg for thrombosis, surgery for a perforated gastric ulcer in 1987, and a thyroidectomy in 1988. No family history of skin cancer in any family member was reported.

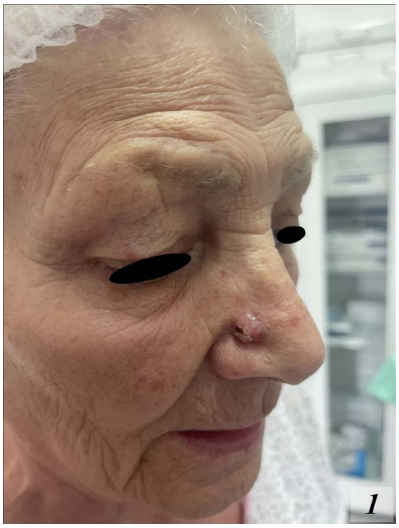

Figure 1. *A solitary nodular formation located on the right perialar nasal region, covered with crust and visible telangiectasias.*

The patient has been on systemic therapy with the following medications: gliclazide 60 mg once in the morning and metformin hydrochloride 850 mg once in the morning, both since 2000; sotalol hydrochloride 80 mg (half a tablet administered in the morning and at noon) since 2022; bisoprolol fumarate 5 mg as needed since 2007; candesartan cilexetil/hydrochlorothiazide 16 mg/ 12,5 mg as needed since 2022; and lercanidipine hydrochloride 20 mg as needed, also since 2022.

The patient requested physical examination and further therapeutic approach to be established.

Routine blood tests were conducted, showing no abnormalities. An ECG was performed, revealing sinus rhythm with a first-degree AV block and no significant ST-T changes.

The dermatological examination revealed a solitary nodular formation located on the right perialar nasal region, covered with crust and visible telangiectasias (Figure 1). The lesion was suspected for basal cell carcinoma. Enlarged lymph nodes were not palpable.

The patient was recommended surgical excision under local anesthesia with lidocaine 2%. The tumor formation located on the right perialar nasal region was excised with an oval excision, which resulted in a circular primary defect (Figures 2 and 3). Primary closure with single interrupted sutures or secondary wound healing were not an option due to the complexity of the anatomical area, as both approaches would likely result in a poor aesthetic outcome. To reconstruct the primary defect, we opted for the one-stage shark pedicle flap reconstructive technique (Figure 4). The postoperative histopathological evaluation was indicative of BCC from nodular type, stage 1.

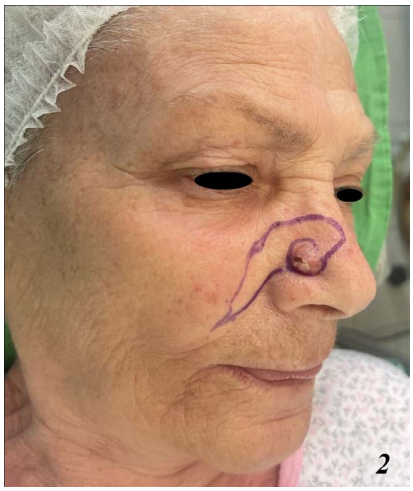

Figure 2. *Preoperative view: Outlining the primary defect and the subsequent shark pedicle flap.*

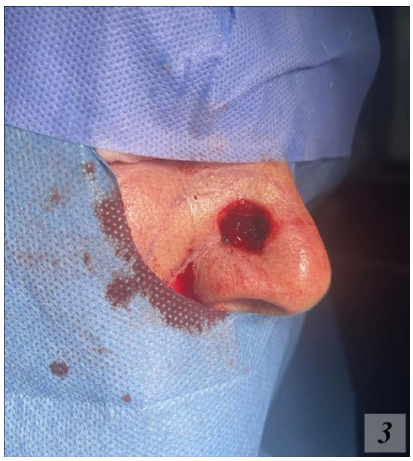

Figure 3. *Preoperative view: Primary wound defect after oval excision of the tumor formation.*

