Subcorneal pustular dermatosis associated with IgG monoclonal gammopathy of undetermined significance

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Abstract

Subcorneal pustular dermatosis is a rare chronic relapsing bullous neutrophilic dermatosis. Because it can be associated with monoclonal gammopathy of undetermined significance and multiple myeloma, screening for these conditions is necessary. Herein, we present a case of subcorneal pustular dermatosis, with concurrent monoclonal gammopathy of undetermined significance, successfully treated with acitretin.

Keywords: monoclonal gammopathy, Sneddon-Wilkinson disease, subcorneal pustular dermatosis, undetermined significance

Introduction

Subcorneal pustular dermatosis is a rare chronic bullous neutrophilic dermatosis first described in 1956 by Ian Sneddon and Darrell Wilkinson (to whom its synonymous eponym 'Sneddon-Wilkinson disease' is owed), [1]. Women are affected four times more often than men; it presents most often in the fifth decade as a relapsing symmetric pustular eruption favoring the trunk, intertriginous areas, and flexor extremities. The classic primary lesion is a pea-sized unilocular pustule with a gravity-dependent fluid level demarcating clear liquid atop sterile pus inferiorly. Although benign, subcorneal pustular dermatosis can be associated with monoclonal gammopathy of undetermined significance, multiple myeloma, and internal malignancies. There are also anecdotal reports of subcorneal pustular dermatosis associated with rheumatoid arthritis, thyroid disorders, mycoplasma pneumonia, and systemic lupus erythematosus. The treatment of choice is dapsone, but retinoids and other therapies have also been used successfully [2,3].

Case Synopsis

A 33-year-old man was referred to the dermatology department with a two-year history of recurrent crops of mildly itchy 'blisters' on his trunk and extremities. He denied other medical problems and use of medications. Examination revealed innumerable symmetrically distributed pea-sized non-follicular pustules, some containing clear fluid sitting atop sterile pus inferiorly. There were well-circumscribed round erosions on his trunk and proximal extremities, most numerous on his superior flanks and proximal flexural arms (**Figure 1**).

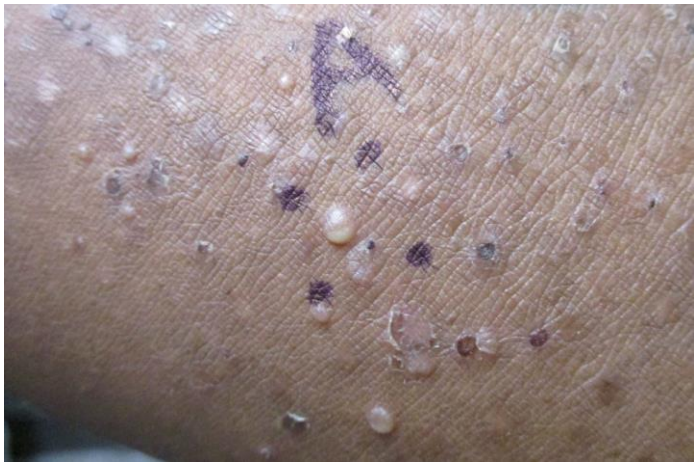

Figure 1. *Pinhead to pea-sized unilocular vesicopustules, erosions, and thin hyperpigmented papules (left flexural arm). The vesicopustule centered between the four inked dots (marked "A") was biopsied for staining with hematoxylin and eosin.*

