A case of Sneddon-Wilkinson disease with hypersensitivity to dapsone successfully managed with colchicine

Jarische Frances S. Lao-Ang, MD[1], Ma. Lourdes Nebrida-Idea, MD, FPDS[2]; and Ma. Lorna F. Frez2, MD, FPDS

Introduction: Sneddon-Wilkinson disease (SWD) is a rare, recurrent neutrophilic dermatosis presenting as sterile pustules, with a predilection for flexural and intertriginous areas.

Case summary: A 49-year-old Filipino female presented with a three-year history of recurrent pustules and papules on the flexural areas of trunk and extremities. Skin punch biopsy was done and histopathology was consistent with subcorneal pustular dermatosis/SWD. She was started on Dapsone but after two weeks of intake, the patient developed generalized erythematous desquamating plaques on the trunk and extremities, with palmoplantar involvement. The patient did not have fever, jaundice, lymphadenopathy, and abdominal tenderness. Laboratory investigation such as complete blood count and liver function tests were normal. The final diagnosis was SWD with hypersensitivity to Dapsone. Dapsone was immediately discontinued and she was shifted to oral colchicine. After six weeks of oral colchicine therapy, the lesions have completely resolved. Patient was in remission for six months thereafter.

Conclusion: SWD is rare and the drug of choice is dapsone. In instances where dapsone is not suitable, oral colchicine can be an ideal alternative treatment.

Key words: Sneddon-Wilkinson disease; dapsone; colchicine

INTRODUCTION

Sneddon-Wilkinson disease (SWD) is a rare recurrent neutrophilic dermatosis presenting as sterile pustules, eventually forming circinate patterns with predilection sites over flexural and intertriginous areas. 3 Though rare, it is important for dermatologists to recognize this disease since it can be associated with underlying systemic disease. In cases of SWD, there is a need to investigate further when confronted with a recurrent pustular dermatosis such as SWD.

[1]Resident, Department of Dermatology, St. Luke's Medical Center, Quezon City, Philippines
[2]Consultant, Department of Dermatology, St. Luke's Medical Center, Quezon City, Philippines

Corresponding author: Jarische Frances S. Lao-Ang, MD
Dermatology Center
12th Floor, Cathedral Heights
Building Complex
St. Luke's Medical Center
Quezon City, Philippines
jajalaoang@gmail.com

Commercial funding: None disclosed
Conflict of interest: None

CASE

This is a case of a 49-year-old female with no known comorbidities, who presented with multiple pustules on erythematous base over the trunk and extremities. Three years prior, the patient reported the appearance of erythematous papules and plaques on the trunk and extremities, with progression into generalized desquamation. She reported use of various topical medications prior to the onset of the lesions. A previous skin punch biopsy was done and findings were consistent with exfoliative dermatitis probably secondary to contact dermatitis. Patient was given unrecalled topical medications, which offered complete resolution.

Two and a half years prior, she noted pustules on an erythematous base on both inguinal areas, and was managed as a case of candidal intertrigo. Patient reported resolution of the lesions with a two-week course of oral itraconazole. However, patient was lost to follow up.

In the interim, she recalled four episodes of recurrent pustules on the inguinal folds and flexural areas of the arms. Hydroxyzine provided relief on the pruritus.

Three weeks prior to consult, numerous pustules and papules started to appear over the bilateral axilla and bilateral inframammary areas. She denied use of any new topical and oral medications. She sought consult and was given clobetasol propionate ointment and an unrecalled antihistamine. Lesions decreased in number and in erythema. However, two weeks later, lesions spread over her abdomen, back, both thighs, and both legs. She also reported swelling of both feet with difficulty of ambulation. Hence, upon follow-up, a skin punch biopsy was done and histopathological findings were consistent with subcorneal pustular dermatosis (Fig.1). She was then admitted for further evaluation.

