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M. E. Zapolskiy https://orcid.org/0000-0001-9284-3539
M. M. Lebediuk https://orcid.org/0000-0001-5674-0196
V. I. Khrushch https://orcid.org/0000-0002-4346-5145
L. M. Tymofieieva https://orcid.org/0000-0002-8708-9460

FOLLICULAR MUCINOSIS CASE IN PATIENT WITH ATOPIC DERMATITIS

Odesa National Medical University, Odesa, Ukraine

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M. E. Zapolskiy, M. M. Lebediuk, V. I. Khrushch, L. M. Tymofieieva
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Follicular mucinosis (scleromyxoedema) is a rare skin disease characterized by follicular degeneration due to the accumulation of mucin in the pilosebaceous unit accompanied with inflammatory changes.

The purpose is to evaluate risk factors for the likelihood of secondary follicular mucinosis.

Materials and methods. Cytomorphology of the patient's skin samples (stains were used: hematoxylin-eosin, toluidine blue, Van Gieson's picrofuchsin).

Results. An observation of a clinical case of secondary follicular mucinosis of the skin, formed against the background of atopic dermatitis and the use of fillers with hyaluronic acid, is presented. The skin lesions of a 33-year-old female patient demonstrate clear clinical and histological features of follicular mucinosis. In the absence of standardized methods for treating this nosology, successful pathogenetic therapy was carried out: dapsone, tacrolimus, phototherapy (UVB 311nm), which led to almost complete regression of the pathological process.

Conclusions. Timely diagnosis, pathogenetic treatment and control of the main disease reduce the risk of skin mucinosis recurrence and improve its long-term prognosis.

Key words: follicular mucinosis, mucin, atopic dermatitis.

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М. Е. Запольський, М. М. Лебедюк, В. І. Хрущ, Л. М. Тимофєєва
ВИПАДОК ФОЛІКУЛЯРНОГО МУЦИНОЗУ У ХВОРОЇ НА АТОПІЧНИЙ ДЕРМАТИТ
Одеський національний медичний університет, Одеса, Україна

Мета дослідження – оцінити фактори ризику розвитку вторинного фолікулярного муцинозу. Наведено спостереження клінічного випадку вторинного фолікулярного муцинозу шкіри, що утворився на тлі атопічного дерматиту та використання філерів з гіалуроновою кислотою. В умовах відсутності стандартизованих методів лікування цієї нозології було проведено успішну патогенетичну терапію з призначенням дапсону, такролімусу, фототерапії, що призвело до практично повного регресу патологічного процесу.

Висновки. Своєчасна діагностика, патогенетичне лікування та контроль основного захворювання дозволяють знизити ризики рецидивів муцинозу шкіри та покращити його віддалений прогноз.

Ключові слова: фолікулярний муциноз, муцин, атопічний дерматит.

Mucinoses (scleromyxoedema) are a heterogeneous group of diseases characterized by mucin deposition in the connective tissue of the dermis (skin mucinoses), hair follicles (follicular mucinoses), or in the epidermis and tumours originating from it (epithelial mucinoses) [1]. Mucins are high molecular weight glycoproteins. The glycosylated part of the stromal mucins is represented by glycosaminoglycans, the main of which are hyaluronic acid, chondroitin sulfate, dermatan sulfate, keratin sulfate and heparansulfate [2].

Mucin is a component of extracellular matrix and is produced by fibroblasts [3]. The reason why its abnormal deposition in the skin occurs is still not clear [4]. In case of primary mucinosis, the deposition of mucin is the main in the histological pattern of the disease; in case of secondary mucinosis, the deposition of mucin is considered as an additional sign against the background of other skin diseases [5; 6].

Both primary and secondary follicular mucinosis of the skin is a rare group of diseases, accompanied by the deposition of mucin in the hair follicles and epidermal-dermal regions. Pathology is manifested by follicular papules or coalesced plaques with enlarged skin pores, increased skin tightness, and impaired hair growth in the affected areas [7].

Follicular mucinosis (FM) was first described by Pinkus in 1957 as an alopecia caused by the degeneration of follicles due to the accumulation of mucin around the outer lining of the hair and sebaceous glands along with a pronounced infiltration of follicles by inflammatory cells [8].

The etiopathogenesis of the disease is not studied sufficiently. Thus, it has been suggested that FM is caused by cellular changes in the affected structures leading to the production of mucin [9]. In addition, the role of circulating immune complexes and cellular immunity, including response to persistent antigens such as Staphylococcus aureus in FM pathogenesis, was considered [10].

