

BRIEF ARTICLES

Subcorneal Pustular Dermatitis Successfully Treated with Acitretin in a Patient with Glucose-6-Phosphate Dehydrogenase DeficiencyHosseinipour, Mojgan DO,¹ Baigrie, Dana DO,² Crane, Jonathan DO²¹Department of Dermatology at St. Barnabas Hospital, Bronx, NY²Department of Dermatology at Campbell University School of Osteopathic Medicine Sampson Regional Medical Center, Clinton, NC

ABSTRACT

Subcorneal pustular dermatosis (SPD) is a rare neutrophilic dermatosis. SPD most commonly presents as a serpiginous pattern of pustules on the trunk or intertriginous areas of middle-aged females. It tends to have a chronic disease course and patients may experience relapses. Dapsone currently remains the treatment of choice for SPD. However, in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, alternative therapies are required. We report a case of subcorneal pustular dermatosis in a G6PD deficient patient successfully treated with acitretin.

CASE REPORT

A 71-year-old African American woman presented for evaluation of a painful and pruritic rash of the right lower extremity that had developed one year prior. She was referred by her primary care physician after treatment with trimethoprim-sulfamethoxazole and clotrimazole for suspected bacterial and dermatophyte infection without resolution. At the dermatology office, she was initially evaluated by a physician assistant and found to have excoriated plaques on the right proximal pretibial region and right distal calf. A shave biopsy was performed revealing an impetiginized nummular dermatitis. Triamcinolone acetonide 0.1% ointment was prescribed for twice daily use with modest improvement in her skin lesions. She was eventually diagnosed with pustular psoriasis

based on clinical findings and started on topical treatment with calcipotriene 0.005% topical ointment to use twice daily. Upon follow-up evaluation four months later, the rash continued to spread and the patient reported draining lesions and worsening pruritus despite compliance with topical therapy. At this visit, she was evaluated by the dermatologist.

On examination, the patient was found to have crops of erythematous scaly papules and plaques studded with pustules distributed on the trunk, upper and lower extremities (Figure 1-4). Two punch biopsies were performed and direct immunofluorescence (DIF) was requested. The patient was instructed to discontinue calcipotriene and begin prednisone 20 mg daily for one week. On follow-up evaluation one week later, annular and serpiginous erythematous patches and peripheral

January 2020 Volume 4 Issue 1

pustules were noted on physical examination. The pathology results revealed subcorneal collections of neutrophils with negative DIF study (Figure 5). Based on clinical and histopathological examination, findings were most consistent with subcorneal pustular dermatosis. The patient was counseled on the risks, benefits and alternatives to starting dapsone therapy. A glucose-6-phosphate dehydrogenase (G6PD) level and baseline labs were ordered prior to initiating treatment with dapsone. She was found to be G6PD deficient on repeated laboratory analysis. Therefore, she was started on acitretin 25mg once daily in addition to a one-week course of oral corticosteroids. The patient was also evaluated by her primary care physician in search of a gammopathy or associated comorbidity, which was unremarkable. The patient has shown immense clinical improvement on acitretin with minimal to no adverse effects. After approximately eight months of therapy with acitretin, the lesions cleared with some residual post-inflammatory hyperpigmentation. The patient experienced a relapse of her skin disease and was restarted on acitretin 25mg once daily and subsequently increased to 25mg twice daily. Once she maintained clearance, she was titrated down to acitretin 25mg once daily and remained well-controlled on a scheduled dose of 25mg every other day.

PRACTICE POINTS

- ◆ Subcorneal pustular dermatosis is a rare, chronic, pustular eruption typically presenting in middle-aged women on the trunk, in intertriginous areas and on the limbs.
- ◆ Although the mainstay of therapy is dapsone, oral retinoids may produce rapid and complete resolution of symptoms for patients in which dapsone is contraindicated.

Figure 1. Scaly erythematous papules studded with pustules distributed on anterolateral upper extremity.



Figure 2. Scaly erythematous papules studded with pustules distributed on posterior upper extremity.