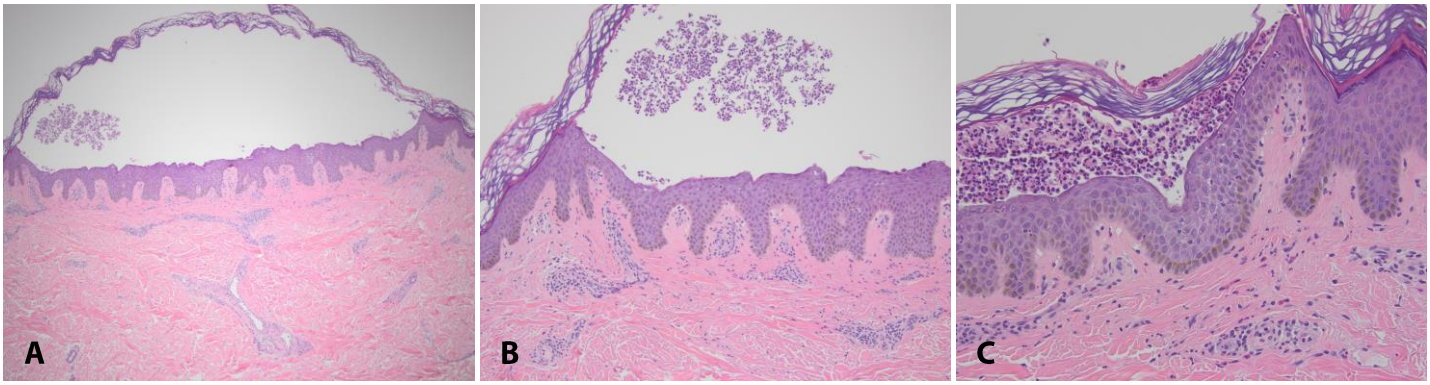

Figure 2. ***A)*** *Subcorneal vesicle with collection of neutrophils. Within the dermis is a mild superficial perivascular infiltrate. H&E, 5×.* ***B)*** *Neutrophilic pustule above a mixed perivascular infiltrate with eosinophils. H&E, 10×.* ***C)*** *High power image with neutrophilic pustule above a perivascular infiltrate containing lymphocytes, neutrophils and eosinophils. H&E, 20×.*

Two punch biopsies were performed of an intact vesicopustule and perilesional skin for histology (**Figure 2**), and direct immunofluorescence. This showed a subcorneal vesicle containing neutrophils and limited acantholysis of epidermal cells in the granular layer above a superficial and mid-perivascular interstitial lymphocytic infiltrate with eosinophils (**Figure 2**). Direct immunofluorescence was negative, arguing against IgA pemphigus. The patient was diagnosed with subcorneal pustular dermatosis based on the clinicopathologic correlation.

Serum IgA level was normal, whereas IgG was elevated at 2960 mg/dL (normal range 600-1600mg/dL) and IgM was slightly elevated at 433mg/dL (normal range 30-190mg/dL). Serum protein electrophoresis revealed elevations of total protein (9.6g/dL, normal range 6.0-7.7g/dL), free kappa light chain (70.90mg/L, normal range 3.30-19.40mg/L), free lambda light chain (39.86mg/L, normal range 5.71-26.30mg/L), and kappa/lambda ratio (1.78, normal range 0.26-1.65). Rheumatoid factor and antinuclear antibodies were negative; thyroid stimulating hormone, glomerular filtration rate, and serum calcium were normal. A hematology consultation recommended annual free light chain serologies to monitor for progression of what they categorized as IgG monoclonal gammopathy of undetermined significance.

The patient's liver function tests were normal, and treatment was started with acitretin 25mg daily and clobetasol ointment twice daily. At four-weeks' follow up, appearance of new lesions had slowed significantly and his pruritus was well controlled. His dose of acitretin was increased to 40mg daily for four weeks, after which his eruption completely resolved. He is now taking 25mg daily and has been instructed to follow-up in three months.

Case Discussion

Subcorneal pustular dermatosis is a rare chronic neutrophilic dermatosis consisting of a symmetric pustular eruption of the trunk, intertriginous areas, and flexor extremities. It must be differentiated from pustular psoriasis, IgA pemphigus, pemphigus foliaceus, dermatitis herpetiformis, and bullous impetigo. Its clinical and histologic findings are identical to IgA pemphigus, but these two entities can be differentiated by direct immunofluorescence. Perilesional skin of the latter demonstrates positive immunofluorescence with intercellular IgA deposits against desmocollin 1, whereas subcorneal pustular dermatosis appears negative on direct immunofluorescence [3].

