

Heterogeneity of clinical manifestations and morphological features of cutaneous mucinosis: clinical cases

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation; D – writing the article; E – critical revision of the article; F – final approval of the article

The aim of this work is to describe clinical cases of primary mucinosis, considering their clinical and morphological heterogeneity.

Materials and methods. Examination of both patients was carried out according to an identical diagnostic algorithm: visual assessment of lesions – morphological diagnostics. An analysis of the clinical manifestations of dermatoses was performed at the Department of Dermatovenereology and Aesthetic Medicine, Zaporizhzhia State Medical and Pharmaceutical University. Final verification of the diagnosis was determined by morphological assessment of the skin biopsy.

Results. Patient 1: a man born in 1961, 6 months ago, first noticed single elements of a rash on the skin of the back and chest, which were almost not accompanied by subjective discomfort. At the time of examination, a papular rash of pink color is visualized on the skin of the décolleté zone, upper and middle third of the back, which in places forms a reticular-polycyclic pattern. However, when palpating individual morphological elements, local marginal indurative areas are noted on the periphery. According to the result of morphological diagnosis, the diagnosis is inserted: reticular erythematous mucinosis. Patient 2: a woman born in 1964 complained of a rash on the skin of the face and hands, which was not accompanied by itching or pain. Objectively: on the skin of the back surface of both hands, there are multiple papules of waxy color and consistency upon palpation, up to 0.2–0.3 cm in diameter with a tendency to group and, in part, merge. At the same time, the linearity of the configuration of these efflorescences is noteworthy. The skin of the forehead presents identical morphological elements, but a more pronounced density of both the affected and visually healthy skin is noted. Due to the formation of induration and deep wrinkles, the face takes on the appearance of a "lion's mask". Within the earlobes and partly the auricle, the rash is similar in appearance and palpatory sensations of compaction. Considering clinical and morphological correlation, it is possible to verify primary mucinosis, with the clinical and morphological pattern of scleromyxedema.

Conclusions. Familiarization of practicing specialists with the clinical manifestations and morphological features of cutaneous mucinosis is necessary for timely diagnosis and avoidance of erroneous interpretation and choice of treatment tactics for these rare but clinically variable dermatoses.

Keywords:

clinical manifestations, morphological diagnostic, mucinosis, reticular erythematous mucinosis, scleromyxedema.

Pathologia.

2026;23(2):161-167

Гетерогенність клінічних проявів і морфологічні особливості шкірних муцинозів: клінічні випадки

Г. І. Макуріна, Л. О. Городокіна

Мета роботи – опис клінічних випадків первинних муцинозів, враховуючи їхню клінічну та морфологічну гетерогенність.

Матеріали і методи. Обох пацієнтів обстежили за ідентичним діагностичним алгоритмом: візуальне оцінювання уражень – морфологічна діагностика. Аналіз клінічних проявів дерматозів проведено на базі кафедри дерматовенерології та естетичної медицини Запорізького державного медико-фармацевтичного університету. Остаточна верифікація діагнозу здійснена на підставі морфологічного оцінювання біоптату шкіри.

Результати. Пацієнт 1 – чоловік 1961 року народження, який 6 місяців тому вперше помітив поодинокі елементи висипу на шкірі спини та грудей, що майже не супроводжувались суб'єктивним дискомфортом. Під час огляду виявлено: на шкірі зони декольте, верхньої та середньої третини спини візуалізується папульозна висипка рожевого кольору, що місяцями формує ретикулярно-поліциклічний патерн. Проте при пальпації окремих морфологічних елементів по периферії визначено локальні крайові індуративні ділянки. За результатом морфологічної діагностики встановлено діагноз: ретикулярний еритематозний муциноз. Пацієнтка 2 – жінка 1964 року народження, котра звернулася зі скаргами на висип на шкірі обличчя та кистей, що не супроводжувався свербіжем чи больовими відчуттями. Об'єктивно: на шкірі тильної поверхні обох кистей множинні папули воскоподібного кольору та консистенції при пальпації, до 0,2–0,3 см у діаметрі з тенденцією до групування та, частково, злиття. Привертала увагу лінійність конфігурації цих ефлорисценцій. На шкірі чола – ідентичні морфологічні елементи, але визначено більш виражену щільність і ураженої, і візуально здорової шкіри. Внаслідок формування індурації та глибоких зморшок обличчя набуває вигляду так званої левиної маски. У межах мочок вух і почасти вушної раковини висип аналогічний за виглядом і пальпаторним відчуттям ущільнення. Враховуючи клініко-морфологічну кореляцію, можлива верифікація первинного муцинозу з клініко-морфологічним патерном склеромікседеми.

