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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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BULGARIAN PATIENT WITH ATROPHODERMA OF PASINI AND PIERINI- DESCRIPTION OF A CASE AND SHORT UPDATE

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Abstract.

Atrophoderma of Pasini and Pierini is a rare, considered benign, skin disease characterized by single or multiple asymptomatic atrophic plaques. Lesions can occur everywhere on the body with the trunk being the most often reported affected site. It appears in the second or third decade of life and affects mostly the female population, with male to female ratio of 1:6, commonly of white European descent.

Different risk factors were described in the literature – genetic predisposition, infections with Epstein-Barr virus, varicella zoster and Borrelia burgdorferi, vaccinations, local trauma and more. Since the pandemic with COVID-19, skin manifestations after the viral infection with COVID-19 were reported. After a thorough search of the existing medical literature, we believe, we present the first case of a rapid progression of Atrophoderma of Pasini and Pierini after COVID-19 infection.

Due to its similarity to morphea in some aspects, the condition is often misdiagnosed, and the proper treatment is often delayed. Sometimes the dilemma "Is it atrophoderma Pasini-Pierini or is it in fact morphea?" stays, but the exact histopathological verification and the "diagnostic clues" which can be used during the examination stage, are usually enough to diagnose the condition.

We present a 63-year-old female with a rapid progression of atrophoderma of Pasini and Pierini after a COVID-19 infection.

The lesion that she presented with was single, asymptomatic, with central hypopigmentation and slight atrophy, with a smooth, shiny surface and ivory color, and peripheral hyperpigmentation, measured 18x5cm, without the presence of perilesional erythema.

The patient was initially diagnosed clinically with localized scleroderma (morphea) and treated with hydroxychloroquine 200 mg once daily for a 5-year period without improvement.

Years later two biopsies from different lesional sites were taken, resulting in absence of sclerosis and dermal atrophy, but - reduction in the thickness of the dermis with fragmentation and hyalinization of collagen fibers forming a parallel orientation, dilated vascular vessels of small caliber and reduced number of skin appendages, confirming the diagnosis of atrophoderma Pasini-Pierini.

The patient's therapy was switched to methotrexate with good therapeutic response.

Often, the two conditions – morphea and atrophoderma of Pasini and Pierini can be mistaken due to its clinical similarity and sometimes coexistence. Therefore, we will shortly review the existing literature with key points on the similarities and differences.

Key words. Atrophoderma of Pasini-Pierini, morphea, COVID-19, hydroxychloroquine, methotrexate.

Introduction.

Atrophoderma of Pasini and Pierini (APP) is a rare cutaneous disease characterized by single or multiple asymptomatic atrophic plaques with violaceous to brown pigmented patches [1]. Its independent nosological entity is highly controversial among clinicians [1]. According to Amano et al. [1] APP could even coexist with the condition - morphea.

Morphea, also called localized scleroderma, is a rare autoimmune disorder characterized by inflammation and sclerosis of the skin and the subcutaneous structures [2]. Typical for the condition are the active periods of inflammation and fibrosis, followed by irreversible damage to different structures – hair loss; cutaneous, soft tissue and bone atrophy, as well as joint contractures and growth restrictions of the affected site [2].

APP sometimes may be challenging to differentiate due to its similarity to other conditions [3]. Since morphea can lead to permanent damage to the affected tissues [2], it is important to have an early diagnosis and treatment.

Different risk factors can contribute to the morphea development, with Borrelia burgdorferi infection being a real possibility [4]. Only a small percentage (26.6%) of the patients with atrophoderma of Pasini and Pierini were found positive for the Borrelia spirochete [5].

Since the pandemic with SARS-CoV-2, the COVID-19 infection has been linked to numerous systemic complications, including the largest organ in the human body – the skin [6]. A rapid progression of localized morphea to disseminated plaque-type morphea following COVID-19 infection has been reported by Rahimi et al. [6].

To our knowledge, there is not a single case in the existing literature describing the development and/or progression of atrophoderma of Pasini-Pierini after a COVID-19 infection.

Hydroxychloroquine is a medication used for morphea due to its high response rate and low adverse drug events [7].

