

Erythema Elevatum Diutinum - Two Case Reports, Two Different Clinical Presentations, and a Short Literature Review

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Abstract

Citation: Wollina U, Krönert C, Koch A, Schönlebe J, Vojvodic A, Lotti T. Erythema Diutinum - Two Case Reports, Two Different Clinical Presentations, and a Short Literature Review. Open Access Maced J Med Sci. <https://doi.org/10.3889/oamjms.2019.765>

Keywords: Leukocytoclastic vasculitis; Infections; Autoimmune disorders; Hematologic disorders; Dapsone; Erythema elevatum diutinum

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Received: 18-Apr-2019; **Revised:** 04-Jul-2019; **Accepted:** 05-Jul-2019; **Online first:** 30-Aug-2019

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Funding: This research did not receive any financial support

Competing Interests: The authors have declared that no competing interests exist

BACKGROUND: Erythema elevatum diutinum (EED) belongs to the spectrum of cutaneous leukocytoclastic vasculitides. EED is a very rare dermatosis presenting with reddish to brownish papules and plaques. EED may be associated with infections, hematologic and autoimmune disorders.

CASE REPORTS: We present two patients with EED, a 50-year-old woman and a 42-year-old man. While the woman shows an association with colitis ulcerosa, the man had an anti-thrombin deficiency. Treatment was started with oral corticosteroid and dapsone, respectively. In both cases, there was a partial and temporary response.

CONCLUSIONS: EED is a rare vasculitis with an unusual clinical presentation and a chronic course. Response to treatment is unsatisfactory and in the long-term run sometimes frustrating.

Introduction

Erythema elevatum diutinum (EED) belongs to the heterogeneous group of cutaneous leukocytoclastic vasculitides. It is a rare disorder, with less than 150 cases reported worldwide. It runs a chronic course with a fluctuating severity [1].

The characteristic clinical features are often symptomless plaques and nodules with a preference of extensor areas. There is neither a racial nor gender preference. The peak incidence seems to be in the fourth to the sixth decade [2].

Histologically, the disease is a leuko-

cytotoxic vasculitis of the mid and upper dermis. Polymorphonuclear cells, macrophages, histiocytes dominate the infiltrate. Some eosinophils may be present. In the early stage, there is papillary oedema causing pseudo-vesiculation. In long-standing lesions, dermal vessels become dilated with hypertrophic and sometimes protruding endothelial cells. Sometimes nodular lesions may be present containing spindle cells which are expressing Mac-387. Immune complexes may become deposited, and granulomas can appear [3], [4].

Infections have been associated with EED such as human deficiency virus and AIDS, hepatitis B or syphilis [5], [6]. There are several reports on the

association of EED with haematological disorders such as clonal gammopathy, or autoimmune connective tissue diseases like lupus erythematosus, dermatomyositis, chronic inflammatory bowel disease, Wegener's granulomatosis or relapsing polychondritis [2]. Cocaine adulterated with levamisole can induce an EED-like vasculitis [7].

Case Report

Case 1

A 50-years-old woman presented with chronic plaques on the extensor surface of both hands for four years. Sometimes, she noted swelling of the hands or suggillations into the plaques. She suffered from colitis ulcerosa. More than 10 years ago a colectomy had been performed. She was treated with ispaghula (Psylla seeds), loperamide, tolterodine tartrate, and topical intra-anal corticosteroid foam.

On examination, we observed multiple erythematous-livid nodules and plaques of a relatively soft consistency on the back of her hands (Figure 1).



Figure 1: Erythema elevatum diutinum late-stage lesion on the hands (case 1)

Laboratory investigations: Anti-thrombin was reduced with 54% (normal range: 75-125), slightly increased were gamma globulins 13.5% (7.2-11.3) and lactate dehydrogenase 3.85 μ kat/L (2.25-3.55). Negative or in the normal range were an immune fixation, HIV-antibodies, cardiolipin antibodies, and rheumatoid factor.

Imaging (endo-sonography, sigmoidoscopy, abdominal magnetic resonance imaging (MRI)) was unremarkable, except for a pouchitis.

Histopathology from a skin biopsy revealed increased vascularity (mainly post-capillary venules) embedded in a slightly fibrotic connective tissue. Perivascular infiltrates consisted of lymphocytes, monocytes, and some neutrophils (Figure 2).