On admission, patient was febrile at 38.4C. On physical exam, multiple well-defined pustules and plaques on an erythematous base, some coalescing into annular patterns, were seen on the chest, both inframammary areas, both axilla, abdomen, back, both upper and both lower extremities (Fig.2). No mucosal lesions were noted.

Laboratory investigation included 1) complete blood count with increase in white blood cell at 19,829; neutrophilic predominance; 2) urinalysis with trace proteinuria; 3) normal creatinine and blood urea nitrogen; 4) normal lipid profile; and 5) normal liver function tests. Dapsone was drug of choice for this case, however, G6PD level result was not available yet at the time hence she was started on colchicine 500mcg/tablet, 1 tablet 2 times a day. Topical treatment regimen was also prescribed as follows: cool normal saline compress followed by emollient, then by clobetasol propionate ointment 2 times a day over affected areas on both arms, legs, chest, abdomen and back, and mometasone lotion once a day over both axilla and both inframammary areas.

After a week of hospitalization, patient was discharged with marked improvement. G6PD test came back normal (patient's result: 11.50, Normal range: 4.6-13.50). She was then started on oral dapsone 100mg daily.

Referral to hematology service was made on an outpatient basis for evaluation of monoclonal gammopathy. Urine protein electrophoresis was negative for urine monoclonal component. As for the serum free light chain panel, findings were suspicious for low level monoclonal free lambda light chains. At this point, the threshold for the patient in developing multiple myeloma is low. However, hematology service still opted to monitor the patient.

Two weeks after oral intake of dapsone, patient experienced pruritus 8/10 with appearance of generalized erythematous patches and plaques on trunk and extremities (Fig.3). Patient did not have associated fever, jaundice, icteric sclerae, and abdominal pain. Laboratory work-ups were done to rule out dapsone hypersensitivity syndrome. Patient's complete blood count, liver functions tests, and renal function tests were all normal. Hence, patient was managed as a case of hypersensitivity reaction to dapsone and said medication was discontinued. She was given oral prednisone at 20mg per day for three days, and topical betamethasone dipropionate ointment. A week after discontinuation of Dapsone, lesions significantly decreased in number.

Colchicine at 0.5mg daily was then re-initiated. After six weeks of intake, previously noted pustules completely resolved, without any recurrence (Fig.4). Hematology service ordered for repeat serum free light chain panel three months after the baseline, and findings were now negative. Colchicine was then discontinued. Patient was in remission for 6 months. She was advised to have close monitoring and follow-up every 6 months thereafter.

DISCUSSION

Sneddon-Wilkinson disease (SWD) is a neutrophilic dermatosis that presents with recurrent sterile pustules primarily affecting the flexural and intertriginous areas of the body. There are 200 cases reported worldwide.1 Based on the Philippine Dermatologic Society Health Information System data, this is the 28th case, with 19 cases affecting females and nine cases affecting males.2 However, its prevalence cannot be truly established since it can be misdiagnosed.

Various factors such as infection, genetic susceptibility, and medications have been reported as underlying triggers in the development of the pustules. However, most cases are still idiopathic. The pathophysiologic cascade leads to the increase in neutrophil chemotaxis to the skin by the activation of the neutrophilic cytokines interleukin-8, interleukin-10 and tumor necrosis factor α. This results in neutrophil collection with eventual formation of pustules.3

Based on a journal by Cheng, S. (2008), clinical findings that strongly support the diagnosis of SWD include presence of superficial pustules in circinate patters over flexural and intertriginous areas; absence of mucosal and nail changes, mostly affecting middle-

aged females. All these criteria are fulfilled by the patient.4 A skin punch biopsy is done to further support the diagnosis. Histopathologic findings would include subcorneal split with collection of neutrophils, usually with minimal to no spongiosis in the epidemis above a normal-appearing dermis.