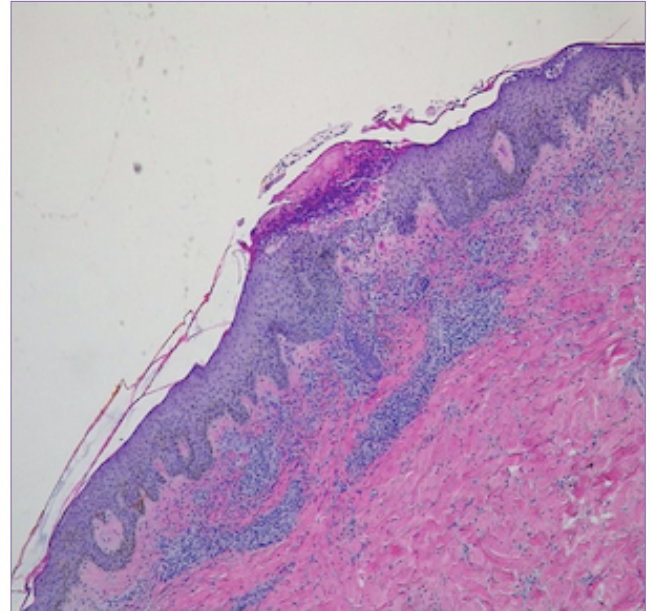
Figure 3. Scaly erythematous papules studded with pustules distributed on lateral lower extremity.



Figure 4. Scaly erythematous papules studded with pustules distributed on upper anterior trunk.



Figure 5. H&E demonstrating subcorneal collections of neutrophils



COMMENT

Subcorneal pustular dermatosis, also referred to as Sneddon-Wilkinson disease, is a rare, pruritic, pustular eruption that is distributed typically on the trunk, intertriginous areas and limbs. It commonly presents in middle-aged women and may be associated with lymphoproliferative disorders such as IgA or IgG gammopathies or myelomas. The condition may also be associated with cancer, infection, medications or systemic or autoimmune diseases.¹ The primary cutaneous lesion is a superficial, flaccid pustule arising on a somewhat erythematous base that subsequently ruptures and develops crusting or scale. The lesions may coalesce to form an annular or serpiginous pattern and tend to be symmetrically distributed.¹

The etiology of subcorneal pustular dermatosis is unknown. The condition tends to have a chronic course with relapses and remissions over many years.² The pathophysiology of subcorneal pustular

January 2020 Volume 4 Issue 1

dermatosis is believed to be migration of neutrophils to the epidermis to form sterile pustules.³ Histopathology is characterized by subcorneal pustules with abundant neutrophils, absence of acantholysis and spongiosis, and negative direct immunofluorescence.⁴ The absence of acantholysis and spongiosis is what distinguishes SPD from impetigo histopathologically. SPD must also be distinguished from IgA pemphigus which will demonstrate immunoblotting with autoantigen human desmocollin 1. Other histologic differentials include pustular psoriasis and superficial bacterial and fungal infections.⁵

The most likely diagnoses to consider in this patient are SPD and pustular psoriasis. We favor SPD because the patient presented with recurrent annular pustular lesions that tended to expand peripherally over a chronic period and resolve with hyperpigmentation. The histopathology exhibited subcorneal pustules without significant spongiform features. Sanchez et al. report a relationship between SPD and pustular psoriasis, and consider SPD a part of the spectrum of pustular psoriasis, specifically the annular presentation. However, these patients tend to present in childhood and have a personal or family history of psoriasis. In many cases, these patients eventually progress into pustular psoriasis, and the typical histopathologic features of acanthosis, parakeratosis and dilated blood vessels are evident.⁶ In pustular psoriasis of the annular pattern, lesions can present with pain and expand more acutely in a centrifugal pattern over a period of days. Patients may also experience systemic symptoms including fever and malaise, and may require hospitalization. In contrast, patients with SPD present with a more benign course.⁷ Both SPD and pustular psoriasis can present clinically and histopathologically similar,