FM is manifested in the form of single or multiple clearly defined erythematous plaques with raised edges above the skin level, with scales, follicular papules, or foci of alopecia forming on their surface. In some cases, clinical manifestations are atypical, have a coalesced nature; there are reports of nodal forms of FM that mimic folliculitis, focal alopecia, scarring alopecia, chronic eczema, acne, and urticaria [9].

Histologically, there is an accumulation of mucin in the outer membrane of the root of the hair follicle and in the sebaceous glands, an inflammatory infiltrate consisting of lymphocytes, macrophages, and eosinophils with lymphocyte tropism to the follicle [6; 11].

The literature describes cases of secondary mucinosis development along with various diseases, in particular, systemic lupus erythematosus [12; 13; 14], eosinophilic folliculitis [15], dermatomyositis [11], acne, and seborrheic dermatitis [15].

Purpose – to analyse the clinical and morphological features of a rare case of a combined course of atopic dermatitis and skin mucinosis on the background of long-term use of topical corticosteroids and the use of hyaluronic acid fillers.

Materials and methods. The case of secondary follicular mucinosis of the skin in a 33-year-old patient was described. A secondary follicular mucinosis was formed against a background of atopic dermatitis and the use of fillers with hyaluronic acid.

Skin lesions with clear clinical and histological signs of FM. Cytomorphological examination of skin samples of patients was performed using haematoxylin-eosin, toluidine blue, Van Gieson's picrofuchsin.

Pathogenetic therapy using dapsone, tacrolimus, phototherapy (UVB 311nm) was conducted. The patient provided informed consent for the examination, treatment and interpretation of the results of the clinical study.

Study results. We present a rare case of secondary follicular mucinosis of the skin, which developed against the background of atopic dermatitis and use of fillers with hyaluronic acid.

A 33-year-old patient came to our clinic with complaints of itchy rashes on the skin of the face, which had been bothering her for 10 months (Fig. 1 A, B). According to the patient, her first rashes appeared in the form of small nodules on the skin of the cheeks after using fillers with hyaluronic acid. Subsequently, the rashes acquired a coalesced nature and spread to the entire face; there is an increase in tightness, periodic itching, and burning sensation. The patient has been suffering from atopic dermatitis for 20 years. Exacerbations of atopic dermatitis were observed mainly in the spring–summer period. The cause of exacerbations was contact with household chemicals and inhalation of pollen of plants. During specific allergic tests, major allergens were identified: birch and ragweed pollen, provoking seasonally atopic dermatitis. The patient refused allergen-specific immunotherapy. According to the family history, her mother has a food allergy and eczema of the hands. The patient denies having other allergic, chronic somatic diseases.

The patient was treated on her own and functional specialists (dermatologist, allergist) repeatedly. She treated her face with emollients and periodically used topical cortico-

