

Leukocytoclastic Vasculitis as an Onset Symptom of Crohn's Disease

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Key Words

Leukocytoclastic vasculitis · Crohn's disease

Abstract

We report the case of an octagenarian who presented with leukocytoclastic vasculitis as the first symptom of Crohn's disease. The patient was admitted with skin rash on the lower extremities and ankles and episodes of bloody diarrhea. Skin and colon biopsies revealed acute leukocytoclastic vasculitis and moderate Crohn's disease, respectively. The patient was treated with intravenous corticosteroids in conjunction with antibiotics and per os mesalazine. Symptoms resolved rapidly within 5 days, and the patient was still asymptomatic on follow-up 3 months later.

Introduction

Extraintestinal manifestations of inflammatory bowel disease (IBD) can be found in 21–36% of affected patients [1]. One third of these patients, preferably those with colonic involvement, reveal skin symptoms [2]. An increased variety of skin lesions usually develop during the course of the disease, while approximately 10% of IBD patients show cutaneous manifestations at the time of diagnosis. These are generally secondary to granulomatous cutaneous disease, reactive skin eruptions, nutritional deficiency and other associated conditions [3].

Apart from the most common cutaneous manifestations that develop in IBD, such as pyoderma gangrenosum (1–2%) and erythema nodosum (3–8%), leukocytoclastic vasculitis is one of the least reported skin lesions that seem to be linked to IBD [3]. Leukocytoclastic vasculitis is a disorder characterized by neutrophilic infiltration and nuclear debris in postcapillary venules [4] and it is believed that it is an immune complex

one [5]. The skin presentation of this type of vasculitis may vary from palpable purpura to necrotic ulcers.

Here we report the case of an octagenarian who presented with leukocytoclastic vasculitis as the first symptom of Crohn's disease (CD). We also review the literature for cases reporting an association between this type of vasculitis and IBD.

Case Report

An 80-year-old white male was initially admitted to the dermatology department complaining of skin rash on the lower extremities and ankles, nonspecific arthralgias and low-grade fever lasting for two months. A week before his admission, a corticosteroid cream had been applied for the skin rash without marked improvement. During his hospitalization he presented episodes of bloody diarrhea and he was transferred to our department in order to investigate the etiology of the diarrhea.

His medical history included chronic obstructive pulmonary disease due to a left partial lobectomy (5 years earlier) and an amputated left arm due to a road traffic accident (10 years earlier). On admission he was hemodynamically stable and the low-grade fever (37.8°C) was confirmed. During physical examination a mild tenderness on the left lower quadrant was found. Skin examination revealed maculopapular purpura with areas of skin hyperpigmentation. On day one, the dermatologists performed a skin biopsy in order to clarify the nature of these lesions (differential diagnosis: hypersensitivity, allergic or leukocytoclastic or septic vasculitis).

The first laboratory results in our ward were indicative of acute inflammation (elevated CRP, ESR, and fibrinogen). Complete blood count, urinalysis, biochemistry, and prothrombin time were normal. Stools, skin, and blood cultures were also negative. Fecal leukocytes and erythrocytes were noted on microscopic examination of the stools and therefore serum antibodies against *Yersinia pseudotuberculosis* and *Yersinia enterocolitica* were examined. The results revealed an old infection. The complement components C3, C4, serum immunoglobulin electrophoresis, and cancer markers were normal; Rose-Bengal, Wright, rheumatoid factor, cryoglobulins, ANA, anti-DNA, ANCA, and PPD test were negative. Hepatitis B and C virus markers were absent. Plain abdominal X-ray was normal. Abdominal ultrasound showed thickening of the intestinal loops and lack of peristalsis. Thus an emergency colonoscopy was carried out. A punctuate congested mucosa with superficial ulceration was observed and five biopsy specimens were taken.

Five days after admission, skin and colon biopsies revealed acute leukocytoclastic vasculitis (neutrophilic infiltration, necrosis of vessel wall, perivascular fibrinoid deposition) (fig. 1) and moderate CD (cryptitis – crypt abscesses), respectively. Therefore the patient received corticosteroids (50 mg i.v. prednisolone) in conjunction with antibiotics (500 mg i.v. ciprofloxacin bid) and per os mesalazine (500 mg tid). Five days after treatment administration, the diarrhea subsided and the skin rash disappeared. He was discharged with per os 30 mg prednisolone (on a slow tapering rate) and 500 mg tid mesalazine. On follow-up 3 months later, the patient was only on mesalazine and asymptomatic.

