SUBCORNEAL PUSTULAR DERMATOSIS – AN UNUSUAL CASE

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Summary

Subcorneal pustular dermatosis (SPD) is an uncommon condition of unknown etiology that usually develops after the age of 40 and has a predilection for the female gender. It is characterized clinically by a chronic, relapsing symmetric sterile pustular rash that predominantly involves the flexure surfaces of the trunk and limbs and histologically by the presence of subcorneal pustules abundant in neutrophils. SPD can be associated with systemic diseases, especially lymphoproliferative diseases, inflammatory bowel disease and rheumatoid arthritis. Dapsone is the mainstay of treatment, leading to complete clinical remission in the majority of cases. Cases refractory to sulphones may respond to oral retinoids, phototherapy, colchicine, cyclosporine or anti-tumor necrosis factor α biologic agents.

We report and discuss the case of a 21-year-old female patient diagnosed with SPD with skin lesions limited to the lower limbs unresponsive to dapsone and colchicine treatment and review the literature.

Key words: *subcorneal pustulosis, sterile pustules, neutrophils, sulphones.*

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Introduction

Subcorneal pustular dermatosis (SPD), described by Sneddon and Wilkinson in 1956 is an uncommon dermatosis of unknown etiology [1]. It presents as a chronic, relapsing symmetric sterile pustular rash that predominantly involves the flexural aspects of the limbs and intertriginous areas. The histopatologic picture is dominated by the presence of subcorneal pustules abundant in polymorphonuclear leukocytes. The onset of SPD usually takes place after the age of 40. The disease has a predilection for the female gender [2]. Despite its prolonged course, SPD is a benign disease. However, in numerous SPD cases underlying systemic diseases have been identified, especially lymphoproliferative diseases, inflammatory bowel disease and rheumatoid arthritis [3].

We discuss the case of a 21-year-old female patient diagnosed with SPD with skin lesions limited to the lower limbs, unresponsive to dapsone and colchicine treatment and review the literature.

Case report

A 21-year-old female patient was admitted to our clinic for a recurrent pustular eruption limited to the lower limbs of 5 months duration. She had undergone topical corticoid treatment without clinical improvement. The patient's past medical history was not significant.

The physical examination revealed the presence of multiple red papules and pustules, as well as older lesions represented by violaceous plaques 5-8 mm in diameter, with a depressed or eroded center and a collarette of scale symmet-

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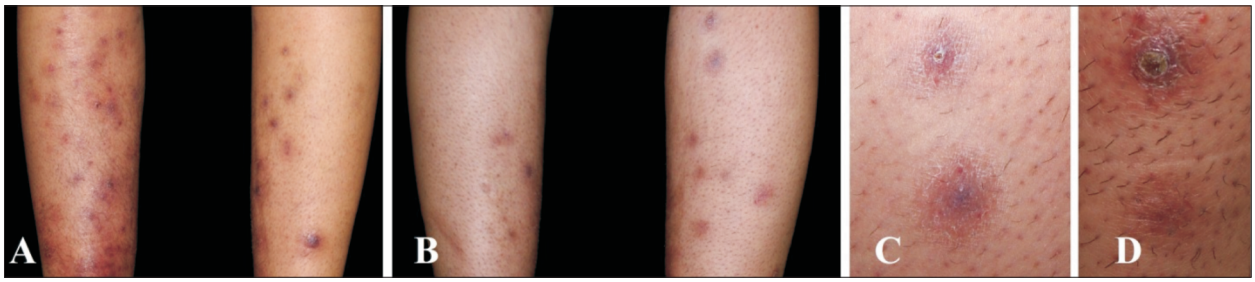

Fig. 1. Red papules and pustules, violaceous plaques with a depressed or eroded center and a collarette of scale (C, D), residual hyperpigmented macules and slightly atrophic scars symmetrically distributed on the lower limbs

rically distributed on the lower limbs (Fig. 1). Residual hyperpigmented macules and slightly atrophic scars could also be seen in the affected area. The rest of the physical examination did not show other pathologic changes.

The results of the laboratory tests were within normal limits. Skin bacterial and fungal cultures did not show the presence of pathogenic infectious agents.

A skin biopsy was performed. The histopathologic examination revealed orthokeratosis and parakeratosis, frequent polymorphonuclear leukocytes in the stratum corneum, with the formation of pustules, acanthosis and reactive epithelial changes (hyperchromasia/nuclear hypertrophy). The dermis underlying the corneal and subcorneal pustules showed a predominantly perivascular moderate mixed inflammatory infiltrate, frequent turgescent capillaries, and numerous extravasated erythrocytes. No hemosiderin deposits or fibrin deposits in the wall of dermal vessels could be noticed. The histopathologic diagnosis was that of subcorneal pustular dermatosis (Fig. 2).

Screening for potential underlying diseases was negative.