which can be diagnostically challenging. The treatment of choice is dapsone at a dose of 50-200mg daily, which typically produces complete remission within 4 weeks. However, our patient had G6PD deficiency, an inherited X-linked metabolic disorder that affects red blood cell function. Unlike most cells in the body, red blood cells only have one enzyme to catalyze dehydrogenase reactions necessary for metabolism. Metabolism of dapsone produces toxic metabolites with directly-acting hemolytic properties.⁸ In patients with decreased activity of the G6PD enzyme, red blood cells become more vulnerable to oxidative stress resulting in acute hemolytic anemia. Retinoids such as acitretin have comparable efficacy to dapsone. They act more rapidly and are better tolerated. Previous literature report eruptions healing within 2 weeks of therapy and complete clearance within 8 months.² Acitretin is believed to exert its therapeutic effects by inhibiting neutrophil migration and function.^{2,3} Most patients tend to have dramatic improvement of symptoms within 1 week of starting low-dose retinoids. Unlike dapsone, toxicities are not a limiting factor for treatment with acitretin. Dapsone has risk for serious toxicities such as hemolytic anemia and methemoglobinemia. Treatment can be refractory in many cases requiring maintenance therapy to prevent relapses.^{1,4} With low-dose acitretin, 0.5mg/kg/day, the most frequently report adverse effect was cheilitis.^{2,3,4} Alternative treatments including corticosteroid therapy and phototherapy are less effective.

CONCLUSION

Subcorneal pustular dermatosis is a rare neutrophilic skin disorder that can significantly impact a patient's quality of life. It typically presents in middle-aged women as polycyclic or serpiginous pustules that

rupture and form superficially crusted plaques. Though lesions may resolve relatively rapidly (within approximately four weeks) when treated with dapsons, certain situations such as failed response or contraindications to therapy may necessitate alternative treatments considerations. Our patient was G6PD deficient, therefore dapsons was dismissed as a treatment option and the patient was started on acitretin, an oral retinoid. She remains clear and off of the medication eight months after treatment initiation.

Conflict of Interest Disclosures: None

Funding: None

Corresponding Author:

Dana Baigrie DO
 Department of Dermatology
 Sampson Regional Medical Center
 1099 Medical Center Drive #201
 Wilmington NC 28412
 Phone: 850-241-6862
 Fax: 910-343-6006
 e-mail: dbaigrie@vcom.edu

Recalcitrant Palmoplantar Eruptions, Pustular Dermatitis, and Erythroderma in *Andrews' Diseases of the skin: Clinical dermatology*. 2011;10(3):185-198.

6. Sanchez, NP, HO Perry, SA Muller, R K Winkelmann. Subcorneal Pustular Dermatitis and Pustular PsoriasisA Clinicopathologic Correlation. *Arch Dermatol*. 1983;119(9):715-721.
7. Khosravi-Hafshejani T, Dutz JP. Chronic annular pustular psoriasis resembling subcorneal pustular dermatosis: A case report. *SAGE Open Med Case Rep*. 2019;7:2050313X19857392.
8. Luzzatto L., Nannelli C. & Notaro R. Glucose-6-Phosphate Dehydrogenase Deficiency. *Hematol Oncol Clin N*. 2016;30:373–93.

References:

1. Cohen PR. Sweet's syndrome - a comprehensive review of an acute febrile neutrophilic dermatosis. *Orphanet J Rare Dis*. 2007;2:34.
2. Canpolat F, Akpınar H, Cemil BC, Eskioglu F, Ozturk E. A case of subcorneal pustular dermatosis in association with monoclonal IgA gammopathy successfully treated with acitretin. *J Dermatolog Treat* 2010; 21: 114-6.
3. Marlière V, Beylot-Barry M, Beylot C, Doutre M. Successful treatment of subcorneal pustular dermatosis (Sneddon–Wilkinson disease) by acitretin: Report of a case. *Dermatology*. 1999;199:153–155.
4. Teixeira M, Alves R, Selores M. Subcorneal pustular dermatosis in association with a monoclonal igA gammopathy: Successful treatment with acitretin. *Eur J Dermatol*. 2006;16:588–590.
5. James, W. D., Elston, D. M., Berger, T. G., & Andrews, G. C. Seborrheic Dermatitis, Psoriasis,