

Dermatitis Herpetiformis in a Young Filipino Male: A Case Report

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Abstract

Background: Dermatitis herpetiformis (DH) is a rare autoimmune blistering disease characterized by pruritic papulovesicular eruptions. It can be differentiated from other vesiculobullous skin diseases by skin biopsy with direct immunofluorescence. DH is most often associated with gluten enteropathy (celiac disease) also an uncommon disease.

Case Presentation: We report a case of a 20-year-old male with a five-week history of multiple vesicles and bullae associated with fever and body malaise. Lesions were symmetrically found on the entire face, axillae, trunk, buttocks and lower extremities. Hematology revealed leukocytosis with neutrophilic predominance. Skin punch biopsy revealed subepidermal blister with neutrophilic predominance. A direct immunofluorescence (DIF) of the perilesional skin showed granular IgA staining at the tips of the dermal papillae, consistent of DH.

Treatment and Outcome: The patient was started with

cloxacillin and mupirocin ointment for the infected skin lesions. Dapsone 100 mg daily was started with significant improvement of lesions after seven days. Endoscopy was suggested to investigate for gluten enteropathy, however patient did not consent. The patient was advised on gluten-free diet (GFD). Complete resolution of lesions with postinflammatory hypo- and hyperpigmented scarring were noted after nine weeks of dapsone therapy.

Conclusion: Bullous skin lesions present as a great challenge to non-dermatologists, hence a thorough investigation was clearly of utmost importance in arriving at a diagnosis of DH in this case. Internists must be aware that skin lesions could provide clues of other internal diseases, such as in DH and gluten enteropathy. Treatment of DH can be as simple as diet modification and avoidance of gluten-containing food.

Keywords: Dermatitis Herpetiformis, Dermatology, Celiac Disease, Gluten Enteropathy, Dapsone

Introduction

Dermatitis Herpetiformis (DH) is a rare autoimmune blistering disease characterized by an intensely itchy, chronic papulovesicular eruption that is usually symmetrically distributed on extensor surfaces.¹ The prevalence of DH in Finland is 10.4 per 100 000 individuals with an annual incidence of 1.3 per 100 000.² Around 15% to 25% of patients with DH have an associated gluten-sensitive enteropathy (celiac disease) that is usually asymptomatic in most patients.^{2,3} Here, we present a Filipino male with DH successfully treated with dapsone and gluten-free diet (GFD).

Case

A previously healthy 20-year-old male consulted at the

outpatient clinic with multiple blistering skin eruptions.

His condition started five weeks prior to consult when he noted appearance of pruritic, tense, erythematous vesicles and bullae on the face. He did not complain of fever, body malaise, abdominal pain, diarrhea or steatorrhea. He self-medicated with an over-the-counter cream (clobetasol propionate + ketoconazole cream) that did not provide any relief. He later consulted a physician and was given ciprofloxacin 500mg tablet twice a day for seven days. However, there were still persistence and spread of lesions to the abdomen, upper back and lower extremities.

The patient was non-hypertensive, non-diabetic, non-asthmatic with no previous hospitalization. His usual diet was rice, noodles, fish, chicken and gluten-containing chocolate milk ("Milo").

Physical examination revealed multiple tense vesicles and bullae with areas of erosions and crusts symmetrically located on the face, axillae, trunk, buttocks and lower extremities (Figure 1. A-F). Mucosal and genital lesions were free of lesions.

Hematologic examination revealed normal hemoglobin and leukocytosis of $13.39 \times 10^9/\mu\text{l}$ with neutrophilic predominance. Serum chemistry was within normal range. Glucose-6-phosphate dehydrogenase (G6PD) test was within normal limits. Chest X-ray and stool exam were unremarkable as well. Wound culture revealed very light growth of non-

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fermenting organism which was sensitive to cloxacillin.

Skin punch biopsy of an early vesicle revealed a subepidermal blister with neutrophilic predominance that was consistent with DH versus linear IgA bullous dermatosis (Figure 2. A & B).

Direct Immunofluorescence (DIF) from a perilesional normal skin showed positive granular IgA deposits at the tips of the dermal papillae that is consistent of DH (Figure 3).