We initiated treatment with dapsone at an initial dose of 50mg daily, afterwards increased to 100mg daily associated with colchicine 1mg daily, but the existing skin lesions did not improve significantly and new pustular lesions continued to appear. After one month of combination treatment with dapsone and cochicine only a slight clinical improvement was achieved. Therefore, administration of colchicine and dapsone was ceased. The patient was recommended treatment with isotretionin 10mg daily, associated with phototherapy (narrow band UVB 311nm), which led to prompt significant clinical amelioration. In a few weeks complete clinical remission was obtained.

Discussions

SPD is a very rare condition, with only a few hundred cases reported to date. Its etiopathogenesis is still unclear, so is its nosological classification. Some authors include SPD in the spectrum of neutrophilic dermatoses [4], while others advocate its affiliation to autoinflammatory pustular disorders due to its similarity to pustular psoriasis [5]. To complicate things even further, some cases of SPD display epidermal intercellular immunoglobulin A (IgA) deposits on direct immunofluorescence [6,7]. These are autoantibodies that target desmocollin-1 and their presence suggests a connection with IgA pemphigus [6,7]. In fact, such cases are currently labeled subcorneal pustular dermatosis type IgA pemphigus [8. Whether the later represents a form of SPD or a distinct condition remains uncertain. Even in these cases neutrophils predominate, acantholysis is either minimal or absent and dapsone is the most efficient treatment [8].

Infection as a potential cause of SPD has been ruled out. However, a fact that warrants attention is its association with haematologic diseases (mainly IgA monoclonal gammopathies, multiple myeloma, but also IgG paraproteinemia, chronic lymphocytic leukemia, and CD30+ anaplastic large-cell lymphoma), inflammatory disorders (especially inflammatory blowel disease, rheumatoid arthritis, pyoderma gangrenosum, rarely systemic lupus erythematosus and Sjogren syndrome), aplastic anemia, as well as solid