Discussion

Leukocytoclastic vasculitis is a form of vasculitis affecting postcapillary venules with the histopathological findings of endothelial swelling, neutrophilic invasion of blood vessel walls, leukocytoclasia (karyorrhexis of nuclei of neutrophils), extravasation of erythrocytes and fibrinoid necrosis of blood vessel walls [4]. It appears on the skin of dependent sites as crops of palpable purpura and is mostly mediated by deposition of immune complexes in postcapillary venules (immune complex vasculitis of small vessels). In the majority of patients the precipitating cause is unidentifiable, but association with drugs, infections (e.g. hepatitis B) or immune complex diseases (e.g. collagen vascular diseases, cancer) should be first excluded [5].

The pathogenetic mechanisms underlying leukocytoclastic vasculitis in patients with IBD remain still unclear. Direct colonic bacterial dissemination of the skin via a hematogenous pathway could explain the onset of skin lesions with the exacerbation and/or onset of active bowel disease. In genetically predisposed IBD patients, alternate pathophysiological mechanisms including the mechanism of immune complex formation in the axis of the inflamed mucosal barrier-immunity [6] and the mechanisms of ‘antigen mimicry’ [7] could be suggested. The former mechanism is frequently revealed by direct immunofluorescence of early lesions by the presence of IgM, IgG and C3 within the walls of small vessels in the upper dermis [8, 9]. On the other hand, the antigen mimicry as a modified immune response to bacteria or other local factors may trigger the activation of T-cell-mediated injury (proinflammatory cytokines) and the secretion of autoantibodies against shared antigens. In this connection a colonic epithelial protein and the human tropomyosin isoform 5, which are shared by different extraintestinal sites including the skin, seem to be the most important targets of the autoimmune attack [10].

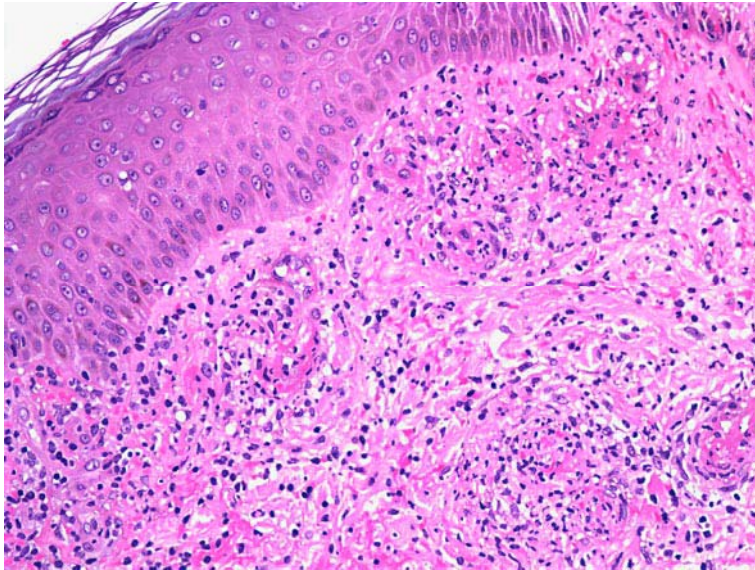
Reviewing the literature, four reports of leukocytoclastic vasculitis (based on a detailed histopathological diagnosis) in association with CD have been found [11–14]. In two of them there was a correlation between the onset of vasculitis and the exacerbation of CD [11, 13], whereas no association was found in the other two cases. To our knowledge, this is the first case reporting leukocytoclastic vasculitis as the initial manifestation of CD. It is apparent that this skin manifestation antedates the onset of CD, although in all the aforementioned cases CD preceded the occurrence of vasculitis. There was no need for specific therapy as the therapeutic management of the underlying CD resulted in resolution of the vasculitis.

Four additional patients with CD have been reported with cutaneous vasculitis of presumed leukocytoclastic type as there was no histological confirmation [15–17]. Among these cases, there was a female pediatric patient who was diagnosed with cutaneous vasculitis secondary to septic thromboembolism as the first symptom of her CD. This skin lesion resolved simultaneously with the resolution of the flare of the CD [17].

Apart from CD, leukocytoclastic vasculitis has also been reported in four patients with ulcerative colitis. In these cases, the cutaneous lesions always preceded the intestinal symptoms with different lag periods, in contrast to CD, where the extraintestinal cutaneous manifestations appear not only as onset symptoms but also during exacerbation periods of the disease [18–20].

In conclusion, we report the case of an elderly patient who presented with leukocytoclastic vasculitis as the first symptom of CD. Although the pathophysiological mechanisms of this rare skin complication are unclear, we observed that the lesion resolved after treatment of the underlying disease.

Fig. 1. Pathology examination: skin biopsies showed neutrophilic infiltration, necrosis of vessel wall and perivascular fibrinoid deposition (acute leukocytoclastic vasculitis).



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