Висновки. Ознайомлення спеціалістів-практиків із клінічними проявами та морфологічними особливостями шкірних муцинозів необхідне для своєчасної діагностики та уникнення помилкової інтерпретації, вибору оптимальної тактики терапії цих рідкісних, але клінічно варіабельних дерматозів.

Ключові слова:

клінічні прояви, морфологічна діагностика, муцинози, ретикулярний еритематозний муциноз, склеромікседема.

Патологія. 2026.

Т. 23, № 2(67).
С. 161-167

Cutaneous mucinoses belong to a group of dermatoses that, unfortunately, receive insufficient attention from practicing clinicians in the differential diagnostic context. First of all, this is due to their nosological heterogeneity, and secondly, such a conceptual gap arises against the background of a lack of understanding of the pathogenetic mechanisms of the formation of this group of dermatoses. The key morphological basis for mucinosis is the direct deposition of excessive amounts of glycosaminoglycans in the skin. The latter are represented by a high-molecular glycoprotein complex based on hyaluronic acid, dermatan sulfate, heparan sulfate, etc. [1,2].

Potential mechanisms that stimulate fibroblasts to actively synthesize these substances include both immune dysregulation with excessive cytokine production (TGF- β , IL-1, TNF- α) and the overall impact of autoimmune compromise in systemic diseases [3,4]. The results of the work obtained by a group of researchers led by S. Steinmann et al. indicate that the synthesis of dermal and follicular epithelial mucin involves different cell types, with CD8+ lymphocytes playing a particularly important role in the formation of follicular epithelial mucin [5]. In turn, differences in the composition of mucin and the nature of its deposition form a significant clinical diversity of this group of dermatoses. In this regard, there is a need to further streamline diagnostic approaches to skin lesions caused by excessive mucin deposition.

The generally accepted classification divides mucinoses into primary and secondary forms depending on the etiopathogenetic basis of glycosaminoglycan deposition. In primary mucinoses, the spontaneous formation of mucin in the skin is the key factor driving the development of dermatosis and, accordingly, its characteristic clinical presentation. In contrast, secondary forms are associated with underlying pathological conditions in which mucin deposition occurs as a consequence or as a kind of epiphenomenon.

Within primary mucinosis, there is a division into degenerative-inflammatory and hamartomatous-neoplastic forms. In degenerative-inflammatory lesions, the emphasis is dichotomously set on the involvement of the dermal and follicular components. In general, the group of primary cutaneous mucinosis includes several nosological entities, including scleromyxedema, localized variants of myxedematous lichen, self-healing cutaneous mucinosis, reticular erythematous mucinosis, angiomyxoma, and others [3]. Such diversity of clinical forms results in a wide spectrum of their external manifestations: primary mucinoses may present as either localized or generalized lesions. At the same time, M. Ghaleb et al. described a case of dermal mucin deposition with the formation of efflorescences even along the lines of Blaschko [4].

The accumulation of glycosaminoglycans in the skin as a concomitant pathological process can be considered both in the context of neoplasia, endocrinopathies, collagenoses, and in the case of skin reactions after taking drugs. For example, C. Dallo et al. demonstrate a case of papulonodular mucinosis in a patient with systemic lupus erythematosus [6].

While the experience of G. Verma et al. indicates the possibility of the debut of focal nodular mucinosis due

to trauma, which acts as a reactive trigger of fibroblast dysfunction [7].

The relationship between pharmacological agents and mucin deposition requires special attention. According to the available pool of scientific data, cases of skin changes have been described with the use of TNF inhibitors, which hypothetically can activate fibroblasts to produce mucin through an indirect effect [8,9,10]. The case presented by X. Zhou et al. demonstrates the occurrence of generalized cutaneous mucinosis in the setting of psoriasis and treatment with ustekinumab [10].

