JAMA Dermatology Clinicopathological Challenge

Circular Erythematous Plaque at the Area of Median Sternotomy

Georgia Kyriakou, MD, MSc; Efthymia Gialeli, MD; Sophia Georgiou, MD, PhD

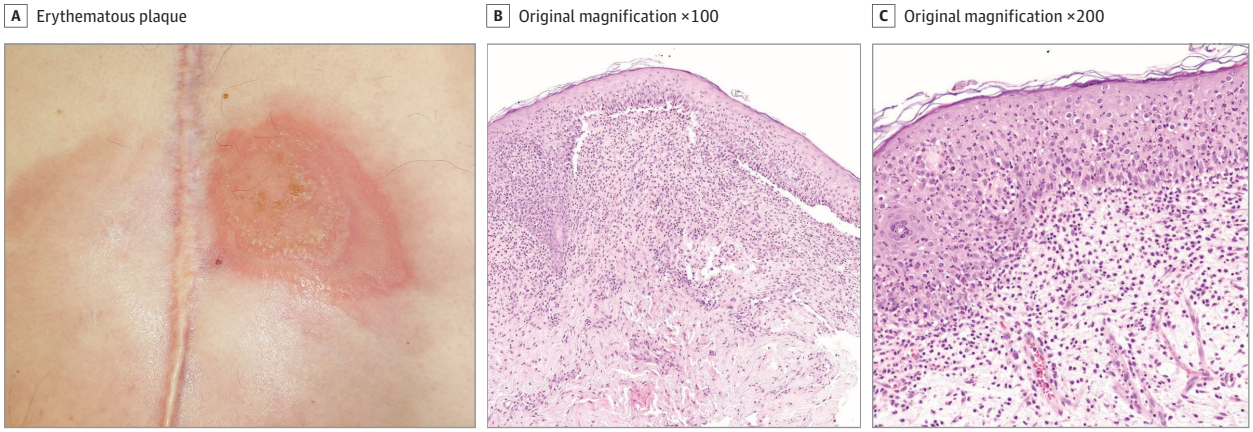

Figure 1. A, A crusted, focally vesiculating, well-demarcated erythematous plaque at the area of median sternotomy. B, Histopathologic examination of lesional skin (hematoxylin-eosin). C, Histopathologic examination of lesional skin (hematoxylin-eosin).

A man in his 60s was referred to our clinic because of a well-demarcated, circular erythematous plaque that had been present at the area of median sternotomy for 3 months. Physical examination findings revealed a 20-cm–diameter plaque that consisted of multiple concentric annular formations with raised erythematous margins and studded with numerous blisters and pustules, some coalescing into lakes of pus (**Figure 1**A). Nikolsky sign was not elicited, and oral, ocular, and genital mucosa involvement was absent. The patient did not report other symptoms, and findings of the overall physical examination were normal.

Over the past 5 years, the patient's medications consisted of metoprolol and acetylsalicylic acid for treatment of established ischemic heart disease. Nine months prior to being referred to our department, he was given oral furosemide and amiloride and then underwent median sternotomy and coronary artery bypass surgery 2 months later. Four days after the operation, he developed a red patch at the area of the incision that was accompanied by mild pruritus. Over the following months, the lesion showed a marked tendency for centrifugal extension over the chest area.

Results of routine laboratory studies, Mantoux test, chest radiography, and chest computed tomography of the area were within the normal range. Gram stain, periodic acid–Schiff stain, and tissue culture results were negative (Figure 1B and C).

WHAT IS YOUR DIAGNOSIS?

- **A.** Annular pustular psoriasis
- **B.** Bullous tinea
- **C.** Linear IgA dermatosis
- **D.** Acute localized exanthematous pustulosis

Diagnosis

C. Linear IgA dermatosis

Discussion

A biopsy specimen showed a subepidermal bulla, prominent neutrophilic infiltrate arranged in a linear fashion, and evidence of dermal papillary microabscesses. Direct immunofluorescence (DIF) study results demonstrated linear deposits of IgA along the basement membrane without C3, IgG, or IgM antibody deposition (**Figure 2**). The diagnosis of linear IgA dermatosis (LAD) was rendered on the basis of clinical, histologic, and DIF findings.