Even though SWD primarily affects the skin, it can be associated with systemic conditions such as connective tissue disease, hematologic disorders and malignancies. Among these, 40% of the cases have underlying hematologic disorders, mostly IgA monoclonal gammopathy. Though benign, 28% of IgA monoclonal gammopathy may ultimately develop into malignant myeloma.5 Hence, referral to Hematology is warranted. In this case, patient's urine protein electrophoresis was normal, but the serum light chain panel was suspicious for low level monoclonal free lambda light chain. Even though the threshold for developing malignant myeloma is low, there is a 5% absolute risk of progression at 20 years. Hence, serum protein electrophoresis is recommended after 6 months and every 2-3 years thereafter.6 The patient in this case had the repeat serum protein electrophoresis three months from baseline and it yielded normal results.

Currently, no gold standard therapy and no treatment guidelines are available for SWD. Dapsone, a sulphonamide, remains to be the first-line treatment. It inhibits neutrophil chemotaxis and decreases release of inflammatory cytokines. Initial dose ranges from 50-200mg daily over 4-6 weeks with dose tapering.7 Since dapsone may cause hemolysis, a baseline G6PD screening is necessary prior to starting therapy. Patient's G6PD level was normal, so she was given dapsone at 100mg daily.

After two weeks, however, patient had hypersensitivity reaction to dapsone, presenting with erythematous desquamating patches and plaques over trunk and extremities. Based on a systematic review by Lorenz. M. et al (2012)8, the overall incidence of dapsone hypersensitivity reaction is 1.4%, with fatality rate of 10%. Hence, prompt recognition and management are necessary.8 Dapsone was immediately discontinued in the case reported here.

Given this clinical scenario where dapsone is contraindicated, an alternative treatment must be considered. Among the 2nd-line systemic therapy, the most common drug given is colchicine. It is an extract from the plant Colchicum autumnale and is known to inhibit neutrophil chemotaxis as well. A starting dose of 0.5 mg twice daily is given for a week, followed by maintenance dose of 0.5 mg once daily for 6-8 weeks.9 Patient was given 0.5 mg of colchicine once daily. During the duration of therapy, she denied any gastrointestinal side effects. After six weeks of therapy, lesions resolved completely with no recurrence.

Given its cyclic and relapsing course, SWD usually has a benign prognosis unless associated with an underlying systemic disorder. At present, there is no definitive cure. Hence, patient monitoring is important since lesions may recur. As for this case, after six weeks of colchicine, medication was discontinued. She has been in remission for 6 months, but is advised to have follow-up every 6 months thereafter.

CONCLUSION

SWD is a rare recurrent, relapsing neutrophilic dermatosis that can be misdiagnosed. Given the presence of recurrent pustules on the intertriginous and flexural areas of the body, a clinical suspicion for this disease entity must be considered. Based on literature, the correlation of clinical history, physical manifestations and histopathologic findings is important for a definitive diagnosis. At present, the drug of choice is oral dapsone. However, in instances where dapsone is not suitable, oral colchicine is an alternative treatment, such as in our case. Though rare, SWD must be recognized early since it can be associated with underlying systemic diseases, most especially hematologic malignancy. Hence, work-up and close monitoring are advised even after treatment.