Methotrexate and corticosteroids can be used for localized scleroderma as well [8]. Methotrexate has been reported to be an effective treatment also for APP [9].

Our aim in the article will be a thorough review of the existing literature regarding both conditions and further diagnosing our patient based on the clinical and histopathological findings– is it morphea or atrophoderma of Pasini-Pierini?.

Case report.

A 63-year-old female came to the dermatology department with primary complaints of a transient pain in the distal phalanges, accompanied by thickening of the skin in the same area. She also reports an increase in the diameter of a painless plaque, dating from 1985, in the left lumbar region of the back, diagnosed over the years as localized scleroderma and treated with hydroxychloroquine 200 mg once daily for a period of 5 years till now. She reported using local medications, each used separately for different periods of time twice daily: methylprednisolone aceponate 0.1% 30gr cream and clobetasol propionate 0.5 mg cream. According to the patient's data, in 2019 during a regular dermatological examination, the lesion was measured 16 cm x 4 cm in size, and she noticed a visible increase in the lesions diameter after a covid infection in 2022.

Several comorbidities were reported as followed: second degree arterial hypertension , ischemic heart disease – rhythmic form; condition after pericardial effusion; Hashimoto's thyroiditis; multiple disc herniations of the cervical and lumbar region, with cervical osteochondrosis and spondyloarthritic changes; peripheral vertigo; organic mood disorders; myopia, keratoglobus and astigmatism. No reported allergies.

The patient is on systemic therapy with Candesartan cilexetil 8mg administrated once at noon, Nebivolol 1,25mg once in the morning, Rosuvastatin 5mg once at noon, Acetylsalicylic acid 75mg once in the evening, Levothyroxine sodium 12,5 mg once daily, Pregabalin 75mg once in the evening, Paroxetine 10 mg in the morning, Hydroxychloroquine 200mg once in the morning and vitamin D: 8 to 10 drops a day for the concomitant diseases.

Routine laboratory tests including a complete blood test and liver function were ordered resulting without abnormalities. ANA profile subtyping was performed: 1:320 (positive), with no increase in the subfraction values, C3 (negative), C4 (negative), as well as IgM and IgG serology for Borrelia Burgdorferi (negative). The anti-dsDNA resulted as 6 (with reference range 6-10 as grey zone).

Consultations with a cardiologist, an ophthalmologist and a rheumatologist were scheduled in order to rule out a possible systemic autoimmune disease and clarify the patient's status, due to the past pericarditis, long-term systemic hydroxychloroquine intake, eye pathology and changes in the distal phalanges.

The dermatological examination showed in the left lumbar region, a single, clearly demarcated from the surrounding skin, elliptical-striped plaque with 18 cm x 5 cm in size, central - with hypopigmentation and slight atrophy, with a smooth, shiny surface and ivory color, and peripheral hyperpigmentation (Figures 1a,b). Separately, in the area of the distal phalanges, bilaterally thickened skin and subcutaneous tissue is observed, in places with limited mobility. Enlarged lymph nodes were not palpable.

Two biopsies from different parts of the lesion were taken. The first one exhibits interface scars for lichenoid dermatitis. The second one showed marked hyperkeratosis of "woven basket" type, intact epidermis, reduction in the thickness of the dermis with fragmentation and hyalinization of collagen fibers forming a parallel orientation, dilated vascular vessels of small caliber and reduced number of skin appendages (Figures 2a,b). The

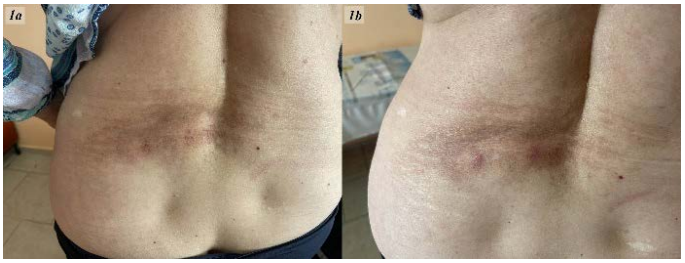

Figure 1a, b. *A single, clearly demarcated from the surrounding skin, elliptical-striped plaque with 18 cm x 5 cm in size, central - with hypopigmentation and slight atrophy, with a smooth, shiny surface and ivory color, and peripheral hyperpigmentation, located in the left lumbar region.*