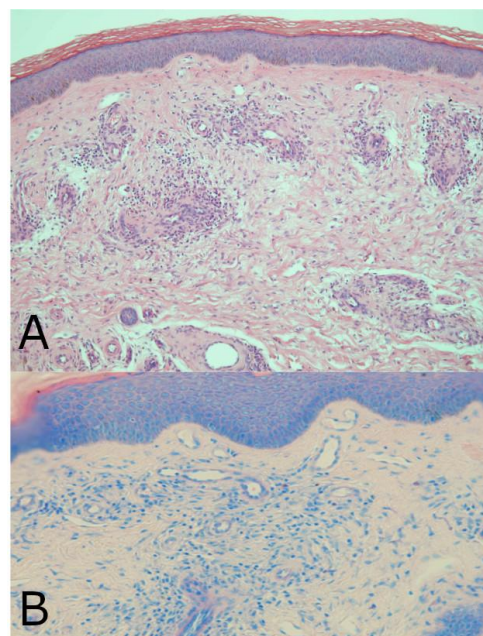


Figure 2: Histopathology of erythema elevatum diutinum (Case 1); A) Hematoxylin-eosin (x 10); B) Giemsa stain (x 20)

The findings were interpreted as a late stage of EED. We compared our findings with an external histopathology report 3 years ago, where the lesions demonstrated the characteristic leukocytoclastic vasculitis signs.

We initiated oral treatment with methylprednisolone 32 mg/day and topical treatment with clobetasol 0.05% ointment. The lesions became flatter, but the patient developed arterial hypertension and headaches. The internal corticosteroid therapy was stopped. Neither cyclosporine A nor methotrexate were effective. Dapsone 100 mg/day was not tolerated due to increased meth-haemoglobin levels.

Case 2

Two years ago, a 42-years-old man developed some papules on the knees with minimal pruritus. Dark red and livid papules and plaques appeared on arms. The course was characterized by waxing and waning. His medical history was otherwise unremarkable. He had no medical drug treatment.

On examination, we observed multiple erythematous to brownish asymptomatic papules on the extremities (knees, forearms, elbows, and back of the hands). The maximum diameter was 2 cm. Some of the lesions disappeared, leaving atrophic scars (Figure 3).

A skin biopsy demonstrated upper dermal leukocytoclastic vasculitis and massive neutrophilic nuclear debris and discrete extravasates of erythrocytes.

Laboratory investigations were unremarkable. Antinuclear antibodies, paraproteins, and anti-

streptolysin titer were negative.



Figure 3: Erythema elevatum diutinum – earlier lesions (Case 2)

The diagnosis of EED was confirmed.

We initiated oral treatment with dapsons 100 mg/day. Lesions showed regression leaving hyperpigmented scars. After dose reduction, a partial relapse was observed, and the dose was increased to 100 mg per day.

Discussion

EED is a rare leukocytoclastic vasculitis of the mid and upper dermis, that can be associated with underlying disorders like autoimmune diseases, haematological conditions or chronic infections [1], [2]. It has a good prognosis in contrast to systemic leukocytoclastic vasculitides although the course is chronic [8].

We report on EED with two different clinical patterns – A) the classical nodules and plaques overlying the joints of upper extremities and B) disseminated papules on legs and arms. Rarely, vesicobullous lesions have been reported suggesting Sweet syndrome [9].

The course of the disease is characterized by chronicity with waxing and waning of lesions. We presented a late-stage and an earlier stage of EED. The characteristics of leukocytoclastic vasculitis are seen in earlier lesions with prominent endothelial cells, but they get lost, and the perivascular connective tissue becomes fibrotic [3], [4].

The most commonly used therapy is oral dapsons, with a response rate of up to 80%. The drug inhibits neutrophil chemotaxis and function. A complete resolution is not always possible. In nodular lesions, this drug has only limited efficacy. Many patients with nodules do not respond [2].

Dapsons is contraindicated in patients with a

glucose-6-phosphate deficiency where it can cause severe hemolytic anaemia. Dapsons hypersensitivity is another important adverse effect. Pancytopenia has occasionally been observed [10],

Second-line therapies are systemic corticosteroids, colchicine, methotrexate, chloroquine and anti-retroviral drugs in case of HIV-associated EED. Antimicrobials with suppressive effects on neutrophils such as tetracyclines, erythromycin or sulfonamides have been used in single cases with success. Nicotinamide may be used in combination with tetracyclines or as a single drug. Topical therapy with corticosteroids, retinoids or dapsons is of limited value [11].

In conclusion, EED is part of the spectrum of leukocytoclastic vasculitides of skin. Although the lesions are commonly asymptomatic, they are disfiguring, and treatment is demanded. Based on experience, dapsons is the most often used drug. In the long-term run, however, medical treatment of EED is unsatisfactory and sometimes frustrating.

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