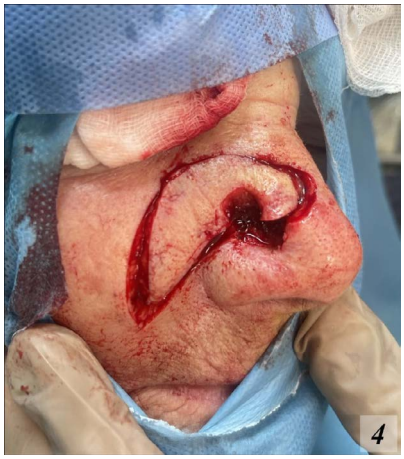

Figure 4. *Preoperative view: Secondary wound defect – shark pedicle flap.*

This approach ensured the preservation of the natural concavities of the nasofacial sulcus and alar groove, while maintaining the nerves and blood vessels beneath. A caudal incision was made along the alar sulcus and nasolabial fold (Figures 2 and 4). The width needed for the "shark's snout" was determined by measuring the distance between the alar sulcus and the medial edge of the defect. The distance was then transferred to the cranial border of the primary defect. The incision line was then extended medially in a curved manner from the cranial edge of the wound, merging into the caudal incision at the nasolabial fold (Figure 4). The right cheek was used as part of the flap (Figures 2 and 4). The secondary defect appears like a "shark with its jaws open". The inferior part of the flap was then dissected down to the hypodermis, and the pedicle was carefully mobilized to preserve the subcutaneous vascular supply (Figure 4). The superior part of the flap was also dissected and mobilized. Levator labii superioris muscle provided an additional blood supply to the area. The underlying cartilage was left intact. The "shark's snout" was then rotated 90 degrees to align seamlessly with the primary wound defect. Closure of the secondary wound defect was achieved using single interrupted sutures (Figure 5). The first suture was placed at the inferior part of the "shark's snout". The histopathological examination confirmed an infiltrative, high-risk basal cell carcinoma with superficial ulceration, prominent desmoplastic stroma, and focal peripheral inflammatory infiltrates. The tumor measured 8 mm in diameter and 4 mm in thickness, with clear margins of at least 2 mm from the lateral resection lines and 1 mm from the deep resection line. A whole-body CT scan with contrast was advised for staging. Daily dressings with povidone-iodine were recommended, along with metamizole sodium ampoules for pain management as needed. Removal of the sutures was performed 14 days post-surgery. A favorable outcome was achieved one month postoperatively (Figure 6).

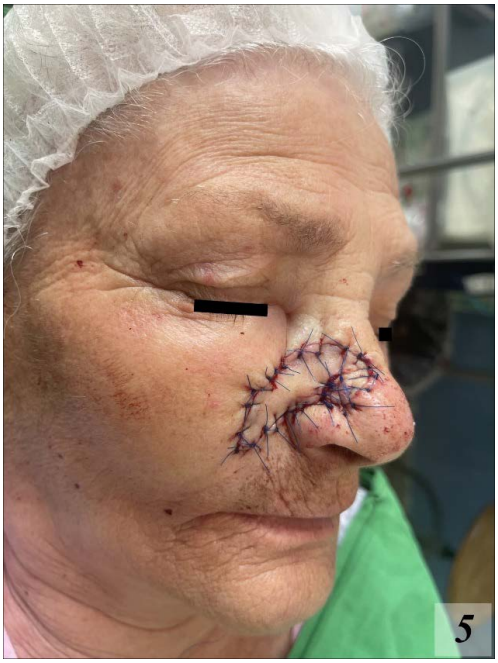

Figure 5. *Preoperative view: The secondary wound defect is closed with single interrupted sutures.*

Figure 6. *1 month follow-up.*

The patient's medication regimen was adjusted to gliclazide 60 mg administered once in the morning, metformin hydrochloride 850 mg once in the morning, and sotalol hydrochloride 80 mg, half a tablet taken both in the morning and at noon.

Discussion.

There are two main external or environmental factors that could be related to the modern vision of skin carcinogenesis and probably determine the incidence of keratinocytic cancers (but not only keratinocytic cancers) through the potentiation of acquired mutations and/or directly through genotoxicity: 2.1 solar radiation and 2.2 the permanent contact of the human body with photocarcinogens/mutagens, also known as nitrosamines/ NDSRIs [7-11]. According to the International Agency for Research on Cancer (IARC), tobacco specific nitrosamines has been found to play a central role in tobacco-smoke mediated cancer initiation [11]. The same or analogous ones have also been identified in drugs, with emphasis on the fact that they are genotoxic and phototoxic [4,5].

It is also interesting that a single drug is capable of being contaminated with up to several carcinogens/mutagens/ nitrosamines/NDSRIs simultaneously: for example (N-nitrosodimethylamine [NDMA] and N-nitrosodiethylamine in losartan [5]. That is, polycontamination with several carcinogens/ nitrosamines could be present or present even with monomedication with only one particular sartan [5].

On the other hand, a given nitrosamine such as NDMA, is able to directly activate RAS oncogenes, and its active methylated metabolite, methyldiazonium, is also mutagenic [12]. In practice, it appears that polycontaminated drug intake, in the context of polymorbidity, could be associated with the intake of twice as many (photo)nitroso-carcinogens/mutagens, also known as nitrosamines or their derivatives [5,12].