He was started with cloxacillin and mupirocin ointment for one week for the infected skin lesions. The patient was on loratadine 10 mg/tab once a day for pruritus. Also, he was started on dapsone 100 mg/tab once a day after G-6-PD test revealed a normal result. Complete blood count was regularly monitored.

During the course of dapsone therapy, the patient developed hemolytic anemia with hemoglobin of 109 g/L and reticulocyte count of 2.8 (Table I). Therefore, dapsone was reduced to half the initial dose once a day on sixth week of therapy. In addition, he was supplemented with ferrous sulfate plus folic acid 325mg/1.0mg tablet daily. After three weeks, the hemoglobin of the patient improved.

The patient was also started on GFD. He was referred to a nutritionist and was advised to avoid the following food such as egg noodle, macaroni, miki, misua, sotanghon, spaghetti, sausages, instant coffee, gluten-containing chocolate milk powder ("Milo"), beer and wheat bread. On the ninth week of therapy, the skin lesions were completely resolved with residual hypo- and hyperpigmented macules and patches (Figure 4). Finally, the patient was diagnosed to have dermatitis herpetiformis.



Figure 1. Multiple tense vesicles and bullae with areas of erosions with crusts symmetrically seen on the A. Entire face, B. Upper trunk, C. Axilla, D. Back, E. buttocks, F. Both lower extremities.

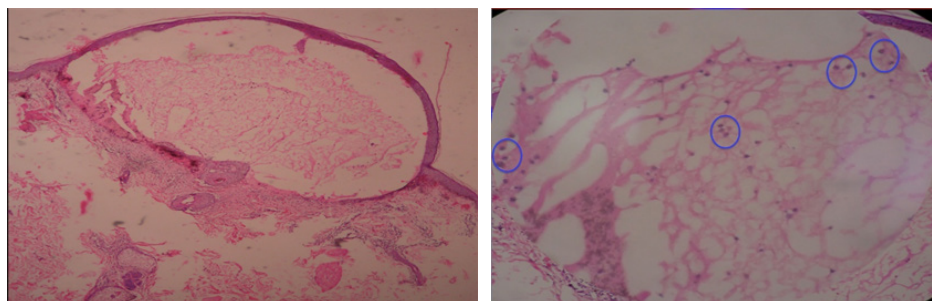


Figure 2. Skin punch biopsy A. Subepidermal blister with neutrophilic predominance (H&E stain, x40) B. Neutrophils contained in the blister cavity (H&E stain, x100)

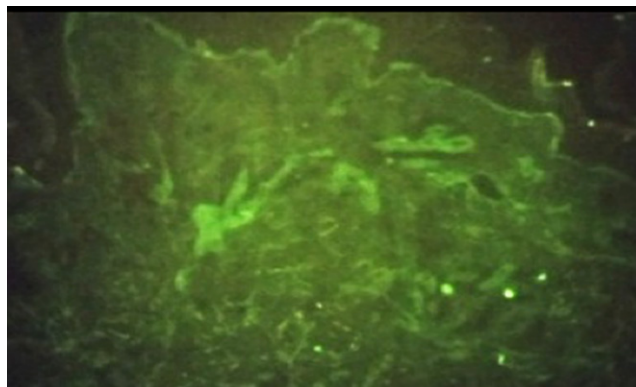


Figure 3. Granular deposition of IgA at the tips of the dermal papillae (DIF, x40).

Table I. Complete blood count (CBC) results on baseline, 3rd, 6th and 9th week.

Complete Blood Count	DAY 0	3rd WEEK	6th WEEK	9th WEEK
Hemoglobin (115 -155)	147	139	109 L	124 L
Hematocrits (0.36 - 0.48)	0.45	0.46	0.34 L	0.42
RBC (4.20 - 6.10)	5.17	4.82	3.62 L	4.27
WBC (5.0 -10.0)	13.39 H	10.32	10.30	9.17
Differentials				
Neutrophils (55 -75)	76 H	56	60	66
Lymphocytes (20 - 35)	13 L	32	28	26
Monocytes (2 - 10)	9	5	6	4
Eosinophils (1 -8)	1	6	5	4
Platelet Count (150 - 400)	340	344	462	330
Reticulocyte Count (1.0 - 2.0)			2.8 H	2.2 H

**Figure 4.** Skin lesions after nine weeks of dapsone. Complete resolution of lesions with residual hyper- and hypopigmented macules and patches. A. Trunk, B. Face, C. Buttocks, D. Back, E. Axilla, F. Both lower extremities.

