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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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GRAHAM-LITTLE-PICCARDI-LASSEUR SYNDROME (GLPLS) IN A BULGARIAN PATIENT: CASE REPORT AND SHORT PATHOGENETIC UPDATE IN RELATION TO THE CONNECTION TO ANTIGEN/ MOLECULAR MIMICRY

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Abstract.

Graham-Little-Piccardi-Lasseur syndrome (GLPLS) is a rare lichenoid dermatosis classified as a variant of follicular lichen planus, also known as classic lichen planopilaris. The condition is characterized by the triad of cicatricial scalp alopecia, noncicatricial alopecia in the axillary and groin regions, and numerous follicular papules distributed across the body.

We present a 64-year-old female with clinically and histologically confirmed GLPLS. Two biopsies were conducted, resulting in lichen planopilaris/ pseudopelade Brocq and lichen planus hypertrophicus. Initial therapy included loratadine and topical clobetasol propionate.

Due to the suspicion of possible drug-induced reaction, the antihypertensive therapy, which consisted of valsartan, bisoprolol, spironolactone, and chlorthalidone, was discontinued and replaced with moxonidine. Urinary infection caused by Escherichia coli and dental infection were noted.

Prescribed outpatient treatment included acitretin, bilastine, and topical prednisolone for the scalp. Improvement was observed in the lesions located on the trunk and upper and lower extremities following betamethasone/salicylic acid ointment was prescribed, and methylprednisolone aceponate cream.

Re-application or return of the old systemic medication on an outpatient basis resulted in a worsening/exacerbation of the clinical picture and a re-need to change medication. It is this fact that suggests that polymedication could also be considered as a trigger of lichen planus and its subforms such as GLPLS.

The hypothesis surrounding alterations in tissue homeostasis as a potential trigger factor for autoimmunity is being discussed, with a specific focus on infectious and drug-induced forms of lichen planus, as well as Graham-Little-Lasseur syndrome.

Key words. Lichen planopilaris, pseudopelade Brocq, Graham-Little-Piccardi-Lasseur syndrome, molecular mimicry, drug-induced, *Escherichia coli*, dental infection, periodontitis chronica granulomatosa, valsartan, bisoprolol, spironolactone.

Introduction.

Graham-Little-Piccardi-Lasseur syndrome (GLPLS) is a rare type of lichen planopilaris [1]. It is characterized by patchy cicatricial alopecia of the scalp, noncicatricial alopecia of the axillae and groin, and the presence of numerous follicular keratotic papules on the body [1]. The condition primarily affects women between the ages of 30 and 70 years [2], with a higher prevalence among those who are postmenopausal [3].

Although the etiology is unknown, some authors suggest that a T-cell-mediated immune response is a key factor in the pathogenesis of both lichen planus [4] and GLPLS [3]. In theory, a contact with an exogenous agent - such as a virus, drug, or contact allergen – leads to alterations in epidermal self-antigens, resulting in the activation of cytotoxic CD8+ T cells [4,5].

Given the various trigger factors associated with the onset of lichen planus, we present a case of a Bulgarian female patient with Graham-Little-Piccardi-Lasseur syndrome that developed in the context of polymedication involving several antihypertensive medications – such as valsartan, bisoprolol fumarate, spironolactone, and chlorthalidone – as well as two infectious sites: one of dental origin (periodontitis chronica granulomatosa) and the other of urinary origin (Escherichia coli infection). Our objective is to conduct a brief retrospective analysis of 12 articles from PubMed and 35 from PMC regarding GLPLS.

Case report.

A 64-year-old female presented to the dermatology department with primary complaints of intense hair loss and severely itchy rash on the trunk and upper and lower extremities, persisting for approximately two months.