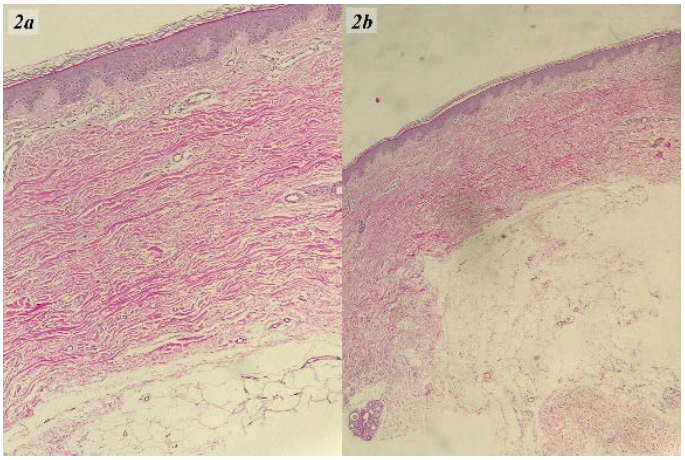

Figure 2a,b. *Marked hyperkeratosis of "woven basket" type, intact epidermis, reduction in the thickness of the dermis with fragmentation and hyalinization of collagen fibers forming a parallel orientation, dilated vascular vessels of small caliber and reduced number of skin appendages.*
2a: *Atrophic dermis with hyalinized collagen bundles and dilated small-to-medium sized vessels x HE x 100.*
2b: *Dermal atrophy with hyalinized, horizontally oriented collagen bundles x HE x 40.*

histological constellation is represented by dermal atrophy, which corresponds to atrophoderma Pasini-Pierini.

The patient was recommended serological tests for hepatitis B (HbSAg) and hepatitis C (anti HCV antibodies) before starting systemic therapy for the disease with methotrexate 15 mg weekly. A control examination every 4 weeks was recommended in order to supervise the disease and manage the dose regimen of the medications.

Discussion.

Atrophoderma is a rare skin condition first described by Pasini [10] in 1923 as "progressive idiopathic atrophoderma" and further connected to morphea by Pierini and Vivoli [11] in 1936.

Later in 1958, Canizares et al. [12] suggests "idiopathic atrophoderma Pasini – Pierini" to be acknowledged as a nosologic entity due to its differences to morphea. Results from Yokoyama et al. [13] implied that glycosaminoglycans metabolism in APP (atrophoderma of Pasini-Pierini) differs from those in morphea.

Idiopathic APP is a rare cutaneous disease, usually benign, characterized as single or multiple asymptomatic hypo- or hyperpigmented well-defined areas of depressed (atrophic) plaques, violaceous to brownish in color, and unlike morphea - without surrounding inflammation in the form of erythema [14].

The hyperpigmented atrophic lesions appear to have no definitive etiology or pathogenesis [14]. They can increase in size over the course of life [14]. Our patient first discovered her lesion in 1985 (when she was 25 years old) and over the years she noticed an increase in size. It occurs in the second or third decade of life with less than 100 cases being reported in the literature [15].

It is usually seen in white Europeans with female predominance, male-female ratio of 1:6 [15]. The lesions can be found for the first time on the trunk and with the disease progressing – later-on on the chest, arms, and abdomen [15]. According to some authors the well-defined depressed (atrophic) lesions with cliff-drop borders are a "diagnostic clue" for the disease [16].

As the name suggests, morphea or localized scleroderma, is a rare autoimmune inflammatory and sclerosing skin condition which affects the skin and the underlying subcutaneous structures [17]. The lesions can be described as active - with signs of inflammation (in the form of erythema), pain and pruritus; and as inactive – with sclerosis and atrophy involving the epidermis, dermis, and the subcutaneous structures [17].

It is primarily seen in children [18] and in women [19]. The inflammatory patches or fibrotic skin are often located on different anatomical sites – the head, neck, trunk, and upper/lower limb areas [20,21]. Despite being considered a skin-limited condition, certain subtypes can exhibit extracutaneous manifestations [21], for example fatigue, arthralgias and myalgias [22]. In some cases, the disease can progress to severe hyperpigmentation and skin atrophy, joint contractures and complications in the neuro-ophthalmological specter [21]. Positive autoantibody serologies are presented in morphea [22].