Thus, even in the presence of a common morphological substrate in the form of mucin and its excessive deposition, the initiating factors, clinical manifestations of mucinosis, and their systematization remain heterogeneous and are determined by the individual characteristics of each individual case. It is this variability that forms a certain "halo of mystery" in the process of their diagnosis. Despite the rarity of registration of these dermatoses, practicing physicians should consider the possibility of patients developing both primary and secondary mucinoses and, if necessary, include them in the list of differential diagnostic search.

Aim

The aim of this work is to describe clinical cases of reticular erythematous mucinosis and scleromyxedema, as representatives of a single nosological group of primary mucinoses, taking into account their clinical and morphological heterogeneity.

Materials and methods

Examination of both patients was carried out according to an identical diagnostic algorithm: visual assessment of lesions, pathomorphological diagnostics. Thus, the analysis of clinical manifestations of dermatoses was performed at the Department of Dermatovenereology and Aesthetic Medicine of the Zaporizhzhia State Medical and Pharmaceutical University; the final verification of the diagnosis was determined by morphological assessment of the skin biopsy.

A 5-mm punch biopsy was performed. The material was immediately placed in 10 % buffered formalin (pH 7.4), followed by fixation for 24 hours, preparation of paraffin blocks, sections 4 μ m thick. Determination of histological patterns of dermatosis was performed by evaluating sections stained with hematoxylin and eosin and colloidal iron. To increase the accuracy of the diagnosis in one of the presented cases, an additional immunohistochemical study was performed to determine the expression of antibodies to vimentin.

This work was performed in accordance with the moral and ethical standards of IGH/GCP, the Declaration of Helsinki (1964 with amendments), the Council of Europe Convention on Human Rights and Biomedicine and the legislation of Ukraine. The study was approved by the Bioethics Commission of the Zaporizhzhia State Medical and Pharmaceutical University (protocol No. 6 dated 16.04.2026).

Results

Clinical case 1. A man born in 1961 first noticed single elements of a rash on the skin of his back and chest 6 months ago, which were almost not accompanied by subjective discomfort. According to the patient, he sometimes noted the presence of itching of minor intensity, but, in general, this did not affect everyday functioning. The patient does not associate the manifestation of this pathological process with any influence of exogenous or endogenous factors, because household and eating habits are unchanged, and there are no occupational hazards. The patient is somatically compensated and is not under the care of any specialist.

The appearance of the first efflorescences prompted him to seek medical attention from a primary care physician, who established a diagnosis of “eczema” and initiated treatment according to established standards of care. As a result of the therapy, which included systemic antihistamines, desensitizing agents, detoxification measures, and topical corticosteroids, the patient experienced a favorable clinical response. This was reflected both in the outpatient medical records as a partial regression of the cutaneous pathological process and, according to the patient, in positive feedback regarding the effectiveness of the treatment regimen.

However, the improvement observed after the first course of therapy was not sustained; therefore, a flare-up of the skin process was noted within several weeks. Gradually, over 4 months, the rash became widespread without a clinically significant response to a repeat treatment regimen similar to the first course. Given the progressive nature of the eruption and the lack of response to prior therapy, the patient was referred for consultation to a secondary care specialist – a dermatovenerologist. At the time of examination, a pink papular rash is visualized on the skin of the décolleté area, upper and middle third of the back, which in places forms a reticular-polycyclic pattern (Fig. 1). When palpating individual morphological elements, local marginal indurative areas are noted on the periphery.

At the same time, there are no signs of atrophy, hyperkeratosis and scarring. Laboratory tests (complete blood count, urine, liver tests) are within the reference values both at the initial examination and in the dynamics over the following months. Taking into account the anamnestic data and clinical manifestations, visual assessment of dermatosis contributes to the formation of only a list of potential nosologies, including erythema migrans, granuloma annulare, erythema annulare, photodermatitis, and even lupus erythematosus.