The patient has a history of an ischemic stroke affecting the vertebrobasilar system, hypertrophic obstructive cardiomyopathy, moderate aortic regurgitation, mild to moderate mitral regurgitation, and mild tricuspid insufficiency. Additionally, the patient has stage III hypertensive disease. Systemic therapy since April 2023 was initiated with valsartan 160 mg half a tablet in the morning, clopidogrel 75 mg once in the morning, bisoprolol fumarate 5 mg half a tablet in the morning, betahistine dihydrochloride 24 mg twice daily – one in the morning and one in the evening, rosuvastatin 10 mg once in the evening, spironolactone 25 mg once in the morning, and chlorthalidone 25 mg once in the morning. Family history of alopecia in her mother was also reported.

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

Routine laboratory tests were performed, resulting in elevated potassium levels, which were monitored over seven days, ranging from 5.91 mmol/L to 5.5 mmol/L measured on the final day (normal range 3.6-5.2 mmol/L). The tests also showed elevated creatinine levels - 142.1 micromol/L (normal range for women 53-97.2 micromol/l), urea at 10.9 mmol/L (normal range 2.1-8.5 mmol/l), and uric acid at 460.0 micromol/l (normal range for women 155-357 micromol/l). Additional tests included Anti-HCV II at 0.07 – nonreactive S/CO ratio (Signal-to-Cutoff Ratio); and HBsAg at 0.29 – nonreactive S/CO ratio. Allergy to ciprofloxacin was noted. An ANA screening was conducted, resulting in positive results with a titer of 1:320, ANA subfractions were without elevations.

The dermatological examination revealed numerous livid hypertrophic papules and nodules with fine desquamation on the extensor surfaces of the trunk (Figure 1a), upper (Figures 1b and 1c), and lower limbs (Figure 2f). The capillitium showed diffuse cicatricial alopecia with plaque-like areas of desquamation (Figures 3a and 3b). Body hair was significantly reduced, particularly in the axillae (noncicatricial alopecia) (Figures 4a and 4b), while pubic and pretibial hair remained intact. Enlarged lymph nodes were not palpable. Several biopsies were performed – from the capillitium and from the papules and nodules from the right lower leg.

The histological examination of the biopsy from the capillitium showed pronounced ortho- and follicular hyperkeratosis, uneven acanthosis, and a reduced number of sebaceous glands throughout the dermis, replaced by diffuse fibrous tracts. A retained hair follicle fragment was covered by a lichenoid

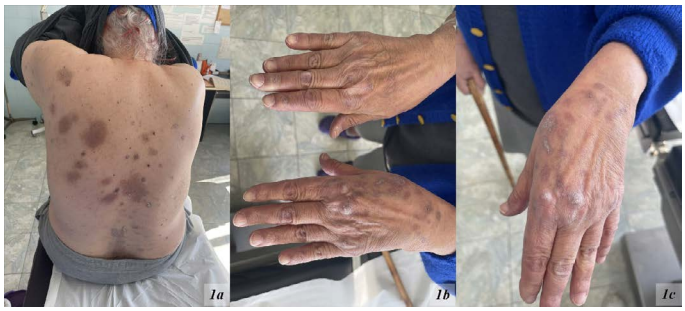

Figure 1a-c. *Numerous livid hypertrophic papules and nodules with fine desquamation on the extensor surfaces of the trunk (a), right (c) and left hands (b).*

