Erythema elevatum diutinum—associated with loss of the uvula

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INTRODUCTION

Erythema elevatum diutinum (EED) is a rare, chronic form of leukocytoclastic vasculitis (LCV) that belongs to the group of neutrophilic dermatoses including Behçet disease, Sweet syndrome, and pyoderma gangrenosum. The exact pathogenesis of the condition is poorly understood, but it is thought to result from immune complex deposition in small vessels, possibly triggered by an unknown antigen.1 Importantly, EED is often associated with underlying conditions such IgA gammopathy, and HIV; thus, it is crucial that patients be appropriately screened for these conditions.2

CASE REPORT

We present the case of a 60-year-old Vietnamese man who was referred to our outpatient dermatology department with a 10-year history of a condition diagnosed by primary care as dermatitis herpetiformis. On examination, the patient had widespread erythematous-to-violaceous papules and plaques affecting the extensor surfaces of the upper and lower extremities and the buttocks (Fig 1). Skin punch biopsy found numerous thick-walled capillaries in the papillary dermis lined by plump endothelial cells, fibrotic intervening stroma with frequent reactive fibroblasts, and a prominent mixed inflammatory infiltrate including numerous eosinophils. Widespread LCV was seen, and direct and indirect immunofluorescence findings were normal. These appearances were consistent with a diagnosis of EED.

Concurrently, the patient was also under the care of ear, nose, and throat surgeons for investigation of recurrent oropharyngeal ulceration and hoarse voice. Initial endoscopy found florid laryngopharyngitis and ulceration. Biopsies found mild dysplasia with nonspecific inflammatory cell infiltrate and no evidence of malignancy. Six months later, during a flare of his cutaneous and oropharyngeal disease, repeat video laryngoscopy found a moth-eaten epiglottis and complete absence of the uvula (Fig 2). There was no history of trauma to the area during this intervening period.

Computed tomography of the thorax found no evidence of granulomatous disease or malignancy. Sputum was negative for acid-fast bacilli and mycobacterial culture. Results of autoimmune serology tests, including antinuclear antibody, anti-double stranded DNA, and antineutrophil cytoplasmic antibody, were negative.

Serum IgA levels were found to be increased at 6.29 g/L (normal range, 0.8–4). Serum protein electrophoresis found a monoclonal IgA λ-type band and no reduction in background γ-globulins. No Bence Jones protein was found in the urine. After referral to the hematology department, a bone marrow biopsy was performed, which showed 3%...
plasma cells. This finding, in combination with normal complete blood count, renal function, and serum calcium level with no evidence of immunopa-
resis, was consistent with a diagnosis of monoclonal gammopathy of undetermined significance.

Shortly after, the patient presented as an emergency with sudden-onset indurated pustular nodules on the abdomen and thighs. Excisional biopsy findings were consistent with superficial pyoderma gangrenosum, which resolved with a course of oral prednisolone.

Colchicine, 1 g daily, was used to minimal effect, and the patient is currently maintained on dapsone, 100 mg daily, hydroxychloroquine, 200 mg daily, and topical clobetasol propionate 0.05% ointment daily. The patient’s monoclonal gammopathy of undetermined significance remains stable, but he continues to have flares and remissions of his EED. He reports that his oral ulcers flare at a similar time to that of his skin, and his voice remains hoarse. The uvula remains absent.

**DISCUSSION**

Clinically, EED manifests as tender reddish-brown papules, nodules, or plaques. Lesions are typically distributed symmetrically with a predilection for the extensor surfaces of the joints, including the hands, feet, elbows and knees, and the buttocks and Achilles tendons. The affected areas may be asymptomatic or painful, often exhibiting a burning sensation after exposure to cold environments. Patients are often systemically well, but symptoms such as arthralgia and myalgia may occur in some cases.2 Histologically, a spectrum from LCV to vessel occlusion and dermal fibrosis may be observed.3 EED may occur at any age, typically affecting adults age 30 to 60, although 1 case series reported 2 peaks of incidence: 1 in the sixth decade with an equal sex ratio and 1 in childhood with a greater incidence in females.4 The natural history of EED is of a chronic course with spontaneous remissions, although duration of disease has been reported to be variable. One series of 13 patients reported that 4 patients had no further episodes after their initial presentation, whereas one patient’s condition persisted for 39 years.4

EED occurs in association with a number of conditions including hematologic disease (IgA gammopathy, multiple myeloma), infectious disease (tuberculosis, HIV, streptococcal infection), immunologic disease (rheumatoid arthritis, inflammatory bowel disease), and malignancy (squamous cell carcinoma, breast cancer, B-cell lymphoma).1,3 Screening for associated disease, particularly hematologic disorders, is crucial to ensure that appropriate treatment is initiated early.
EED is a chronic, recurrent condition, and the treatment of choice is dapsone, which is reported to be effective in 80% of cases. However, colchicine, mycophenolate mofetil, hydroxychloroquine, tetracycline or sulphonamide antibiotics, systemic and intralesional corticosteroids, and cyclophosphamide may also be beneficial. Although not a typical feature, there are reports of EED occurring in association with oral ulceration. It has been proposed that this may represent an overlap with the other neutrophilic dermatoses, Sweet syndrome and Behçet disease, in which oropharyngeal ulceration is commonly observed. Taking into account the 6-month period between endoscopic visualizations of the pharynx and history of the patient suffering exacerbations of his oral lesions at a similar time to his skin disease, we postulate that ulceration and destruction of the uvula are a result of the patient’s EED.

This case highlights the importance of screening patients for underlying hematologic disease when the diagnosis of EED is established. In addition, we report an unusual case of EED associated with absence of the uvula.

Granulomatosis with polyangiitis is another condition of autoimmune etiology that may present with LCV and pyoderma gangrenosum—like lesions and severe oropharyngeal ulceration. However, a negative antineutrophil cytoplasmic antibody test, normal renal function, and unremarkable thoracic imaging make this diagnosis unlikely. This patient displayed features associated with a number of neutrophilic dermatoses including EED, Sweet syndrome, Behçet disease, and pyoderma gangrenosum, all of which may be associated with hematologic disorders—particularly IgA gammopathy. This case suggests that an overlap syndrome between the neutrophilic dermatoses may exist, potentially making the establishment of the correct diagnosis even more challenging.

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