Therefore, histological evaluation of this pathological process has become key to the final determination of the nature of the skin lesion and is presented as follows: epidermis with orthokeratosis and focal hyperpigmentation of basal keratinocytes. In the superficial and deep parts of the dermis, a dense perivascular lymphohistiocytic infiltrate with an admixture of single eosinophils is determined. Also, in the dermis, there are signs of solar elastosis. When performing additional multiple sections from the paraffin block, the histological picture did not change. Periodic acid – Schiff (PAS) staining showed no thickening of the basement membrane. Grocott staining



Fig. 1. Clinical manifestations of dermatosis on the skin of the back in the form of pink papules that, when merged, form polycyclic outlines.

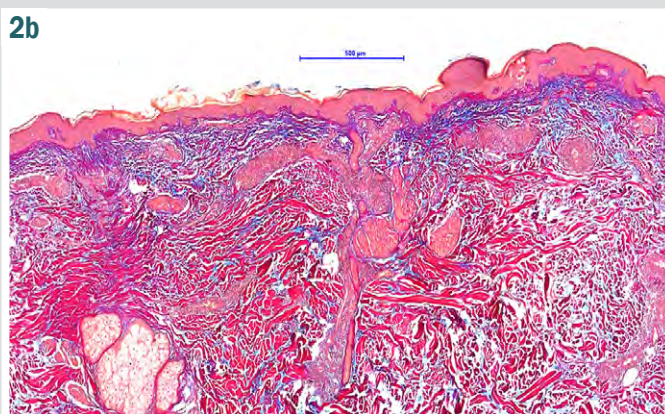
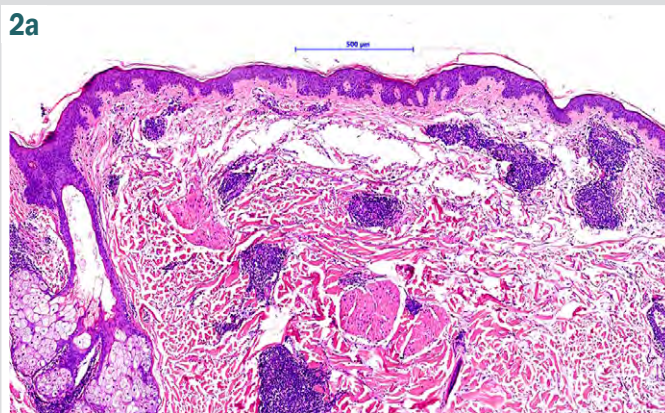


Fig. 2. Morphological features of reticular erythematous mucinosis.
a: H & E, mag. $\times 50$; b: Coll. Fe, mag. $\times 50$.



Fig. 3. Skin lesions within the forehead and hands in the form of multiple dense papules of white-light pink color with a waxy texture, and deep wrinkles in the area between the eyebrows.

revealed no fungal elements. When stained with colloidal ferum, accumulation of mucin is observed between the collagen fibers.

This morphological picture allows us to attribute dermatitis to the perivascular group (superficial and deep perivascular dermatitis) and, taking into account the clinical manifestations of the disease, most closely corresponds to reticular erythematous mucinosis (Fig. 2).

Clinical case 2. A woman born in 1964 complained of a rash on the skin of her face and hands, which was not accompanied by itching or pain. The gradual dynamics of the spread of efflorescences were noted: from single ones only within the extensor surface of the hands to their appearance on the skin of the forehead, earlobes. In addition to the rash, the patient constantly paid attention to changes in facial features. Thus, comparing the patient's photo a year ago, the formation of deep longitudinal wrinkles in the interbrow area, as well as edema of the upper third of the face, which leads to a decrease in the mobility of the facial muscles, is observed.

Regarding the cutaneous lesions, the patient had not previously sought medical attention, and this consultation represents the first clinical encounter. The allergy history is unremarkable, and she denies exposure to any triggering factors. No dermatological diseases are documented in the medical record or identified based on the obtained anamnesis. The patient also denies any history of travel abroad, particularly to tropical regions. Over the past five years, the patient has had stage II, grade 2 hypertension, which is pharmacologically compensated.