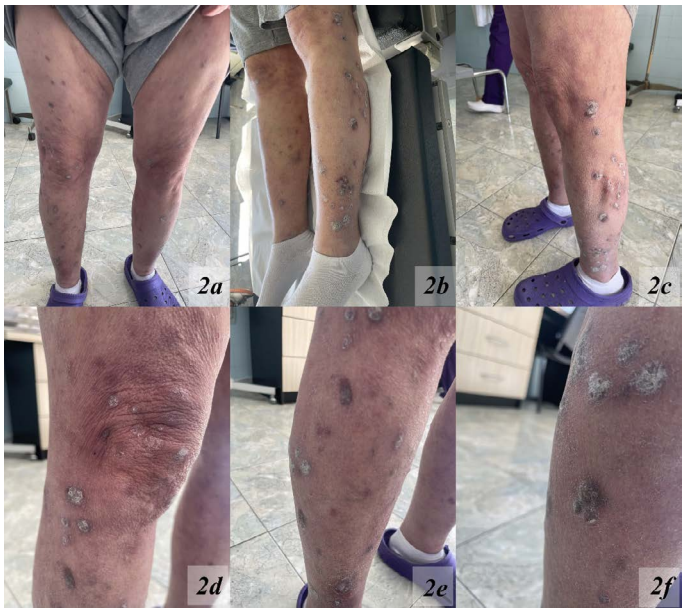

Figure 2. *Numerous livid hypertrophic papules and nodules with fine desquamation on the extensor surfaces of lower limbs.*
2a: *anterior prospective: front view of the right and left lower legs.*
2b: *lateral view of the lower left leg. The medial side of the right lower leg is also visible.*
2c: *a closer view of the distal lesions, left lower leg.*
2d: *a closer view of the anterior genu region (patellar area), right lower leg.*
2e: *antero-lateral view, right lower leg.*
2f: *a closer look at the lesions in the crural region – calf area.*

Figure 3. *Capillitium: diffuse cicatricial alopecia with plaque-like areas of desquamation.* ***3a:*** *left lateral view,* ***3b:*** *right lateral view.*

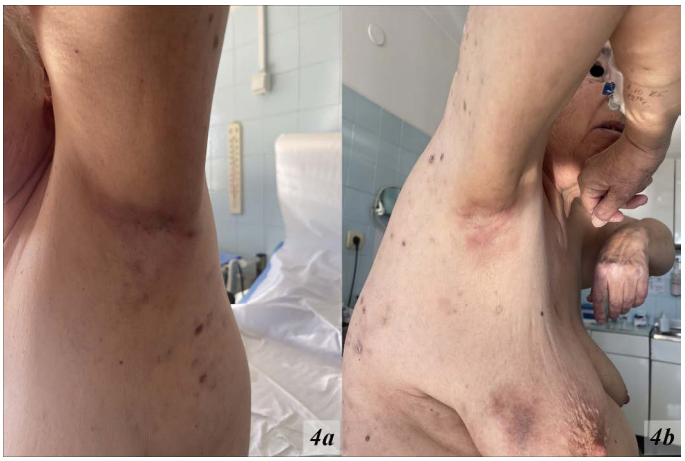

Figure 4. *Reduced body hair, particularly in the axillae (noncicatricial alopecia).* ***4a:*** *Left axillary region,* ***4b:*** *Right axillary region.*

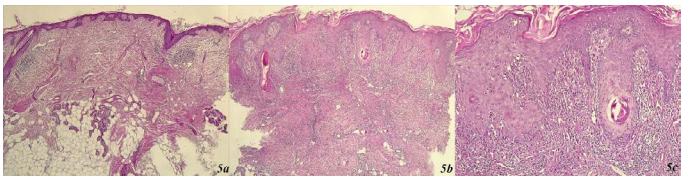

Figure 5. *Histology panel.*
5a: *cicatricial alopecia HE x 40*
5b: *Lichen planus hypertrophicus HE x 40*
5c: *Lichen hypertrophicus HE x 100.*

inflammatory reaction, with round cells destroying the external epithelial sheath. These findings were consistent with lichen planopilaris/ pseudopelade Brocq (Figure 5a).

The histological examination of the biopsy from the lower leg region revealed marked ortho- and follicular hyperkeratosis, irregular acanthosis alternating with pseudoepitheliomatous hyperplasia, vacuolar degeneration of basal keratinocytes, and a lichenoid lympho-plasmocytic inflammatory infiltrate obscuring the dermo-epidermal junction and lining the papillary dermis. These findings were consistent with lichen planus hypertrophicus (Figures 5b and 5c).

Based on the histological and dermatological findings, the diagnosis of Graham-Little-Piccardi-Lasseur syndrome (GLPLS) was confirmed.