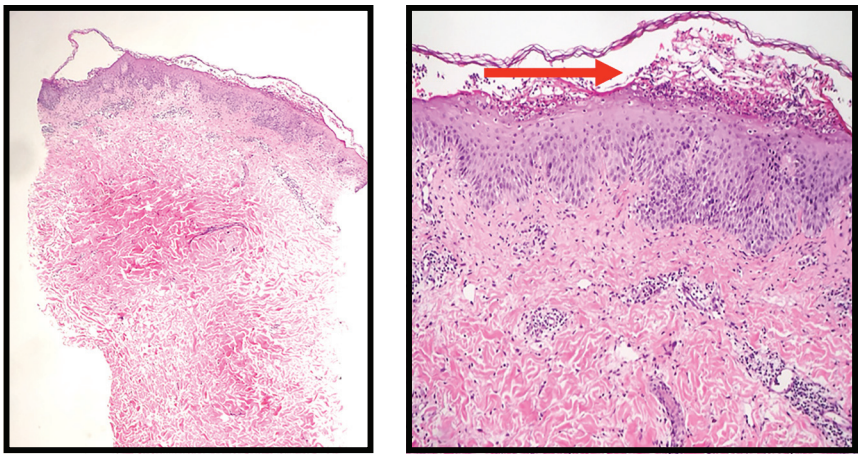

Figure 1. Biopsy of lesion on abdomen a. epidermis shows subcorneal split (H & E x 100 b. collection of neutrophils with occasional eosinophils at subcorneal split (red arrow, H & E x 400)