According to Wojas-Pelc et al. [23] 47% to 76% of the patients with scleroderma had antinuclear antibodies (ANA) and antibodies to the B. burgdorferi spirochete. The study included 50 patients with circumscribed sclerosis (plaque, deep linear, atrophoderma Pasini-Pierini) and the antinuclear antibodies were detected in 18% of the patients (in titer of 1:40 to 1:320) [23].

Although the patient we present had several comorbidities, including ophthalmological disorders, her laboratory tests were normal, without present antibodies to the spirochete. Her ANA profile subtyping was 1:320 (positive), with no increase in the subfraction values. This result alone could not exclude either of the conditions.

In genetically predisposed patients, certain trigger factors can contribute to the disease - different infections with Epstein-Barr virus, varicella zoster and Borrelia burgdorferi, medications, vaccinations, surgical interventions, or local trauma [21]. Our patient did not recall any certain medication intake or past event involving infection or local trauma in her adulthood.

Infection with Borrelia burgdorferi spirochete has been described as a potential triggering factor also for atrophoderma of Pasini and Pierini [24]. 38% of the patients in the study done by Buechner et al. [24] had elevated serum antibodies to B. burgdorferi. In our case presented, the IgM and IgG serology for B. burgdorferi was negative and therefore the infectious agent was ruled out as a possible disease inductor for both morphea and APP, excluding the antibiotic therapy as a possible therapeutic option.

COVID-related diseases have become a hot and interesting topic for many clinicians worldwide. Skin manifestations after a COVID-19 infection are already described in the literature -exanthematous rashes, urticarial rashes, and mucosal lesions [25]. A case presented by Lotfi et al. [25] showed a 57-year old woman with pan sclerotic morphea that rapidly progressed after a COVID-19 infection. The laboratory tests that were conducted showed high elevations in ANA, anti-ds DNA and CRP and the skin biopsy – sclerodermoid changes [25]. After a thorough search of the medical literature, we could not find any relationship between APP and Covid-19 infection. If so, this could be the first case reported in the scientific literature of a rapid progression of atrophoderma Pasini-Pierini after a Covid-19 infection.

When the clinical findings and laboratory tests are indecisive, the diagnosis is often made with the help of histopathology. Different parts from the morphea lesion are showing different histological patterns [26]. A skin biopsy taken from the erythematous border of an inflammatory lesion will present with inflammatory cell infiltrate (lymphocytes, macrophages, plasma cells, eosinophils, and mast cells) and a biopsy from the atrophic site will present with loss of the inflammatory infiltrate, less sclerosis and missing appendageal structures [26].

Three different patterns of vascular changes in morphea are described by Kobayasi et al. [27]: the first, mostly found in unaffected skin, is presented with stimulated endothelial cells and thickened vascular wall with infiltration of mast cells and macrophages; the second, found in inflammatory and sclerotic lesion sites, described with pericytes with thick basal lamina and the third pattern, found also in inflammatory and sclerotic areas, described with activated pericytes with infiltration of plasma cells and lymphocytes [27]. Activated pericytes were concluded to be the most important vascular change in morphea [27].

The different types of collagen in the cellular and fibrotic stages of localized and systemic scleroderma were studied by Fleischmajer et al. [28]. The cellular stage is presented by perivascular or diffuse cellular infiltration consisting mainly of lymphocytes, plasma cells and macrophages and type III collagen (which can be seen also in the lower dermis) [28]. In the fibrotic stage, the type III collagen in the papillary layer can be reduced or agglutinated in contrast to the normal skin's architecture [28].Compact collagen consisting of type I or of type I&III collagen, can be seen in the adipose tissue or the lower dermis [28]. Collagen bundles surrounding the eccrine glands and blood vessels can be seen extending into the reticular dermis in older sclerotic morphea lesions [29].