Therapy was initiated with loratadine 5 mg once daily and topical clobetasol propionate applied twice daily. Due to the suspicion that the condition may have been triggered by the antihypertensive medications – valsartan 160 mg, bisoprolol fumarate 5 mg, spironolactone 25 mg, and chlorthalidone 25 mg – they were discontinued and replaced with moxonidine 0.2 mg twice daily when blood pressure exceeded 145/90 mmHg.

Given the elevated creatinine and urea levels, along with evidence of a urinary infection with Escherichia coli (urine sediment with significant bacteriuria, leukocyturia and mild hematuria, positive uroculture for *E coli*), sulfamethoxazole/ trimethoprim 480 mg two tablets twice daily for five days was prescribed.

To rule out infectious causes, hepatitis markers were tested, and the results were negative for hepatitis B and hepatitis C.

Additionally, after dental consultation, periodontitis chronica granulomatosa was established and further treatment was recommended.

The patient was discharged with an improvement in the dermatological status. The prescribed outpatient treatment included acitretin 45 mg daily (25 mg in the morning, 20 mg at noon), bilastine 20 mg once daily at 5 p.m., and topical prednisolone 0.2 g solution once daily in the evening for the scalp. For the lesions located on the trunk and upper and lower extremities, betamethasone/salicylic acid ointment was prescribed once in the morning, and methylprednisolone aceponate once in the evening. Regular blood tests every four weeks for monitoring were recommended.

Due to elevated arterial pressure in the outpatient setting, cardiac medication was changed, and old medication was resumed. This led to an exacerbation of the clinical picture and the appearance of new lesions on the trunk and extremities. After dermatologic examination, a referral was made to discontinue the triggering medication and continue systemic treatment with neotigasone, and significant improvement was achieved.

Discussion.

Lichen planus (LP) is a chronic, immune-mediated inflammatory condition that involves the skin, mucous membranes, nails and hair [6]. Cutaneous lichen planus (CLP), most frequently observed in middle-aged individuals, usually appears as pruric, violaceous papules, primarily affecting the flexor surfaces of the extremities [6]. CLP is further classified into various subtypes based on the morphology of the lesions and the site of involvement (lichen planopilaris, nail involvement, and palmoplantar involvement) [6]. These subtypes include papular, vesiculobullous, hypertrophic, atrophic, annular, linear, actinic, erosive, follicular, lichen planus pigmentosus and lichen planus pigmentosus-inversus [6]. Oral lichen planus may present as the primary manifestation or occur alongside other mucosal sites, such as the gastrointestinal tract, genital or/and ocular regions [6].

Initially described in 1914 by Piccardi as a progressive cicatricial alopecia of the scalp, noncicatricial alopecia in the axillary and pubic area, along with follicular papules on the trunk and extremities [7], Graham-Little-Piccardi-Lasseur syndrome received its full name later in 1915 when Graham Little described a similar condition as “folliculitis decalvans et atrophicans” [8]. The syndrome is a rare lichenoid dermatosis, classified as a variant of follicular lichen planus (classic lichen planopilaris) [9].

Although familial cases of lichen planus are well-documented in the literature [10], familial GLPLS is extremely rare, with only two published articles on the subject in PubMed [9,11]. In the case we present, no direct link could be established between our patient and her mother, as the patient recalled that her mother only had alopecia (scarring or nonscarring) without any other skin manifestations. Although these conditions share similarities, they are distinct. However, they may have a similar underlying autoimmune basis contributing to both. In this case, we cannot classify it as familial Graham-Little-Piccardi-Lasseur syndrome.

Some authors suggest that a T-cell-mediated immune response plays a crucial role in the progression of lichen planus to Graham-Little-Piccardi-Lasseur syndrome [12,13]. However, in cases of severe inflammatory reactions, additional antigens may be damaged and released, potentially also triggering B-cell immune activation [12,13]. The heterogeneous cutaneous manifestations observed in patients with lichen planus and GLPLS may be attributed to the discovery of new antigens through processes like antigen mimicry or epitope expansion [13,14]. Those two events could help explain the potential transition to other rare forms of the condition [14].

