Erythema Elevatum Diutinum in a Patient With Well-Controlled Crohn's Disease

Brian McKenna, PhD, Adam Blechman, MD, Alejandro Gru, MD, R Hal Flowers, MD

Abstract

We present a case of erythema elevatum diutinum (EED) in a 23-year-old female with well-controlled Crohn's disease. EED is thought to result from circulating immune complexes secondary to systemic diseases including infections, autoimmune diseases, and hematologic disorders. To our knowledge, EED has been reported in only three other cases of Crohn's disease, in which eruptions of EED were associated with features of active Crohn's. Our patient was in clinical remission at the time of EED onset, making this report significant not only for its uncommon presentation, but more importantly, to aid readers diagnosis and clinical management of similar cases.

Case

A 23-year-old female with a PMH notable for Crohn's presented to clinic with a rash on her legs first noticed eight months prior, and raised lesions on her feet, knees, and elbows that began two months later. The leg rash was associated with a burning and itching sensation and had a waxing and waning course. These lesions typically resolved several days after appearing, leaving behind darkened skin. The raised lesions on the feet, knees, and elbows were persistent, and chronically painful. Prior treatment of the leg rash with topical mupirocin and fluocinonide, and the raised lesions with cryotherapy, provided no relief of symptoms.

Physical exam revealed erythematous, urticarial linear plaques, irregularly shaped macules, and post inflammatory hyperpigmentation on the lower legs. Multiple red-brown papules and nodules varying in size from 3mm to 2.5cm were observed on the knees, elbows, and dorsal feet (Figure 1).

Histopathologic examination of a punch biopsy from a nodule on the right dorsal foot demonstrated a superficial and deep perivascular and interstitial inflammatory infiltrate composed of numerous neutrophils and lesser numbers of lymphocytes, histiocytes, and eosinophils (Figure 2). There was evidence of a small vessel vasculitis with fibrinoid necrosis and endothelial cell swelling. The inflammation extended around adnexal structures into the deep dermis and subcutaneous adipose tissue. Concentric fibrosis was observed surrounding multiple vessels within the deep dermis, and karyorrhectic debris was also seen. The overlying epidermis was uninvolved. Grocott methenamine silver (GMS), acid fast bacilli (AFB), FITE, and Mycobacterium tuberculosis species-specific monoclonal antibody stains showed no evidence of infectious organisms.

Based on the clinical findings, histopathologic features of perivascular fibrosis and leukocytoclastic vasculitis, and history of Crohn's disease, a diagnosis of erythema elevatum diutinum (EED) was made. EED is a benign disorder that often resolves spontaneously 5-10 years after onset, but has been reported to last up to 40 years.[1] Many patients are asymptomatic and pursue treatment due to the chronically disfiguring nature of the lesions.[2] However, similar to our patient, reports of pruritis and pain associated with lesions are not uncommon.[2] Due to the rarity of this disorder, a paucity of evidence exists to guide therapy. Oral dapsone is generally considered the first-line therapy for EED, with the majority of patients showing complete or partial resolution with treatment.[2] Among other well documented adverse effects, dapsone causes some degree of hemolysis in all patients.[3] Shortly after initiating dapsone, our patient experienced acute worsening of her chronic anemia and therapy was discontinued.

Alternative treatment options include intralesional corticosteroids or methotrexate injections, oral chloroquine, colchicine, NSAIDs, and surgical removal.[2] The patient agreed to a trial of intralesional triamcinolone injections of several of the more prominent nodules on her feet. After two rounds of injections, however, this proved to be ineffective, with exception to reducing pain in the treated nodules. Surgical removal of two lesions was subsequently performed, one from the right knee and left elbow with shave removal and punch excision, respectively. At next appointment these lesions had healed well, especially the elbow. The patient was lost to follow-up after this point.

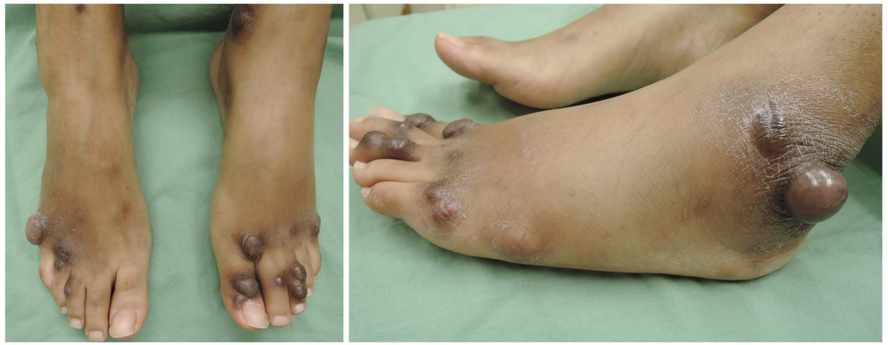

Figure 1. Multiple red-brown papules and nodules varying in size from 3mm to 2.5cm on the dorsal toes, feet, and ankles.