Discussion

DH commonly occurs among Europeans, while it is uncommon among Asians.^{1,2} A research study done in Utah found a prevalence of 11.2 per 100 000 and an incidence of 0.98 per 100 000 per year. It also noted that the mean age of onset for men was 40¹ years and for women 36.2 years.⁴

In the Philippines, we have a very limited data about DH and gluten enteropathy (celiac disease). This is the first documented case in our institution. Our patient is a young male Filipino who does not fit the stereotype of a DH patient.

Patients presenting with vesiculobullous skin diseases can be challenging to non-dermatologists because most of these conditions have similar appearances. Skin diseases that present with multiple tense vesicles and bulla include DH, bullous pemphigoid (BP), pemphigus vulgaris (PV), linear IgA bullous dermatosis (LABD) and epidermolysis bullosa acquisita (EBA). These differential diagnoses are difficult to distinguish both clinically and in plain histopathology, hence the need of DIF staining.⁵ In H&E staining, both DH and LABD demonstrate subepidermal blister containing neutrophils.¹ Thus, DIF was done on our case to determine the definitive diagnosis. A granular deposition of IgA is seen in the tips of the dermal papillae in DH, while linear deposition of IgA at basement membrane is found in LABD.⁶

The four findings that confirmed our diagnosis of DH were the presence of excoriated papules or pruritic papulovesicles on typical locations, neutrophilic predominance of infiltrates of the dermal papillae with cleft formation at the dermal-epidermal junction, a granular deposition of IgA within the dermal papillae and the response of the skin lesions to gluten restricted diet and dapsone therapy.^{1,6}

Majority of DH patients are associated with gluten enteropathy.^{7,8} The bowel abnormality is due to the ingestion of gluten, such as wheat, rye, and barley.⁹ Gluten is processed by digestive enzymes into antigenic gliadin

peptides, which are transported across the mucosal epithelium. CD4+ T cells in the lamina propria recognise gliadin peptides presented by HLA-DQ2 or -DQ8 molecules on antigen-presenting cells, resulting in the production of Th1 cytokines and matrix metalloproteinases that cause mucosal epithelial cell damage and tissue remodeling.⁸ Our patient had gluten-containing diet.

A GFD is suited for patients with DH and gluten enteropathy since both the cutaneous rash and the enteropathy depend on the ingestion of gluten.¹⁰ A prompt diagnosis of enteropathy should be made since continuous exposure to gluten promotes chronic inflammation that can lead to malignancy such as lymphoma.¹¹⁻¹² It will take around two years of GFD for a complete resolution of cutaneous lesions, which can recur within 12 weeks after the reintroduction of gluten.¹³⁻¹⁴ IgA antibodies may disappear from the dermal-epidermal junction after many years of a strict GFD, while the reintroduction of gluten will lead to IgA deposition in the skin and the rash recurs.¹⁵⁻¹⁶ Because GFD takes a long time for a response to occur, a concurrent use of dapsone is usually necessary.^{1,17}

Strict compliance with GFD will, after variable periods of time (from six months to one year), reduce or completely eradicate the need for medication in most patients.¹⁸ Hence, the importance of proper counseling by a dietitian.

Pruritic lesions are usually relieved within 48-72 hours of starting dapsone (4',4'-diamino-diphenyl sulfone). The lesions may abruptly recur within 24-48 hours of discontinuation of therapy.¹⁷ Unfortunately, dapsone has no effect on the intestinal pathology, thus the importance of GFD.¹⁹

Dapsone was only started after screening for G6PD deficiency because it may cause severe hemolysis due to the effects of oxidant stress on aging red blood cells among susceptible individuals.¹⁹ The average maintenance dose in adults is 100 mg daily which can be regulated on a weekly basis to optimize control.¹⁹

Despite having a negative result for G6PD test, our patient developed decreased hemoglobin on his third week of treatment with dapsone. Hence, the initial dose given was reduced to half during his sixth week of treatment that led to the improvement of the blood parameters.