The pathogenicity of lichen planus lesions involves autoimmune-mediated lysis of basal keratinocytes, driven by cytotoxic T lymphocytes (CD8+ lymphocytes) [15]. Alterations in tissue homeostasis can arise from the presence of exogenous antigens, such as medications or infections, and/or endogenous antigens, such as neoplastic cells [14].

The triggering of lichen planus by various classes of antihypertensive medications has been well-documented in the literature, including beta blockers (like nebivolol) [16], angiotensin II receptor blockers (such as valsartan) [17], aldosterone antagonists (such as spironolactone) [18] and thiazide diuretics (such as hydrochlorothiazide) [19].

Beta blockers have long been recognized as a potential trigger for the development of autoimmune responses [20]. Since 1974, drug-induced eczema, lupus erythematosus, lichen planus and erythematous psoriasiform eruption have been reported as adverse reactions to practolol [21]. A case report documented the occurrence of a bullous lichen planus induced by labetalol [22]. A more recent article by Tchernev et al. [16] described a rare case of lichen planus localized on the penis following the administration of nebivolol. An article reported the reoccurrence of erosive lichen planus lesions on the palms and feet of a patient following the administration of metoprolol, suggesting that the recurrence was likely secondary to the medication [23]. Topical application of beta blockers has also been found as a potential inducer of lichen planus [24].

Lichen planus-like drug eruptions (LDE) can present with features that closely resemble those of idiopathic lichen planus [25]. It is suggested that LDE may arise from cross-reactivity or from a suppressed skin adrenergic system [25]. Upon discontinuation of the medication (labetalol), the lichenoid reaction in the patient resolved [25].

A lichenoid drug eruption secondary to propranolol was also reported by Massa et al. [26]. A case report describing a possible multi-drug-induced palmoplantar lichen planus was presented by Tchernev et al. [27], involving the medications metoprolol, rosuvastatin, ramipril, and acetylsalicylic acid.

An article highlighted a case of telmisartan-induced lichen planus eruption in a patient with vitiliginous skin [28]. Based on the patient's medical history in the article, telmisartan was used in a combination with hydrochlorothiazide [28], prompting us to consider whether telmisartan alone could trigger the lichen planus or if the reaction resulted from a possible cumulative effect of both medications, indicating a potential case of multi-drug-induced lichen planus.

The second and final article we found on PubMed concerning angiotensin II receptor blocker-induced lichen planus described a linear lichenoid drug eruption associated with valsartan [17].

No cases of bisoprolol-induced or chlorthalidone-induced lichen planus were found in the literature.

A single case report of spironolactone-induced lichen planus was identified on PubMed [18].

Hydrochlorothiazide has been reported in the literature as a potential inducer of lichen planus [19].

A case report published in the 1990s described erosive lichen planus of the oral mucosa associated with the use of alpha-methyldopa and hydrochlorothiazide [29].

A case report by Halevy et al. [30] described a lichenoid photosensitive eruption induced by hydrochlorothiazide. The authors employed a macrophage migration inhibition factor test to identify hydrochlorothiazide among several suspected medications the patient was taking [30]. Notably, the colleagues suggested that an allergic reaction to the drug contributed to the onset of the photosensitive lichenoid eruption [30]. While other "trigger" medications are discussed in the literature, this case report will focus exclusively on those most relevant to ours.