This case demonstrates unique features, namely our patient's gender, young age, and concurrent IgG monoclonal gammopathy (IgA monoclonal gammopathy is more frequent), [3]. Treatment was successful with acitretin, which we elected over the more traditional dapsone (considered first-line) because of reports of acitretin's comparable efficacy, more rapid decline in symptoms, and better

tolerability [2]. A literature review of cases treated with acitretin is summarized in **Table 1**. Acitretin is a metabolite of etretinate, which has also been reported as yielding varying success in a prior review of 10 cases [4].

This dermatosis can be associated with monoclonal gammopathy of undetermined significance, and it is recommended that multiple myeloma be ruled out in these patients [3]. Abnormal serum free-light chain ratio in the presence of non-IgM monoclonal gammopathy of undetermined significance (both present in our patient) confers a 20% risk of progression to multiple myeloma or another plasma-cell or lymphoid disorder at 20 years [5]. Consultation with a hematologist and long-term observation may be necessary to monitor for this important possibility.

Conclusion

We present this case to highlight a rare neutrophilic dermatosis, its known association with monoclonal gammopathy of undetermined significance, and the importance of monitoring such patients for progression to multiple myeloma. Although dapsone is considered first-line, acitretin may also be used with rapid efficacy and good tolerability.

Potential conflicts of interest

The authors declare no conflicts of interest.

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Table 1. *Published cases of subcorneal pustular dermatosis treated with acitretin. Direct immunofluorescence was negative for all cases (except one, which was not specified).*

Age	Sex	Monoclonal gammopathy	Histology	Prior treatments	Acitretin dose	Response time	Follow-up	Reference
78	Male	IgA	Subcorneal pustules filled with neutrophils, mild diffuse epidermal spongiosis with focal exocytosis of neutrophils without acantholysis; patchy superficial infiltrate of lymphocytes, histiocytes, and neutrophils	Dapsone	35mg	'Good control of lesions and symptoms in 2 weeks'	Reduced to 10mg daily after 1 year, well controlled after 20 months of follow-up	[6]
58	Male	IgA	Subcorneal pustule with neutrophils; edema and dense perivascular infiltration of lymphocytes and eosinophils in upper dermis; no acantholysis	Dapsone + topical steroids	40mg	'Complete response' in 8 days	Well controlled at 15 months follow-up	[4]
55	Female	IgA	Subcorneal pustules with superficial perivascular infiltrate of lymphocytes and neutrophils without acantholysis	Dapsone + topical steroids	25mg for 3 months, then 10mg	'Eruptions were completely healed' in 2 weeks	Reduced to 10mg for 3 months, 'virtually clear' at 4 months; then discontinued with no relapses after 30 months	[7]
40	Female	IgM	Not specified	Dapsone, colchicine, sulphameth-oxypyridazine, etretinate	10mg + PUVA*	Not specified	Maintained for 5 years, then switched to uvb + sulphameth-oxypyridazine	[8]
33	Male	IgG	Subcorneal vesicle containing neutrophils with limited acantholysis of epidermal cells in the granular layer above a superficial and mid-perivascular and interstitial lymphocytic infiltrate with eosinophils	None	25mg (1st month), 40mg (2nd month) + topical clobetasol	Near-cessation of new lesions at 1 month	Completely resolved 2 months after starting acitretin	this case
25	Female	None	Subcorneal pustule filled with neutrophils and some eosinophils, under a slightly acanthotic epidermis; superficial perivascular infiltrate	Dapsone	25mg + dapsone 100mg	'Almost total' resolution in 3 months	Not specified	[9]
10	Female	None	Subcorneal pustules containing neutrophils with mixed perivascular infiltration of mostly neutrophils	None	10mg (0.5mg/kg)	'Almost completely healed' at 4 weeks	Continued 10mg every other day for 1 month, no relapses	[10]
2.5	Male	None	Subcorneal pustules; irregular epidermal acanthosis and spongiosis;	None	10mg (0.8mg/kg)	2 months	After 5 months, switched to topical steroids	[11]

			perivascular monocyte infiltration				only; relapsed 6 weeks later with mild exacer-bations and remissions in the following year	

*PUVA: psoralen and long-wave ultraviolet radiation.