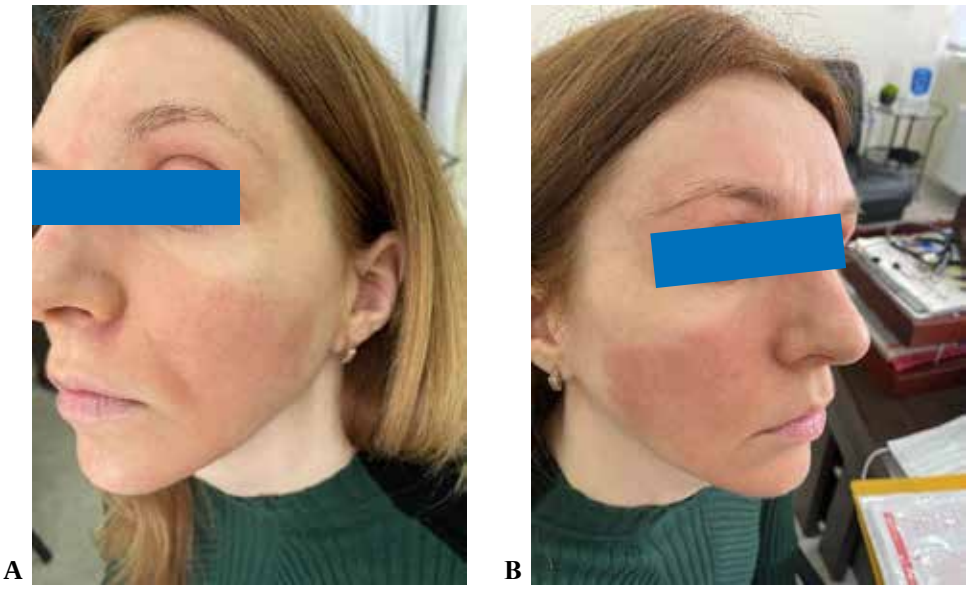


Fig. 1. Clinical manifestations of secondary follicular mucinosis of the skin in the face: persistent erythema, skin induration, enlargement of the skin pores, clear boundaries of the skin induration, small follicular papules are visible here and there. A – on the left side of the face, B – on the right side of the face

steroids with a short-term positive effect. For an aesthetic purpose, stabilized hyaluronic acid was injected several times in the affected areas, which, according to the patient, deteriorated her condition and increased skin tightness. Five months before coming to our clinic, the patient noted an increase in skin density, as well as a feeling of tissue compression in the foci of the disease.

Status localis. Visual examination showed hyperaemia, coalesced infiltrated pink papules, having a uniform density throughout the affected area, on the skin of her cheeks, nose, and chin, enlarged skin pores and slight flakiness on the surface of the damaged skin. Lanugo hairs are absent or feebly marked in the affected areas. In the periorbital region, additional skin folds and pronounced xerosis are visible. Regional lymph nodes are not enlarged, soft, freely movable, not matted together and in relation to surrounding tissues. In the cheek area, the boundaries of the skin induration are clearly defined, and a brown tint is visible above the affected areas. There is an increase in skin tightness when the affected areas are palpated, sensitivity is not impaired. The skin beyond the affect: moderate lichenification, isolated excoriations, and postatopic leukoderma remain on the skin of the flexural surfaces of the upper and lower extremities. Dermographism is white and persistent.

Preliminary diagnosis: Atopic dermatitis? Skin lymphoma?

For the purpose of differential diagnosis, a number of examinations were carried out:

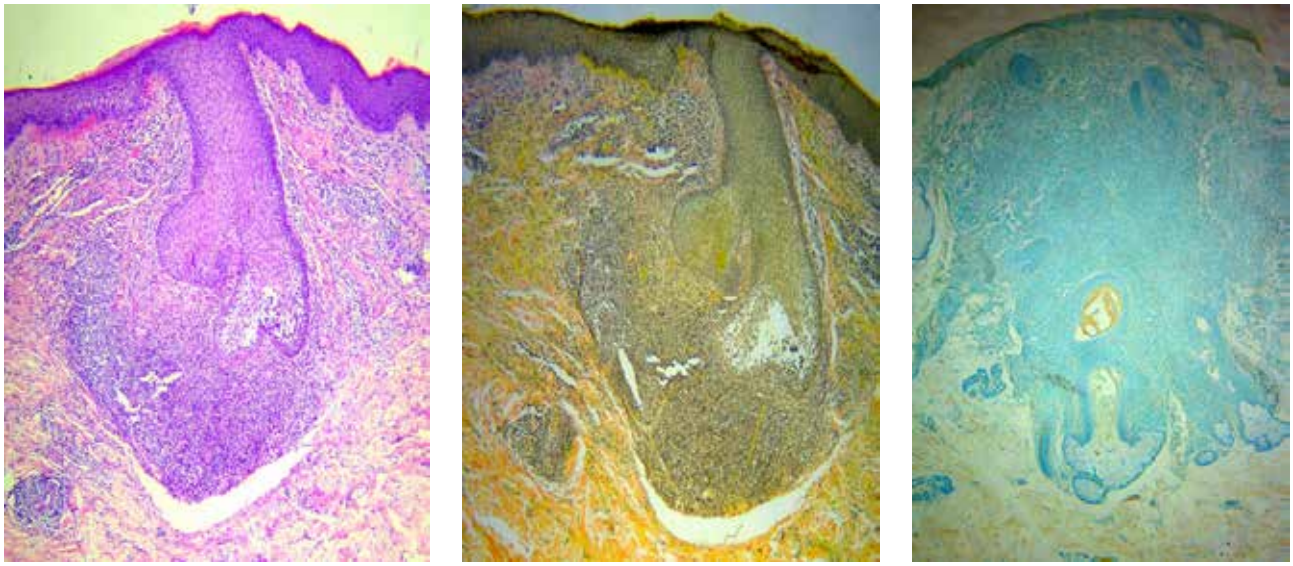
1. Complete blood count: no abnormalities.
2. Biochemical blood count: increase in direct bilirubin to 4.5 μmol/l.
3. Total IgE – moderate increase – up to 270 pg/μL.
4. Determination of thyroid hormone levels: no abnormalities were detected.
5. HIV, hepatitis B, C blood test: negative.
6. Analysis of scaly crusts for mycelium of pathogenic fungi: no pathogenic fungi detected.
7. Determination of antinuclear antibodies: negative.
8. Skin biopsy: epidermis on histologic preparations exhibits patchy acantosis with mild spongiosis. Epidermal papillae appear reduced in height. Openings of the hair follicles appear enlarged with profound hyper- and parakeratosis, deposition of cornified cell mass and sebaceous glands' discharge. Hairs are fully absent or destroyed. Cells of the outer epithelial root sheath of the hair follicles exhibit dystrophic changes which vary from intra- and intercellular edema of epidermal cells with loss of intercellular contacts between them (spongiosis) to cyst-like cavities which show presence of faintly basophilic content in the form of small threads and granules.