The permanent , combined, potentially nitrosamine-contaminated intake of drugs (in our presenting patient) such as metformin [9,13], gliclazide, hydrochlorothiazide [8,9], bisoprolol/sotalol [10], lercanidipine [14,15] and candesartan [8], could (and according to other literature data) also be

associated with or considered as the intake of a cocktail of heterogeneous photo/nitroso carcinogens, carcinogens/ mutagens that also determine the appearance of multiple cutaneous tumors (keratinocytic/melanocytic) in areas exposed to solar radiation [8-10,13-15].

Foreign authors collectives believe that the use of antihypertensives (HR [95% CI]: 1.12 [1.07-1.18]), ACE inhibitors (1.09 [1.01-1.18]), calcium channel blockers (1.13 [1.05-1.22]), diuretics (1.20 [1.12-1.27]), loop diuretics (1.17 [1.07-1.28]), and thiazides (1.17 [1.03-1.33]) could be each associated with higher NMSC risk [16]. NMSC risk linearly increased with use of multiple antihypertensives (p-trend = 0.02) and with longer duration of use (p-trend < 0.01) [16].

Similar data have been reported for hydrochlorothiazide and the subsequent development of skin cancer: keratinocytic and melanoma: with increased risks with longer durations and cumulative doses [17].

According to data from German authors, hydrochlorothiazide intake could be associated with the development of up to 4 types of nonmelanocytic tumors: HCTZ was significantly higher in patients with AFX/PDS (44.5%) compared to patients with SCC/BCC (25.3%) [18]. ″Additionally, diabetes mellitus or its comorbidities may be associated with an increased risk for AFX/PDS″ [18]. In all likelihood, the comorbidities shared by the colleagues (diabetes mellitus) [18] could also be related to the potential intake of metformin and sitagliptin, for which there is already strong evidence that, in the context of polymedication polycontamination, they could also have pro-carcinogenic effects [9,13].

Unfortunately, none of the aforementioned articles [16-18] address the fact that each of the drugs presented in them (after or during whose intake skin cancer occurs) is actually also on the 2024 FDA list for nitroso-contaminated products [6]. That is to say, in the groups in question, one could also make the suggestion that it is a probable case of concentrated (or normal daily) intake from a cocktail of nitroso carcinogens [16-18]. Or the intake of substances whose presence has not been officially declared to this day by regulators in the face of the EMA and the FDA.

Surgical treatment of tumors in the nasal area is challenging for dermatosurgeons, with options for adequate single-stage surgical treatment often hesitating between shark pedicle island flap and bilobed flap [19,20].

Incorrect planning or performance of a shark flap could be associated with necrosis of part of the area mobilized for transposition and adaptation, subsequent nasal asymmetry or marginal promination in the area of the ″shark tail″ [21].

The shark pedicle island flap is ideally suited for the surgical treatment of tumors in the perialar area and the alar sulcus area [22].

Proper performance of this procedure also guarantees perfect postoperative results [23,24]. Shark pedicle island flap was first described as a surgical technique in the nasal area in 2006 by Cvancara and Wentzell [24]. In practice, it is a myocutaneous island flap in the form of a shark [24]. The jaws of this shark are formed by the tumor formation or defect that occurs after its removal. Correction or closure of this defect corresponds to a ″Smiling shark″ (Figure 5). The intraoperative finding of this defect could be likened to an ″Angry shark″ with open jaws (Figure 4).

An interesting analogy could be drawn based on a number of available literature data. Tobacco-specific nitrosamines are carcinogenic to the human genome, in fact inducing mutations that affect the tumour suppressor gene p53 and RAS oncogenes [25]. These genes also belong to the genes affected by acquired mutations responsible for the occurrence and progression of skin cancers: melanoma and keratinocytic cancers [26-33]. It would be logical to think in direction of drug-mediated phototoxicity and photo nitroso carcinogenesis [7-10], both modelled or distinguished in the context of permanent contaminated Nitroso-drug intake.

Nitrosamines and/or nitroso compounds could also be defined as multipotent carcinogens [34].

Precisely because of the above-mentioned facts, their future cataloguing and detailed analysis with respect to skin carcinogenesis should be considered as a priority.

In conclusion, we present a patient with a new basal cell carcinoma localized in the perialar area/alar sulcus area arising within the context of a potentially/actually nitrosamine-contaminated drug intake. The role of nitroso contamination in the context of photo-nitrosocarcinogenesis and oncopharmacogenesis is commented.

The so-called shark pedicle island flap appears to be a good therapeutic option for tumors with similar or analogous localization.

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