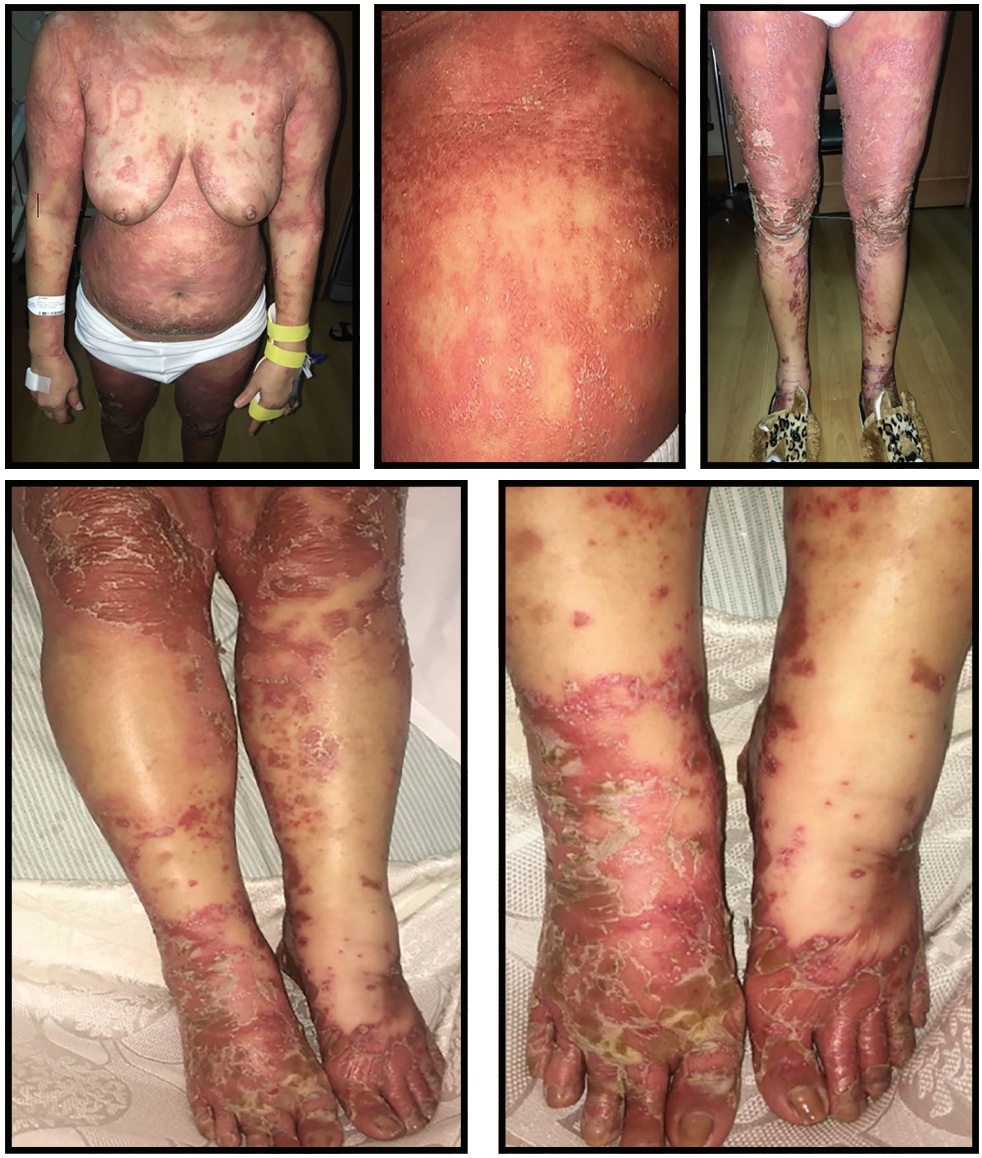

Figure 2. Multiple pustules and plaques, some in circinate patterns, over trunk and extremities

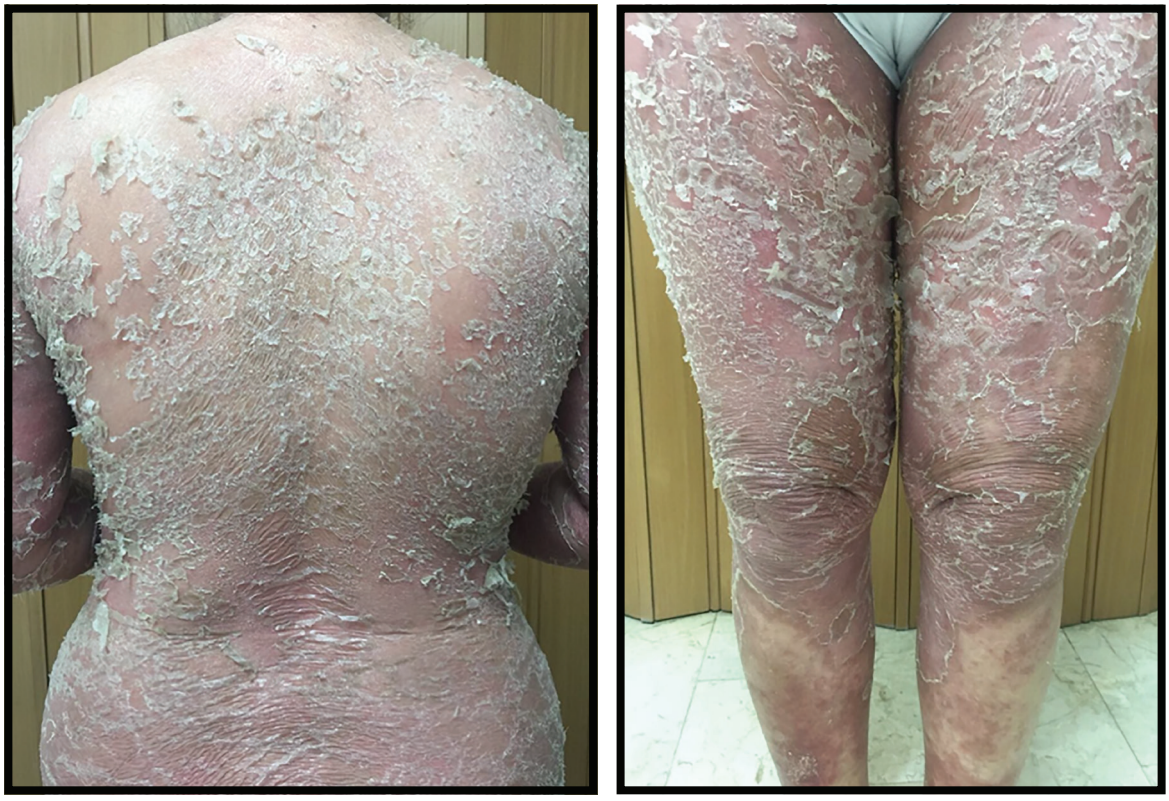

Figure 3. Erythematous desquamating patches and plaques on two weeks of dapsone therapy