Infectious causes that are reported to induce lichen planus are well-documented in the literature, with several notable examples such as localized lichen planus triggered by COVID-19-Vaccination (following both doses of the mRNA vaccine) [31], lichen planus pemphigoides after COVID-19 infection [32], and oral lichen planus following Candida albicans infection [33], as well as Hepatitis C (HCV) infection [34]. The exact cause or mechanism behind adverse reactions following COVID-19 vaccination remains a mystery [31]. However, some authors hypothesize that the spike protein from the vaccine triggers the T cells, leading to the release of proinflammatory cytokines, which in turn target epidermal basal keratinocytes and contribute to the development of lichen planus [31]. Another hypothesis suggests that the vaccine stimulates CD4+ type 1 helper T cells (Th1), which produce cytokines, interferon-alpha, and tumor necrosis factor-alpha, ultimately inducing apoptosis of basal keratinocytes and triggering the formation of lichen planus [35]. In a study by Sood et al. [36], a hypothesis was proposed suggesting that in patients with COVID-19, altered T-cell responses, cross-reactive antibodies, elevated cytokine levels, disrupted immune permeability barrier, and nutrition deficiency (vitamin D deficiency) may contribute to the development of lichen planus or exacerbation of pre-existing oral lichen planus [36].

A case report described a drug-induced cutaneous lichen planus triggered after the first dose of the Pfizer-BioNTech COVID-19 vaccine [37]. In addition to the single case reports, a retrospective cross-sectional study involving 648,110 patients with lichen planus, COVID-19 infection, and COVID-19 vaccination was conducted [38]. The study found that 181 patients developed lichen planus after receiving the COVID-19 vaccine, while 24 patients developed lichen planus following a COVID-19 infection [38]. The calculated risk of developing lichen planus post-COVID-19 infection was 1.143, compared to 1.573 following COVID-19 vaccination was [38].

The meta-analysis by Ma et al. [33] included 1,124 patients with oral lichen planus and 1,063 healthy controls, revealing a significantly higher detection rate of Candida albicans in the oral lichen planus group compared to healthy controls (OR = 1.74, P = 0.003, 95% CI: 1.20, 2.52). Furthermore, the study indicated an increased risk of Candida albicans infection in patients with erosive oral lichen planus compared to healthy controls (OR = 3.97, 95% CI: 2.31, 6.84, P < 0.00001) [33]. Zhang et al. [39] employed a random-effects model (REM) across several literature databases to assess the link between the infectious agent Helicobacter pylori and oral lichen planus. A significant correlation was found, with an odds ratio (OR) of 4.69 (95% CI: 1.36 to 16.19; P < 0.01) [39]. Using sensitivity analysis, the pooled ORs ranged from 3.69 (95% CI: 1.01 to 13.44; P = 0.05) to 6.77 (95% CI: 2.65-17.30; P < 0.001) [39]. Another meta-analysis identified a significant correlation between oral lichen planus and Human papillomavirus (HPV) [40].

Data from Bankvall et al. [41] revealed a distinct bacterial composition in the oral cavity of patients with oral lichen planus, suggesting that these bacteria may play a role in the aetiology of the condition. While an article by Baek et al. [42] identified four strains of Escherichia coli in oral lichen planus lesions, no data on PubMed suggests that lichen planus can be triggered solely by Escherichia coli. In future studies, clinicians should consider expanding their focus to include various infectious agents, especially regarding their role in molecular mimicry.

Extrahepatic manifestations of hepatitis C virus (HCV) infection predominantly affect the oral region [43]. HCV has been shown to replicate in the oral mucosa, attracting HCV-specific T lymphocytes, which suggests a potential role of the virus in the pathogenesis of oral lichen planus [43]. A systematic review with meta-analysis by Lodi et al. [44] analyzed 33 studies comparing the seroprevalence of HCV in lichen planus patients, alongside 6 studies reporting the prevalence of lichen planus in individuals with HCV infection. The findings indicated that lichen planus patients have a significantly higher risk (OR 4.85; 95% confidence interval 3.58-6.56) compared to controls of being HCV seropositive [44]. Additionally, the ORs for HCV patients developing lichen planus were found to be 4.47 (95% confidence interval 1.84-10.86) [44]. Although not very common, a rare variant of lichen planus follicularis tumidus was diagnosed in a patient with a history of hepatitis C [45].