Currently, the patient is out of dapsone therapy and is maintaining a GFD. There was no recurrence of skin lesions or other associated symptoms upon subsequent follow-ups.

Conclusion

Bullous skin lesions present as a great challenge to non-dermatologists, hence a thorough investigation, such as biopsies with immunohistochemical staining is needed in arriving at a diagnosis. Internists should be aware that skin lesions could provide clues of other internal diseases, such as in DH and gluten enteropathy. A GFD and increased surveillance can prevent the development of lymphoma among DH patients.

References

1. Hull CM, Zone J. Dermatitis Herpetiformis and Linear IgA Bullous Dermatitis. In: Bologna JL, Jorizzo JL, Schaffer JV. *Dermatology*. Third edition. Elsevier; 31: 475-499; 32: 501-513.
2. Reunala T. Incidence of familial dermatitis herpetiformis. *Br J Dermatol*. 1996; 134: 394-8.
3. Bolotin D, Petronic-Rosic P. Dermatitis herpetiformis: part I. Epidemiology, pathogenesis, and clinical presentation. *Journal of the American Academy of Dermatology*. 2011;64(6):1017-1024.
4. Smith JB, Tulloch JE, Meyer LJ, Zone JJ. The incidence and prevalence of dermatitis herpetiformis in Utah. *Arch Dermatol*. 1992;128:1608-10.
5. Sousa L, Bajanca R, Cabral J, Fiadeiro T. Dermatitis Herpetiformis: Should Direct Immunofluorescence Be the only diagnostic Criterion? *Pedi Dermatol* 2002;19(4):336-339.
6. Preisz K, Sárdy M, Horváth A. Immunoglobulin, complement and epidermal transglutaminase deposition in the cutaneous vessels in dermatitis herpetiformis. *Journal of the European Academy of Dermatology and Venereology*. 2005;19(1):74-79.
7. Ronagly A, Katz SI, Hall RS. Dermatitis Herpetiformis. In: Goldsmith L, Katz S, Gilchrest B, Paller A, Leffell D, Wolff K. *Fitzpatrick's Dermatology in General Medicine*. 8th edition. New York: McGraw-Hill; 2008. P.642-648
8. Alonso-Illamazares J, Gibson LE, Rogers RS. Clinical, pathologic and immunopathologic features of dermatitis herpetiformis: Review of the Mayo Clinic experience. *International Journal of Dermatology*. 2007;46(9):910-919.
9. Farrel RJ, Kelly CP. Celiac Sprue. *N Engl J Med*. 2002;346:180-8.
10. Fry L. Effect of gluten free-diet on dermatological, intestinal and hematological manifestations of dermatitis herpetiformis. *Lancet*. 1968; 1:557-561.
11. Hervonen K, Vornanen M, Kautiainen H. Lymphoma in patients with dermatitis herpetiformis and their first degree-relatives. *Br J Dermatol*. 2005;49(52):82-86.
12. Vilijamaa J, Kaukinen K, Pukkala E. Malignancies and mortality in 47 patients with coeliac disease and dermatitis herpetiformis: 30-year population-based study. *Dig Liver Dis* 2006;38:374-380.
13. Godkin A, Jewell D. The pathogenesis of Celiac disease. *Gastroenterology*. 1998;115:206-10.
14. Cardones ARG, Hall RP. Pathophysiology of dermatitis herpetiformis: A model for cutaneous manifestations of gastrointestinal inflammation. *Dermatologic Clinics*. 2011; 29(3): 469-477.
15. Fry L. Clearance of skin lesions in dermatitis herpetiformis after gluten withdrawal. *Lancet*. 1973; 1: 288-291.
16. Hull CM, Liddle M, Hansen N. Elevation of IgA anti-epidermal transglutaminase antibodies in dermatitis herpetiformis. *Br J Dermatol*. 2008;159:120-4.
17. Duhring LA. Dermatitis herpetiformis. *JAMA*. 1893;3: 225.
18. Turchin I, Barankin B. Dermatitis herpetiformis and gluten-free diet. *Dermatol Online J*. 2005;11:6.
19. Sener O, Doganci L, Safali M. Severe dapsone hypersensitivity syndrome. *J Invest Allergol Clin Immunol*. 2006;16:268-270.