Significant lymphohistiocytic infiltration is seen in the dermis spreading into the deep areas of the dermis and hypodermis rich in adipose tissue. Cellular infiltrate is found lying closer to epithelium of hair follicles, sebaceous, and sweat glands. The most prominent cellular infiltrations are observed around the hair follicles (Fig. 2A).

Their constituents include not only lymphocytes and histiocytes but plasma cells, solitary eosinophils and tissue basophils as well. Some of hair follicles exhibit signs of atrophic changes or sclerosis. Sebaceous glands are hypertrophied with foci of dystrophy. Sweat glands are normal in appearance.

Blood vessels of the upper third of the dermis have thickened walls and appear somewhat dilated and plethoric. They are invested by cuff-like lymphohistiocytic infiltrates. Content of cyst-like epidermal cavities stained with toluidine blue appears metachromatic which indicates that it mostly consists of acid mucopolysaccharides, namely mucin (Fig. 2B).

Metachromasia reduces after digestion with hyaluronidase but don't not vanish which tells us about the presence of not only hyaluronic acid but sulfated glycosaminoglycans as well. Staining with Van Gieson's picrofuchsin reveals extensive areas of connective tissue around hair follicles which lost their normal histologic architecture (Fig. 2C).



A B C

Fig. 2. Dystrophied hair follicle with forming cavity and profound perifollicular lymphohistiocytic infiltration. A – hematoxylin-eosin, ×40; B – toluidine blue, ×40; C – Van Gieson's picrofuchsin, ×40

Taking into account the peculiarities of the course of the disease, according to the diagnostic criteria as to the classification of Hanifin & Rajka (1980), as well as the results of clinicopathologic studies, a diagnosis was established: secondary follicular mucinosis of the skin, developed against the background of atopic dermatitis.

The patient was prescribed the following therapy: dapsone 50 mg/day for 2 months with two-day breaks once a week, cetirizine 10 mg/day for 1 month. Topically: tacrolimus ointment 0.03% once a day for 2 months, and emollients that restore the lipid composition of the epidermis, 2 times a day. From the 14th day of treatment, phototherapy (UVB 311nm) was added three times a week (15 sessions in total). In the first week of the therapy, a phase of moderate exacerbation with increased itching and hyperaemia was noted, but these symptoms faded within 7 days, the tightness of the skin in the affected areas was gradually decreasing. The process almost completely regressed, which was not observed over the past 5 months; the skin acquired its normal colour and tightness; infiltration almost completely disappeared (Fig. 3A, B).

Discussion. The manifestation of FM in the form of coalesced follicular erythematous, papular elements in the face is not typical. At the same time, clearly defined, raised edges of the affected areas with impaired growth of lanugo hairs, typical induration and thickening of the skin are pathognomonic signs of skin mucinosis. According to the description by a number of authors, the clinical symptoms of the disease are sometimes atypical with the creation of forms that mimic folliculitis, nodular elements, cicatricial alopecia, and the erythrodermic form of mucinosis rarely develops [2].

So, it is possible to suspect an atypical deposition of mucin in the skin in case of a change in the nature of the chronic dermatosis course (including atopic dermatitis), an increase in tightness, induration of the skin, a change in the nature of subjective sensations (itching was replaced by a steady burning sensation). An important factor contributing to the deposition of mucin in the tissues was probably the repeated inserting of fillers with hyaluronic acid, retaining moisture in the skin.