Malignant transformation occurs in approximately 1% of cases of oral lichen planus, with erosive lichen planus recognized as a significant risk factor for such transformation [46]. A retrospective study by Roberts et al. [46] evaluated

1,920 patients with suspected oral lichen planus, and found that 1.39% developed oral squamous cell carcinoma over an average follow-up period of 5.8 years. The transformation rate for erosive oral lichen planus into malignancy was found to be 5.98% exhibiting an aggressive clinical course [46].

A case of unilateral lichen planus triggered by dental metals was reported by Fukumoto et al. [47], who examined the roles of metal allergy and sweating in its development [47]. The authors conducted patch tests with metal allergens, including SnCl2, H2 PtCl6, ZnCl2, and MnCl2 which yielded positive results [47]. They also performed thermoregulatory sweat test using the starch-iodine method, which involved heat stimulation to provoke sweating [47]. Immunohistochemical staining for dermcidin confirmed sweat leakage in the subpapillary dermis within the affected area [47]. These findings suggested that a coexistence of metal allergy and sweat leakage in a hypohidrotic region may contribute to the development of unilateral lichen planus [47]. Three cases of linear lichen planus localized to the lower extremities, without accompanying mucosal lesions, were reported as early as 1996 by Sasaki et al. [48]. In two of these cases, patients exhibited a positive patch test reaction to gold (HAuCI4) and a positive lymphocyte stimulation test to gold compound (Gold sodium thiomalate), while one patient showed a positive patch test reaction to mercury (HgCI2) [48]. The study suggested that T cells responsive to metal compounds might play a role in the development of linear lichen planus [48].

Lichen planus has occasionally been linked with paraneoplastic pemphigus [49]. Bowen et al. [49] observed six patients diagnosed with paraneoplastic pemphigus, finding that lichen planus was both clinically and histopathologically evident in five of the patients. They concluded that lichenoid eruptions might predispose individuals to an early evolutionary stage of paraneoplastic pemphigus, with epitope spreading serving as a potential explanation [49].

The various types of lichen planus discussed so far, can be triggered by infections, medications, paraneoplastic syndromes, or remain idiopathic [50]. In the case of the first three trigger factors, individual susceptibility likely plays a significant role, influenced by each person's genetic predisposition and the reactivity of their immune system in response to specific stimuli [51].

Since the organism's internal homeostasis can be disrupted by the presence of exogenous antigens – whether drug-related, bacterial, or viral- clinicians should focus on identifying these antigens through various laboratory tests and thorough patient history evaluations [14]. Following the hypothesis by Tchernev G [13], infectious pathogens – specifically Escherichia coli and different periodontal pathogens [52] - could act as triggers of exogenous antigen mimicry in the early stages, potentially resulting in the heterogeneous clinical presentation of GLPLS in our case.

After conducting a thorough review of the 12 articles on PubMed, we filtered out those without available abstracts or full text access. Among the available articles, we identified one case that suggested an exogenous infectious cause potentially linked to the development of GLPLS [53]. In this case, a 48-year-old man received the HBV vaccine Recombivax (Merck-Sharp & Dohme, MSD) [53]. One to two months after the second dose, the patient developed numerous, polygonal, red, and itchy papules on the trunk, limbs, and wrists [53]. The only notable laboratory findings were the positive HBsAb and HBcAb [53]. The author suggested a possible dose-dependent response to the HBV vaccine, with lichen ruber planus being the initial sign of GLPLS [53]. A strong correlation has been observed not only with hepatitis B vaccination but also with HLA DR-1 positivity in both mother and daughter, vitamin A deficiency, hormonal dysfunction, androgen insensitivity syndrome, and neuropsychological issues [9,54].

Conclusion.

The diverse and complex clinical presentation of lichen planus and its subtypes may be influenced by the interactions among different infectious and drug-related factors, along with the immune responses they trigger. This immune response is associated with the phenomenon of molecular/ antigenic mimicry, which, although not currently measurable through specific tests, is supported by clinicopathological correlations observed in the context of these interactions.

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