In APP, a decrease in thickness of the dermis and absence of sclerosis can be found with additional interstitial edema, mild perivascular infiltrate and normal-looking sweat glands and skin appendages [30,31]. Macrophages and lymphocytes were present around vessels and in the dermis – between the fibers [32]. Although the presence of inflammatory infiltrate has been

described in both conditions (morphea and APP), the absence of inflammation in our histology might be due to the years of local therapy with clobetasol propionate and long-standing systemic immunosuppressive therapy with hydroxychloroquine. The atrophic appearance of the lesions results from changes in the organization of collagen and elastic fibers and not from the tissue content [31]. The same study concluded that horizontal collagen fiber organization in the lesional biopsy was increased in the lower dermis and the elastic fibers had greater disorganization in the upper dermis [31]. Normal to severe reduction and fragmentation of elastic fibers were described by Saleh et al [33]. Dermal atrophy with hyalinized, horizontally-oriented collagen bundles were present in our patient' biopsy (Figure 2b).

Patients presenting with asymptomatic atrophic skin lesions should be considered on the differential diagnosis with atrophoderma Pasini-Pierini [30]. Clinical features and tissue biopsy can help differentiate the condition from morphea and other skin diseases [30]. Taking into consideration the given information above and the histological constellation made in our case report, a diagnosis of Atrophoderma Pasini-Pierini was made.

In terms of treatment options, hydroxychloroquine is a great option for plaque morphea with high response rate and low adverse drug events [7]. The medication is a first-line drug option for many rheumatologic and/or dermatologic conditions [34]. During the COVID-19 pandemic it was also used for the treatment of viral infection due to its immunomodulatory, anti-inflammatory, antibacterial and antiviral properties [34]. The retrospective study performed by Kumar et al. [7] showed complete response greater than 40% and partial response rate of nearly 50% to the drug [34]. The patient presented to us was diagnosed over the years as localized scleroderma and treated with hydroxychloroquine 200 mg once daily for a period of 5 years till the second consultation was made.

Lupus-associated APP can be also treated with a hydroxychloroquine [35].

In the case of Lyme disease (infection with Borrelia burgdorferi spirochete), antibiotics can be optioned for a treatment [24]. Topical and systemic steroids, antimalarials, antibiotics and phototherapy can be found effective for the atrophoderma Pasini-Pierini treatment [36]. Clinical improvement of hyperpigmentation can be seen with the Q-switched alexandrite laser [37].

Methotrexate is a widely used medication in the dermatology field due to its antiproliferative and anti-inflammatory properties [38].

Morphea can also be treated with methotrexate [39]. It is considered a drug with overall mild and reversible drug adverse events [39]. Positive response to methotrexate was found in patients with APP after 3 months of initial therapy with the drug [16]. She was initiated with methotrexate at a dose of 20 mg/wk and topical treatments for her psoriatic areas on the body [16]. Major improvements in the atrophic skin sites on her back and shoulders were administrated [16].

Conclusions.

Atrophoderma of Pasini and Pierini (APP) is a rare cutaneous condition which alters the collagen organization in the dermal layer of the skin resulting in depressed (atrophic) changes. APP can sometimes exhibit similar characteristics to other skin conditions, such as morphea.

Thorough clinical examination followed by histopathological verification has proven its efficiency during the diagnostic stages of the disease.

Several key points in the case report were crucial for the diagnosis of atrophoderma of Pasini and Pierini:

1) The patient was presented with a single asymptomatic plaque characterized by central hypopigmentation and slight atrophy, with a smooth, shiny surface and ivory color, and peripheral hyperpigmentation.

2) Surrounding inflammation in the form of erythema was not observed, unlike in morphea lesions. However, the absence of inflammation in our histology might be due to the years of local therapy with clobetasol propionate and immunosuppressive systemic therapy with hydroxychloroquine.

3) Absence of sclerosis and dermal atrophy with hyalinized, horizontally oriented collagen bundles, which are specific for atrophoderma of Pasini and Pierini.

It is important to differentiate the disease since the therapeutic approach may sometimes be different even for similar skin conditions. Choosing the right therapy for every patient must be a number one priority for not only every dermatologist but also for every clinician. In such cases, when the clinical picture is very similar, a drug of choice for both morphea and APP can be methotrexate.

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