Prior to the patient's clinical admission, the lesion was treated as a surgical wound infection, and the patient was sequentially prescribed amoxicillin and clavulanic acid, doxycycline, ciprofloxacin and clindamycin, and fluconazole as an add-on therapy, with minimal clinical response. After confirmation of the diagnosis, the furosemide and amiloride were discontinued and replaced by hydrochlorothiazide and valsartan. He started a regimen of dapsone and achieved a short clinical improvement followed by important clinical deterioration.

Oral colchicine and a class III topical steroid cream were administered instead of dapsone because the patient was not a candidate for treatment with prednisone owing to severe coronary heart disease. Within 6 weeks, the patient achieved complete remission, and the colchicine and steroid were tapered without any rebound effect.

Linear IgA dermatosis is a rare autoimmune subepidermal bullous disease that may be idiopathic or acquired. Acquired LAD is often associated with drug intake, predominantly vancomycin.[1] Furosemide has also been implicated in 2 reported cases.[2,3] Lesions appear within 1 month of drug initiation, and withdrawal of the agent causes remission within several weeks. Other triggers include systemic autoimmune diseases, infections, and malignant neoplasms.[1,4]

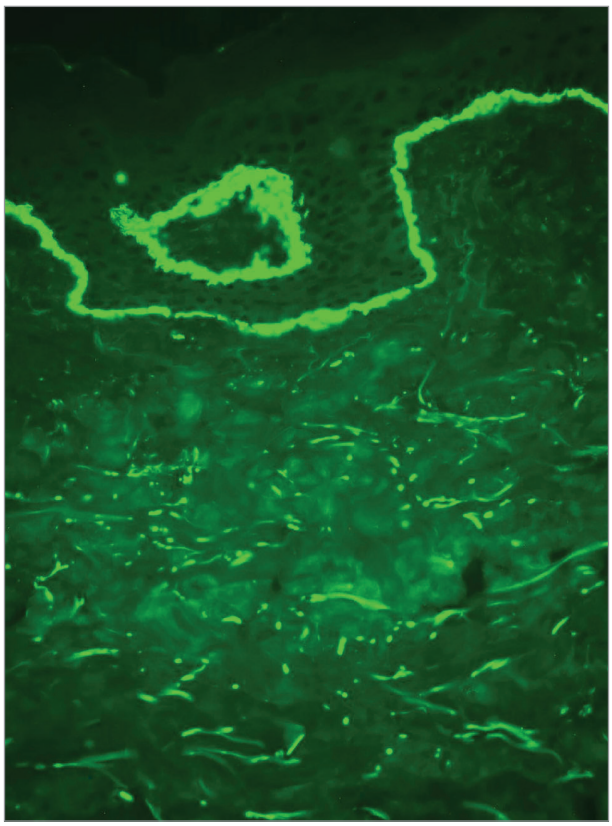

Figure 2. Direct immunofluorescence analysis of lesional skin showing high-intensity linear deposition of IgA antibodies at the dermal-epidermal junction.

Linear IgA dermatosis is characterized by the specific binding of IgA antibodies to the epidermal basement membrane, which leads to complement activation and neutrophil chemotaxis with release of proteolytic enzymes and blister formation.[5] Clinically, considerable variation exists regarding age at disease onset, clinical morphology, and mucosal involvement.[1,5] Typical cutaneous manifestations include tense arciform bullae in a cluster-of-jewels configuration or, less commonly, grouped papulovesicles.[5,6] Atypical lesions owing to Koebner phenomenon have also been reported in areas where adhesives were previously applied.[7,8] This patient developed a lesion on the median sternotomy scar, which was highly suggestive of koebnerization. Although isomorphic response on operation scars has been described in other bullous dermatoses, to our knowledge, only 1 case has been described in LAD.[8]

The histopathologic features are represented by the presence of subepidermal bullae with neutrophil-predominant infiltrate at the dermal-epidermal junction, which are characteristically arranged in a linear array.[1,9] The criterion standard for establishing an LAD diagnosis is DIF revealing linear IgA antibody deposition along the basement membrane.[5]