Objectively: multiple waxy-colored papules of firm consistency on palpation are present on the dorsal surfaces of both hands, measuring up to 0.2–0.3 cm in diameter, with a tendency to group and partial coalescence. Notably, a linear configuration of these efflorescences is observed. The skin of the forehead presents identical morphological elements, but there is a more pronounced density of both the affected and the visually healthy skin. Due to the formation of induration and deep wrinkles, the face takes on

the appearance of a “lion mask”. Within the earlobes and partially the auricles, the rash is similar in appearance and palpatory feeling of compaction. Changes in the mucous membranes are not detected during visual examinations.

The phenomena of self-regression of efflorescences during the observation period were not recorded. The presence of the above-mentioned clinical manifestations in the form of indurative papular changes, edema, and deformation of facial features primarily requires confirmation or exclusion of autoimmune diseases of the connective tissue, in particular scleroderma.

During morphological evaluation of the biopsy, a slight atrophy of the epidermis, thickening of the dermis due to fibrosis with compaction, and thickening of collagen bundles are determined. In the superficial and deep parts of the dermis, a slight perivascular lymphohistiocytic infiltrate is determined. In the examined material, within the dermis and during differential diagnosis using additional histochemical methods, congo red staining showed a negative reaction, and gentian violet staining was also negative. On PAS-AB staining, a positive reaction was detected, manifested as mucin deposition. On immunohistochemical examination with anti-Vimentin antibodies, strong cytoplasmic expression was detected in dermal fibroblasts (more than 85 % around the foci of mucinous deposition). The obtained data, considering the clinical manifestations of dermatosis, do not exclude the presence of cutaneous scleromyxedema.

Discussion

Pathological processes on the skin in both patients presented in this work belong to the group of primary mucinoses. But despite belonging to the same nosological category, the clinical manifestations are not homogeneous and demonstrate individual features both in the nature of efflorescences and in the pattern of their distribution on the skin. Therefore, we will consider each individual case in more detail.

Reticular erythematous mucinosis (REM) is a relatively rare nosological entity, which is confirmed by the absence of a clearly established population-based prevalence of this dermatosis. According to approximate estimates reported in the scientific literature, approximately 100 cases of this dermatosis have been documented in total [11]. REM can occur in individuals of either gender, but there is a female predominance [12,13]. In the clinical case presented by the authors, a male patient is described. Identification of the provoking factor for this dermatosis is significantly complicated and often remains uncertain. Possible trigger factors include ultraviolet radiation, hormonal changes, immunological dysregulation, or previous infections [12,14].

Thus, D. Tenea et al. described a case of REM occurrence in a woman with verified HIV infection [11]. In our patient's case, REM appears to have an idiopathic basis, as no potential triggering factors could be identified. From the available anamnestic data and the medical information system, it is known that the patient has no facts about prolonged exposure to the open air, harmful habits, or the presence of chronic diseases. During laboratory examination, the indicators of general clinical tests (blood and urine), biochemical indicators of liver and kidney function, examination for hepatitis, and HIV infection did not reveal any changes.

Analyzing the clinical picture from case 1, the appearance of a symmetrical rash on the skin of the chest and back in the form of erythematous-papular efflorescences, forming a reticular pattern in places, really corresponds to the manifestations of REM. However, the density on the periphery, the appearance on exposed areas of the body, and the partial clinical response to rather non-specific therapy require differential diagnosis. This, in turn, indicates a high level of clinical mimicry of this diagnosis and the need to exclude various nosologies, from granuloma annulare to mycosis fungoides. Special attention is required to differentiate it from lupus erythematosus. Despite the absence of atrophy and hyperkeratosis typical of discoid changes in our patient, lupus tumidus may still demonstrate certain clinical and morphological similarities [15,16,17].

To confirm such multivectorality in differentiation and clinical imitation, we can also cite a clinical case presented by B. Kenny et al. regarding an atypical manifestation of REM, which was clinically assessed as cutaneous larva migrans [13].

Thus, given the gender characteristics, atypical disease course, and clinical manifestations with high potential for visual mimicry, the management of the patient from the first case necessitated a clear correlation between clinical symptoms and morphological changes.