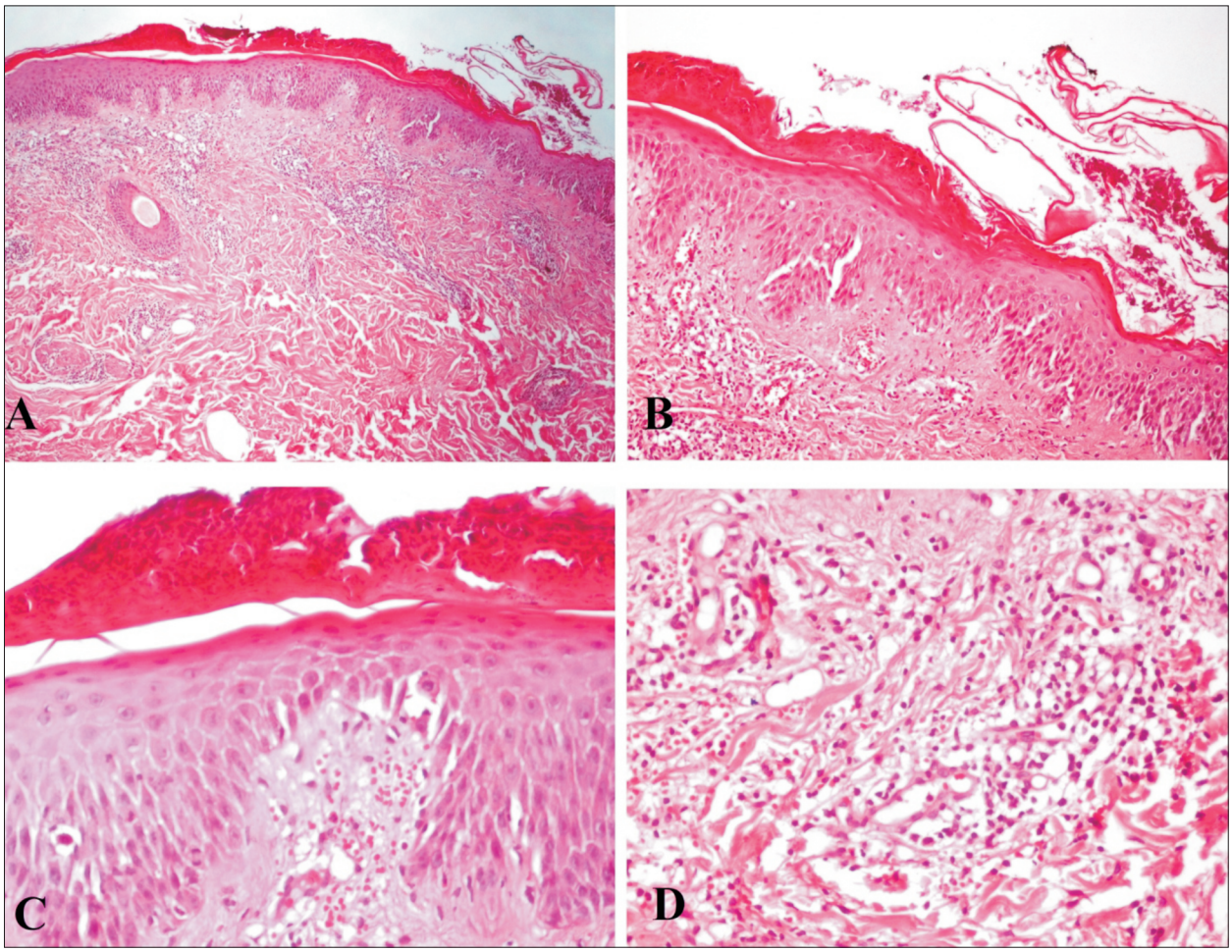

Fig. 2 Haematoxylin & eosin stain (A) magnification x 40, (B) magnification x 100, (C,D) magnification x 200 showing ortho- and parakeratosis, frequent neutrophils in the stratum corneum that form pustules, acanthosis and reactive epithelial changes (hyperchromasia/nuclear hypertrophy), a predominantly perivascular moderate mixed inflammatory infiltrate in the dermis underlying the corneal and subcorneal pustules, turgescent capillaries, and numerous extravasated erythrocytes

tumors (metastatic thymoma, epidermoid carcinoma of the lung) [3]. These associations might reflect common pathogenic mechanisms.

In our patient, the history, physical examination and the results of the laboratory tests and paraclinical investigations did not reveal any underlzing systemic disorder.

SPD usually develops after the age of 40. Women are more often affected than men [2]. The onset of SPD took place at a very young age in our patient.

Clinically, SPD manifests as a chronic, relapsing rash initially composed of vesicles that appear on normal or erythematous skin and rapidly turn into flaccid pustules. Tipically, the pus drops in the lower part of the lesion, generating the aspect of „half-and-half" blister. The lesions tend to coalesce and form serpiginous, arcuate, or annular plaques. The pustules rupture easily and leave erosions covered by thin crusts or superficial scales that often heal with postinflammatory hyperpigmentation. The lesions predominantly involve the intertriginous areas and the flexor aspects of the limbs. The face, palms and soles are rarely affected [3]. The scalp and mucous membranes are not involved. In our case, the distribution of the skin lesions was atypical as they were limited to the lower limbs. Skin lesions are usually asymptomatic, although some patients complain

of mild pruritus. Systemic symptoms are absent or minimal. In the absence of specific treatment the disease has a chronic course, with periods of inactivity of days or weeks and acute exacerbations over many years [3].

Histopathologically, SPD is characterized by the presence of subcorneal pustules abundant in neutrophils and only occasional eosinophils. The rest of the epidermis shows little or no changes.

Rarely, minimal spongiosis is noticed. Older lesions may display minimal secondary acantholysis. A predominantly neutrophilic perivascular infiltrate is also observed in the dermis [1,2]. In most SPD cases, direct and indirect immunofluorescence studies are negative. Cases currently designated subcorneal pustular dermatosis type IgA pemphigus show epidermal intercellular IgA deposits on direct immunofluorescence and circulating IgA antibodies that target desmocollin-1 on indirect immunofluorescence [3].

The main differential diagnoses of SPD are pustular psoriasis, bacterial or dermatophyte infections, acute generalized exanthematous pustulosis, immunobullous diseases, and necrolytic migratory erythema.

Patients diagnosed with SPD should undergo paraclinical investigations in order to exclude potential associated disorders, particularly malignancy. Screening for underlying lympho-proliferative or inflammatory diseases is mandatory at diagnosis and every few years. Long-term monitoring of patients diagnosed with SPD is recommended as such associated diseases may develop many years after the onset of SPD.

The treatment of choice is dapsone 50-150 mg daily. Sulfapyridine 1-3 g daily has also proven beneficial [3]. The use of systemic corticosteroids should be limited to severe, widespread exacerbations. Oral retinoids and phototherapy as monotherapy or in combination with sulfones are the main alternatives for the treatment of SPD [9-11]. Other therapeutic agents that have been reported to induce clinical amelioration are colchicine, cyclosporine, topical tacalcitol, and anti-tumor necrosis factor α biologic agents [12].

Our patient responded poorly to agents that inhibit neutrophilic migration, such as dapsone and colchicine. Although the preferred oral retinoid in recalcitrant SPD cases is acitretin, given the young age of the patient and her desire to have children in the next few years, we opted for isotretinoin 10mg daily combined with narrow band UV 311 nm, which led to complete clinical remission.

Our case has several atypical features: the young age of the patient, the localization of the skin lesions, which were limited to the lower limbs, the lack of response to dapsone and colchicine, and the prompt response to very low dose isotretinoin treatment and phototherapy.

Conclusions

Physicians should be aware of this uncommon condition and consider it in the differential diagnosis of sterile pustular eruptions with no systemic symptoms in patients without a history of psoriasis. A thorough physical examination and screening for associated diseases are mandatory. Sulphones remain the treatment of choice, leading to complete clinical remission in the majority of cases. Refractory cases may respond to oral retinoids, phototherapy, cyclosporine or anti-tumor necrosis factor α biologic agents.

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Conflict of interest
NONE DECLARED

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