Treatment modalities vary with the degree of involvement and identification of inciting factors.[9] Drug-induced LAD is usually self-limiting and gradually resolves after discontinuation of the causative agent. Additional therapy, such as dapsone, sulfonamides, corticosteroids, colchicine, tetracyclines, and nicotinamide, may be required.[1,6,10]

A presumptive clinical diagnosis of annular pustular psoriasis was supported by the annular lesion morphology, formation of pustules, centrifugal expansion, and potential koebnerization; however, pustular psoriasis was unlikely given the DIF positivity and histologic findings. Bullous tinea is a clinical mimicker, and 2 cases have described basement membrane DIF positivity. Nevertheless, the presence of subepidermal rather than intraepidermal bullae, the temporal relationship with medications, and the negative periodic acid–Schiff stain exclude this diagnosis. Acute localized exanthematous pustulosis, a rare localized variant of acute generalized exanthematous pustulosis, may also present with multiple nonfollicular, sterile pustules on a background of edematous erythema in the context of recent drug administration. Distinguishing differences are that in acute localized exanthematous pustulosis, skin reaction occurs within a few hours, is usually accompanied by fever and neutrophilic leukocytosis, and does not exhibit DIF reactivity. Given the potential for koebnerization, this patient's case emphasizes the importance of including LAD in the differential diagnosis for atypical lesions with an isomorphic response.

ARTICLE INFORMATION

Author Affiliations: Department of Dermatology, University General Hospital of Patras, Patras, Greece.

Corresponding Author: Georgia Kyriakou, MD, MSc, Department of Dermatology, University General Hospital of Patras, Patras, PO Box 265 04, Greece (geo_kyr@yahoo.gr).

Published Online: December 11, 2019. doi:10.1001/jamadermatol.2019.3883

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for granting permission to publish this information.

Self-assessment Credit: This article is eligible for journal-based self-assessment (1 credit) for Maintenance of Certification (MOC) from the American Board of Dermatology (ABD). After completion of an activity, please log on to the ABD website at www.abderm.org to register your credits. This may be done after each exercise or after accumulating many credits.

REFERENCES

1. Fortuna G, Marinkovich MP. Linear immunoglobulin A bullous dermatosis. *Clin Dermatol*. 2012;30(1):38-50. doi:10.1016/j.clindermatol.2011.03.008

2. Cerottini JP, Ricci C, Guggisberg D, Panizzon RG. Drug-induced linear IgA bullous dermatosis probably induced by furosemide. *J Am Acad Dermatol*. 1999;41(1):103-105. doi:10.1016/S0190-9622(99)70414-7

3. Obaidat NA, Awamleh AA, Nu'eimi RF. Furosemide-induced linear IgA bullous dermatosis. *JRMS*. 2008;15(3):46-49.

4. Fortuna G, Salas-Alanis JC, Guidetti E, Marinkovich MP. A critical reappraisal of the current data on drug-induced linear immunoglobulin A bullous dermatosis. *J Am Acad Dermatol*. 2012;66(6):988-994. doi:10.1016/j.jaad.2011.09.018

5. Chaudhari S, Mobini N. Linear IgA bullous dermatosis. *J Clin Aesthet Dermatol*. 2015;8(10):43-46.

6. Patsatsi A. Chronic bullous disease or linear IgA dermatosis of childhood—revisited. *J Genet Syndr Gene Ther*. 2013;4(6):151. doi:10.4172/2157-7412.1000151

7. Lopez I, Callahan GB, Grimwood RE, Le LQ. The role of the isomorphic phenomenon in distinguishing drug-induced linear IgA bullous dermatosis. *J Clin Exp Dermatol Res*. 2010;1:104. doi:10.4172/2155-9554.1000104

8. Mori T, Yamamoto T. Vancomycin-induced linear IgA bullous dermatosis with isomorphic response. *Our Dermatol Online*. 2013;4(suppl 3):619-620. doi:10.7241/ourd.20134.154

9. Chen S, Mattei P, Fischer M, Gay JD, Milner SM, Price LA. Linear IgA bullous dermatosis. *Eplasty*. 2013;13:ic49.

10. Navi D, Michael DJ, Fazel N. Drug-induced linear IgA bullous dermatosis. *Dermatol Online J*. 2006;12(5):12.