Scleromyxedema, despite the fact that it also belongs to the group of primary mucinosis in the form of diffuse myxedematous changes, is characterized by a more persistent, severe course with potential damage to various organs and systems, even with a possible fatal outcome [18,19]. This condition usually debuts in middle-aged people; according to some authors, the average age of registration of scleromyxedema is 59 years [19,20]. At the time of dermatological consultation, the patient

from case 2 was 60 years old, which corresponds to the characteristics of a typical onset of the pathological process. Scleromyxedema is a condition characterized by the following diagnostic triad: diffuse / generalized papular and scleroderma-like skin involvement, specific histological features in the form of mucin deposition, fibrosis, and fibroblast proliferation, as well as monoclonal gammopathy [19].

In our own described case, the patient has dense waxy papules on the hands and face, ears, edema, skin density, formation of folds on the forehead, with a tendency to facial expression disorders, as well as morphologically verified changes. The presence of efflorescences with dense infiltrate, edema primarily prompts the clinician to think about scleroderma-like changes; however, as the last case demonstrates, this may be a condition associated with mucinous deposition as well [21,22]. At the time of examination, there were no complaints about the patient's general condition, and the examination by specialists of the therapeutic profile, except for hypertension, did not reveal any changes. The indicators of general clinical and biochemical examinations were within the age norm. It should be noted that no structural or functional changes of the thyroid gland were identified. The patient was informed of the necessity to exclude or confirm monoclonal gammopathy and received a referral for consultation with an oncohematologist.

However, the described clinical case occurred prior to the full-scale invasion, specifically in February 2022, and the patient was subsequently lost to follow-up, making it impossible to determine her further diagnostic and therapeutic trajectory regarding the concomitant hematological diagnosis.

Therefore, in this case, precise nosological categorization is considerably challenging: according to certain studies, scleromyxedema in its classical sense is associated with paraproteinemias, whereas this form of mucinosis may also occur without the aforementioned concomitant changes. In the latter case, this may correspond to the manifestations of atypical lichen myxedematosus, which is likewise characterized by papular skin eruptions with a tendency toward widespread sclerosis, development of restricted facial mimetic mobility, and specific histological changes [19,23,24].

Since the presence or absence of gammopathy is a key diagnostic criterion for classical scleromyxedema, the cutaneous changes observed in our patient may be attributed either to her early presentation and the initial stages of this chronic and potentially protracted pathological process, or to the manifestation of atypical scleromyxedematous changes. Given the inability to definitively differentiate between these conditions, it was decided in this clinical situation to retain a generalized diagnostic definition of primary mucinosis, emphasizing the presence of a characteristic clinical and morphological pattern inherent to scleromyxedema.

That is why, even after morphological evaluation of the skin biopsy, in each individual case of dermatosis suspected of mucinosis, an interdisciplinary and comprehensive algorithm is important: visual assessment, histological picture – analysis of the comorbid background.

Conclusions

1. Primary mucinoses are characterized by significant clinical variability, which necessitates a broad differential diagnostic approach. In the case of reticular erythematous mucinosis, key mimicking conditions include both forms of lupus erythematosus and dermatoses with a polycyclic pattern, while scleromyxedema is primarily associated with scleroderma-like features of lesions.

2. Morphological correlation is crucial for the diagnosis of primary mucinosis, since it is the comparison of clinical manifestations with histological changes that allows for a correct diagnostic algorithm.

3. Familiarization of practicing specialists with the clinical manifestations and morphological features of cutaneous mucinoses is necessary for timely diagnosis and avoidance of erroneous interpretation and choice of treatment tactics for these rare but clinically variable dermatoses.

AI statement

The following artificial intelligence tool was used in the preparation of this manuscript: Gemini 3.5 Flash. It was used for language editing and translation. All AI-generated or AI-assisted content was carefully reviewed and edited by the authors, who assume full responsibility for the content of the manuscript.

Funding

The description of this clinical case is a fragment of the research project of the Zaporizhzhia State Medical and Pharmaceutical University: "Development of personalized approaches to the treatment of inflammatory dermatoses, hair diseases, STIs, and correction of age-related skin changes, taking into account comorbid pathology, aesthetic, and psychopathological factors", state registration 0124U003220 (2024–2029).

Conflicts of interest: authors have no conflict of interest to declare.
Конфлікт інтересів: відсутній.

Надійшла до редакції / Received: 08.05.2026

Після доопрацювання / Revised: 13.07.2026

Схвалено до друку / Accepted: 23.07.2026

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