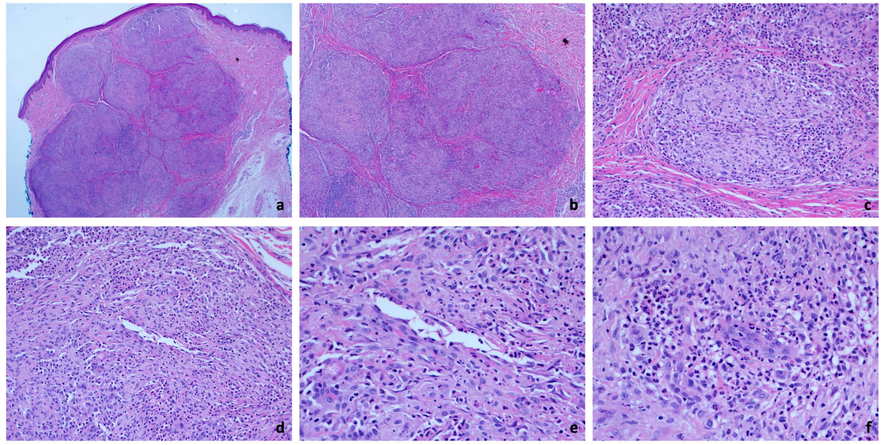

Figure 2. H&E staining of punch biopsy shows a nodular infiltrate in the dermis with prominent fibrosis (a and b, 20x and 100x). The nodules are composed of areas of fibrosis with a concentric appearance (c, 200x). The nodular areas of fibrosis are centered around distinctive small vessels with vasculitis and leukocytoclastic foci (d-e, 200x and 400x).

Discussion

EED is a rare, chronic cutaneous leukocytoclastic vasculitis (LCV), with prominent fibrosis at its later stage.[4] Clinically, EED manifests as a symmetric eruption of violaceous, red-brown, or yellow papules, plaques, or nodules.[4] Lesions predilect acral and periarticular skin, especially the extensor surfaces of the fingers, hands, elbows, feet, ankles, and knees.[2,4]

The pathogenesis of EED remains unclear. The leading hypothesis is that circulating immune complexes in the setting of systemic disease deposit in the perivascular dermis, inducing subsequent complement activation, neutrophil infiltration, tissue damage and fibrosis.[4-8] This theory is supported by direct immunofluorescence revealing perivascular deposition of complement, IgG, IgM, IgA, and fibrin, although these studies are typically not required for diagnosis.[8]

EED has been associated with a number of systemic diseases including infections (Group A Streptococcus, hepatitis B virus, HIV, tuberculosis), autoimmune diseases (granulomatosis with polyangiitis, inflammatory bowel disease, celiac, relapsing polychondritis, systemic lupus erythematosus, rheumatoid arthritis), and both benign and malignant hematologic disorders, especially monoclonal IgA paraproteinemia.[8] Eruptions of EED typically correlate with underlying disease activity. Therefore, once a diagnosis of EED is made, evaluation for underlying disease with a thorough history, complete review of systems and physical exam, and specific laboratory tests should be performed. Our patient was found to have elevated IgA and IgG, however, serum protein electrophoresis revealed this to be a polyclonal gammopathy, with no evidence of anomalous monoclonal immunoglobulins. Although in clinical remission, these findings were most likely related to the patients Crohn's disease, as opposed to an underlying lymphoproliferative disorder.

In summary, EED is a rare, chronic cutaneous LCV thought to result from circulating immune complexes in the setting of infections, autoimmune diseases, and hematologic disorders. Here, we report a case of EED associated with Crohn's disease. To our knowledge, EED has been reported in only three other cases of Crohn's disease, in which eruptions were associated with features of active Crohn's.[9-11] Notably, despite being in clinical remission, our patient exhibited characteristic clinical and histological findings of both early and late-stage EED lesions. Early-stage lesions revealed LCV, while late-stage lesions showed increased prevalence of histiocytes, spindle cells, and concentric perivascular dermal fibrosis. Oral dapsone provides an effective clinical response in most patients and is considered first-line therapy for EED. For those unable to tolerate dapsone, a variety of other local, systemic, and surgical therapies have been reported with varying degrees of success in small numbers of patients.[2] Surgical excision showed promise as a treatment option for our patient, however, the long-term effectiveness of this, or trials of alternative treatment strategies was precluded by lack of follow-up.

References

1. Wilkinson SM, English JS, Smith NP, Wilson-Jones E, Winkelmann RK. Erythema elevatum diutinum: a clinicopathological study. Clin Exp Dermatol. 1992;17(2):87-93.
2. Momen SE, Jorizzo J, Al-Niaimi F. Erythema elevatum diutinum: a review of presentation and treatment. J Eur Acad Dermatol Venereol. 2014 Dec;28(12):1594-602.
3. Ghaoui N, Hanna E, Abbas O, Kibbi AG, Kurban M. Update on the use of dapsone in dermatology. Int J Dermatol. 2020;59(7):787-795.
4. Sangüeza OP, Pilcher B, Martín Sangüeza J. Erythema elevatum diutinum: a clinicopathological study of eight cases. *Am J Dermatopathol*. 1997;19(3):214-222.
5. LeBoit PE, Yen TS, Wintroub B. The evolution of lesions in erythema elevatum diutinum. Am J Dermatopathol. 1986;8(5):392-402.
6. Wetter DA, Dutz JP, Shinkai K, Fox LP. In Dermatology 4th ed. Elsevier; 2018. Accessed July 30, 2022. https://www.clinicalkey.com/#!/content/book/3-s2.0-B9780702062759000246?scrollTo=%23top
7. Wilkinson SM, English JS, Smith NP, Wilson-Jones E, Winkelmann RK. Erythema elevatum diutinum: a clinicopathological study. Clin Exp Dermatol. 1992;17(2):87-93.
8. Doktor V, Hadi A, Hadi A, Phelps R, Goodheart H. Erythema elevatum diutinum: a case report and review of literature. Int J Dermatol. 2019;58(4):408-415.