

Erythema elevatum diutinum as a differential diagnosis of rheumatic diseases: case report

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ABSTRACT

Erythema elevatum diutinum is a chronic and rare cutaneous leukocytoclastic vasculitis, characterized by red, purple and yellow papules, plaques and nodules, distributed symmetrically on the extensor surfaces of the limbs. It is associated with several autoimmune, neoplastic and infectious processes, mainly hematological malignancies in about 30% of the cases. Joint pain and arthritis are frequent symptoms, affecting approximately 40% of the patients, indicating the need for its inclusion in the differential diagnosis of rheumatic diseases, chiefly the other presentations of leukocytoclastic vasculitis, which are characterized by the combination of rheumatic manifestations and peculiar cutaneous lesions. We report the case of an 18-year-old female patient who developed erythema elevatum diutinum and whose diagnosis was based on the morphologic characteristics, the distribution pattern of the cutaneous lesions and the histopathological findings of leukocytoclastic vasculitis. The major systemic symptom was severe arthritis.

Keywords: arthritis, dapsone, skin diseases, erythema, vasculitis.

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INTRODUCTION

Erythema elevatum diutinum (EED) is a chronic and rare dermatosis, considered a variant of leukocytoclastic vasculitis. It was originally described by Hutchinson¹ in 1888 and Bury² in 1889. The name EED, however, was used for the first time by Radcliffe-Crocker et al.,³ who found similarities between the clinical findings of their patients and the cases described by Hutchinson and Bury. The name EED is due to the characteristics of the cutaneous lesions, which are red (erythema), elevated (*elevatum*, in Latin) and persistent (*diutinum*, in Latin), and tend towards a symmetrical distribution on the extensor surfaces of the joints of the limbs and buttocks.⁴

EED etiology remains unknown. It is believed to be mediated by the deposition of circulating immune complexes in the perivascular dermis, secondary to streptococcal infections and

hematological or autoimmune diseases, inducing an inflammatory cascade that damages the vascular walls, resulting in fibrosis.⁵

Erythema elevatum diutinum can occur at any age. Its incidence peaks between the third and sixth decades of life, and few cases have been reported in pediatric patients. Erythema elevatum diutinum is equally seen in both genders. In women, it usually occurs at an earlier age and is accompanied by a rheumatologic disease.⁶

Joint pain is the most common symptom, observed in up to 40% of the cases.⁷ Erythema elevatum diutinum can also be associated with important arthritis and an elevation in the inflammatory activity assays, and should always be considered in the differential diagnosis of rheumatologic diseases.

We report the case of an 18-year-old female patient, whose cutaneous lesions had morphological characteristics, distribution pattern and histopathology of a leukocytoclastic vasculitis.

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The findings were consistent with the diagnosis of EED, in which the major systemic complaint was severe arthritis in the wrists, elbows, and knees.

CASE REPORT

The patient is an 18-year-old white female, single, student, referred to rheumatologic assessment due to polyarthritis associated with Raynaud's phenomenon and cutaneous lesions in upper and lower limbs for three years. The patient denied the use of any medication prior to the clinical findings.

On physical examination, her wrist, elbow and knee joints were warm and showed erythema, edema, and pain. The cutaneous lesions were characterized by persistent erythematous, purplish to brownish papules and plaques, symmetrically distributed on the dorsal feet, legs, buttocks, and extensor surfaces of the metacarpophalangeal joints, wrists, elbows, and knees. Erythematous, purplish plaques of xanthomatous aspect were observed on her anterior legs (Figure 1). The patient reported being treated with prednisone (40 mg/day) and non-steroidal anti-inflammatory drugs for five months with little improvement of the cutaneous and articular findings.