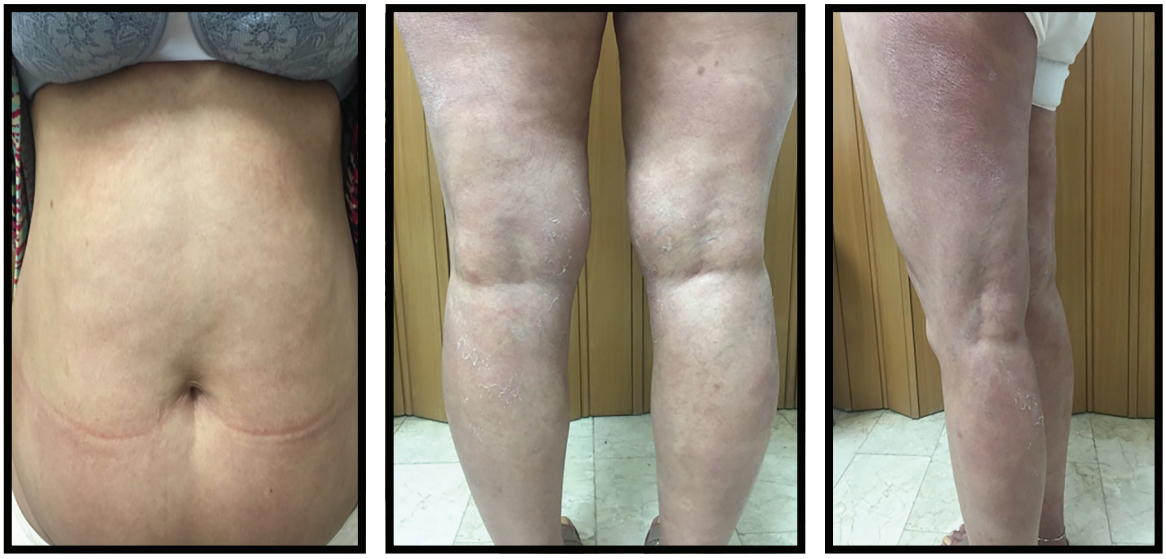

Figure 4. Complete resolution of lesions after six weeks of colchicine therapy

REFERENCE

1. Watts, P. and Khachemoune, A. (2016). Review Article: Subcorneal Pustular Dermatosis: A Review of 30 Years of Progress. Am J Clin Dermatology Dec; 17(6):653-671.

2. Philippine Dermatologic Society Health Information System data. Retrieved: February 2018

3. Cheng S, Edmonds E, Ben-Gashir M, Yu RC. Subcorneal pustular dermatosis: 50 years on Clin Exp Dermatol 2008;33:229.

4. Razera F, Olm GS, Bonamigo RR. Neutrophilic dermatoses: part II. An Bras Dermatol. 2011;86(2):195–209

5. Kasha EE, Epinette WW. Subcorneal pustular dermatosis in association with a monoclonal IgA gammopathy. A report and review of the literature. J Am Acad Dermatol 1988;19:854

6. Lipe,B., and Kyle,R. (2016) Monoclonal Gammopathy of Undetermined Significance (MGUS): Predictor of Progression and Monitoring. Downloaded from: http://www.hematology.org/Guidelines-Quality/Quick-Ref/6973.aspx

7. Cohen PR. Neutrophilic dermatoses: a review of current treatment options. Am J Clin Dermatol. 2009;10(5):301–12

8. Lorenz,M., Wozel,G. and Schmitt,J. Hypersensitivity reactions to Dapsone: a review article. Acta Derm Venereology 2012; 92:194-199

9. Pavithran K. Colchicine in the treatment of subcorneal pustular dermatosis. Indian J Dermatol Venereol Leprol 1995;61:56-7

10. Laifaoui JA, Guillen E, Worret WI, Ring J. A case of subcorneal pustular dermatosis (Sneddon-Wilkinson disease) not responding to dapsone: Therapeutic alternatives. Acta Dermatoven APA 2003;12:109.