The most reliable criterion for skin mucinosis in this case was a histomorphologic study, which revealed the intradermal deposition of mucopolysaccharides in reaction with alcian blue. The follicular form of mucinosis was also accompanied by the accumulation of mucin mainly around the hair follicles; in addition, dyskeratosis of some cells was revealed in the spinous layer of epidermis (probably as a result of chronic inflammation). The basic membrane under the epidermis was not thickened, and there were no signs of increased proliferative activity of epidermal cells. Thus, the combination of the case history data, peculiarities of clinical manifestations and histologic examinations gave grounds to establish a diagnosis: Secondary follicular mucinosis of the skin.

There are currently no standardized methods of FM treatment. Cases of intralesional application of systemic corticosteroids, dapsone, antimalarial drugs, isotretinoin, indomethacin, interferon, minocycline, and photodynamic therapy have been described [14]. However, not one of the methods has fully justified itself. In this regard, the successful elimination of the symptoms of secondary follicular mucinosis is of scientific and practical interest.

In the case of our patient, we used dapsone in combination with external application of tacrolimus ointment 0.1%; from day 14, the treatment was enhanced with phototherapy (UVB 311 nm), which caused improvement and a complete regression of rashes. The positive effect of dapsone, topical calcineurin inhibitor, and narrowband phototherapy application was probably associated with the combined

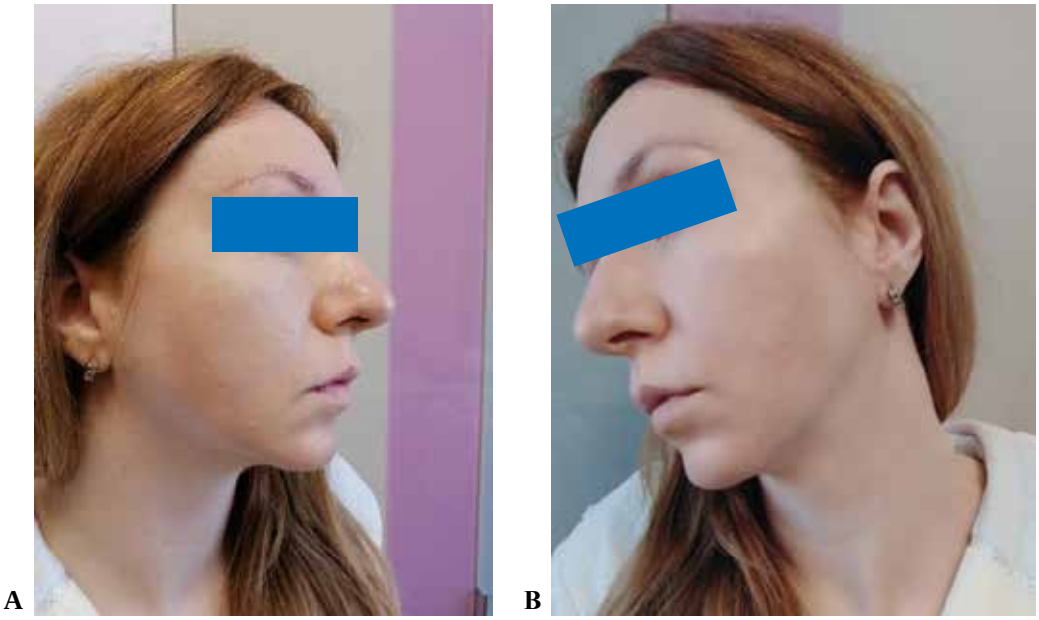


Fig. 3. The patient 2 months after the beginning of therapy. Resolution of follicular skin mucinosis, restoration of normal skin tightness, moderate hyperaemia persists. A – on the right side of the face, B – on the left side of the face

cytostatic effect of the therapy, suppression of the activity of epithelial cells, and a subsequent decrease in mucin synthesis. Given the association of the disease with atopic dermatitis, it can be assumed that the control and timely treatment of the underlying disease will reduce the risk of recurrence of skin mucinosis and improve its long-term prognosis.

Conclusions. The presented clinical observation of rare follicular mucinosis of the facial skin against the background of atopic dermatitis deserves the attention of dermatologists, as it is associated with certain diagnostic difficulties, requires an individual approach to the choice of laboratory screening, treatment, proactive therapy and prevention of the disease.

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