The diagnosis of EED was proposed on joint assessment with the service of dermatology, and the following complementary exams were ordered: complete blood count; platelet count; biochemistry; liver and kidney function; fasting glycemia; total cholesterol and fractions; serum triglycerides; glucose 6-phosphate dehydrogenase; creatine phosphokinase; lactic dehydrogenase; VDRL; ASO; thyroid hormones; serology for HIV and hepatitis; rheumatoid factor; Waaler-Rose test; antinuclear antibodies; autoantibodies (anti-Ro, anti-La, anti-DNA and anti-RNP antibodies); cryoglobulins and cryoagglutinins; chest radiography; and computed tomography of the facial sinuses. All those tests were within the normal range. However, increased inflammatory activity (erythrocyte sedimentation rate of 66 mm in the first hour, and C-reactive protein of 10.91 mg/L), positive P-ANCA (titer of 1:40), and gamma-globulin peak (30%) on protein electrophoresis were observed.

The histopathological examination of the left leg lesion showed a focal area of epidermal necrosis, and, on the superficial and deep dermis, perivascular inflammatory infiltrate composed of lymphocytes, neutrophils, and eosinophils, in addition to endothelial neutrophilic infiltrate, leukocytoclasia, and red blood cell leakage (Figure 2). These are histological findings of a leukocytoclastic vasculitis.

Then, treatment with dapsone (100 mg/day) and prednisone (20 mg/day) was initiated, which resulted in partial improvement of the articular symptoms and cutaneous lesions after three months of treatment. Some lesions on the metacarpophalangeal joints of both hands and on the dorsal feet persisted. Residual hyperpigmentation persisted on the extensor surfaces of her wrists, elbows, and knees.



Figure 1
Brownish and purplish papulonodular lesions and erythematous and purplish plaques on the anterior region of the lower limbs.

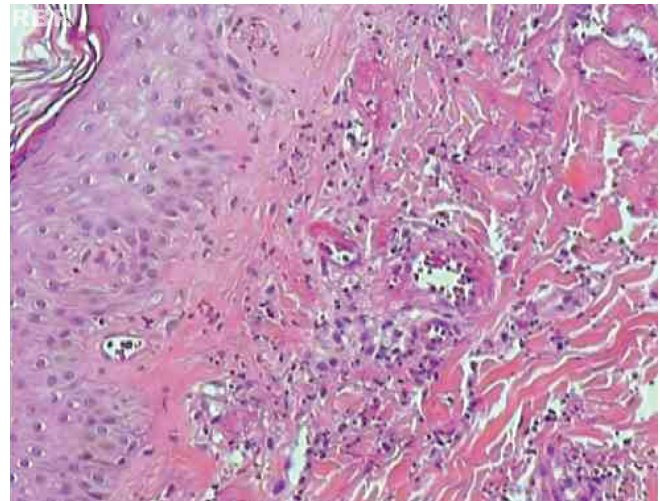


Figure 2
Leukocytoclastic vasculitis. Epidermis with no changes. In the dermis, disperse and perivascular infiltrate is seen, composed predominantly of neutrophils, some lymphocytes and eosinophils, associated with nuclear fragmentation (leukocytoclasia), in addition to endothelial neutrophilic infiltrate. The dermal vessels show edema of the endothelial cells and markedly eosinophilic deposits in their walls, compatible with fibrinoid degeneration. Mild red blood cell leakage is seen. (hematoxylin-eosin – 100x).

DISCUSSION

Erythema elevatum diutinum is a chronic and rare disease that manifests with erythematous and purplish plaques, papules and nodules, which, most of the time, have a symmetrical and persistent distribution, preferentially on the extensor surfaces of the hands, feet, elbows, and knees, in addition to buttocks, legs and Achilles tendons. The initial lesions tend to be soft, but, over time, they become hard and firm, reflecting their tendency towards fibrosis.⁸ Our patient had lesions with the typical distribution pattern (buttocks and the extensor surface of the joints of the hands, elbows, and knees), in addition to purplish and brownish lesions on the lower limbs.

Less commonly, atypical distribution of the cutaneous lesions have been reported on the trunk, retroauricular region, palms, and soles.⁹ Burnett et al.¹⁰ have reported the possibility of exacerbation of the cutaneous lesions with concomitant bacterial infection.

Usually the patient's general state of health is not affected, and the systemic involvement is almost inexistent.⁴ Joint pain is the most common systemic symptom, and there have been reports of severe and vesperine burning pain in the cutaneous areas involved, pruritus, and constitutional symptoms.⁷ In our case, there was important arthritis in the wrists, elbows, and knees, and Raynaud's phenomenon in association with an elevation in the inflammatory activity assays (erythrocyte sedimentation rate and C-reactive protein), requiring the differential diagnosis with several rheumatological diseases that have a similar course.

Hematological malignancies, present in approximately 30% of the cases, of which the most frequent is IgA monoclonal gammopathy, are considered the most commonly associated factors.^{11,12} The hematological anomaly of the patient reported was a gamma globulin peak of 30%.

Association of that vasculitis with neoplastic, autoimmune and infectious diseases has been reported, especially with the acquired immunodeficiency virus infection. In the latter, the clinical presentation can differ, with the presence of nodular lesions and palmoplantar involvement.¹⁰

The major rheumatological diseases reported in association with EED are as follows: rheumatoid arthritis; relapsing polychondritis; systemic lupus erythematosus; Sjögren's syndrome; and juvenile idiopathic arthritis.^{4,8,13} Such associations are most often seen in young female patients.⁶ Although no rheumatological disease was characterized in the case reported, arthritis was severe and caused patient's initial consultation.

The histopathologic findings are not pathognomonic, although they can be highly suggestive.⁴ The early lesions of EED evidence signs of a leukocytoclastic vasculitis, with fibrin, neutrophils and fragments of neutrophils in the wall of small vessels of the middle and superficial dermis.^{13,14} All such elements are compatible with the description of our patient's histopathologic findings. In late lesions, the findings include the combination of granulation or scar tissue along with proliferation of fusiform cells in the dermis, and the possible association with multinucleated giant cells. The deposition of circulating immune complexes in perivascular dermis triggers the inflammatory cascade, which causes vascular injury and consequent fibrosis.^{9,11}

Some rheumatological diseases, such as Behçet's disease, cryoglobulinemic vasculitis, Henoch-Schönlein purpura, and hypersensitivity vasculitis, can show the histopathologic findings of leukocytoclastic vasculitis in association with characteristic cutaneous manifestations, and should always be considered in the differential diagnosis of EED. The typical distribution pattern of the skin lesions in that pathology helps to confirm the diagnosis.⁸

EED treatment is difficult because of the chronic and recurring course of the disease.⁹ The most efficient treatment is with dapsone.^{14,15} Dapsone's exact mechanism of action is not completely known, but that drug is known to stabilize the lysosomes of neutrophils or interfere with the deposition of complement factor 3. Other hypotheses about dapsone's mechanism of action are: suppression of the excessive chemotactic activity of neutrophils; inhibition of cytotoxicity of neutrophils; decrease in the concentration of inflammation-induced oxygen intermediates; and inhibition of prostaglandins D2, which are vasoactive and increase the chemotactic potential of leukotrienes B4.⁴

When resistance to dapsone occurs, some therapeutic options are as follows: colchicine; niacinamide associated with tetracycline; systemic corticosteroids; and even intermittent plasma exchange in cases associated with IgA paraproteinemia.^{8,13}

Although the lesions are characteristically persistent, EED course is variable and unpredictable, with reports of spontaneous resolution without relapse and cases of recurrence in previously involved sites.¹⁰ With the regression of the lesions, residual hyperpigmentation with occasional atrophy is commonly seen.⁴

We report a case of EED, a chronic and rare form of leukocytoclastic vasculitis, whose diagnosis should be always considered in patients with rheumatological complaints associated with characteristic cutaneous manifestations and compatible histopathology.

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