Leukocytoclastic vasculitis with features of flagellate purpura: a comparison with flagellate erythema

Antonio Ji-Xu[1,2] MA BM BCh, Kushal Mansatta[2] BA BM BCh, Radhika Bali[2] MA MB BChir, Carine J Moezinia[3] MBBS

Affiliations: [1]Department of Dermatology, University of California Davis, Sacramento, California, USA, [2]Oxford University National Health Service Hospitals Foundation Trust, Oxford, United Kingdom, [3]University College London Centre for Rheumatology and Connective Tissue Diseases, Royal Free London National Health Service Foundation Trust, London, United Kingdom

Corresponding Author: Carine Moezinia, University College London Centre for Rheumatology and Connective Tissue Diseases, Royal Free London National Health Service Foundation Trust, London, NW3 2QG, United Kingdom, Tel: 44-20-7794-0500, Email: cmoezinia@gmail.com

Abstract

Leukocytoclastic vasculitis is a histopathologic term describing a type of small-vessel vasculitis characterized by a predominantly neutrophilic inflammatory infiltrate and nuclear debris. Skin involvement is common and can have a heterogeneous clinical presentation. Herein, we describe a 76-year-old woman with no history of chemotherapy or recent mushroom ingestion that presented with focal areas of flagellate purpura secondary to bacteremia. Histopathology revealed leukocytoclastic vasculitis and her rash resolved after antibiotic treatment. It is important to distinguish flagellate purpura from a similar condition, flagellate erythema, as they have been reported in association with distinct etiological and histopathological features.

Keywords: bacteremia, flagellate purpura, leukocytoclastic vasculitis

Introduction

Leukocytoclastic vasculitis is a histopathologic term that describes a form of small-vessel vasculitis in which the inflammatory infiltrate is predominantly neutrophilic [1,2]. Cutaneous involvement is frequent and can manifest as a wide spectrum of morphologies [1,2]. When presenting as flagellate purpura, leukocytoclastic vasculitis typically presents as an eruption characterized by "whip-like," palpable purple or violaceous streaks or plaques that are typically nonblanchable. It is important to differentiate this clinically from flagellate erythema, which presents with pink to red-brown streaks that are typically blanchable [3,4]. Herein, we describe a patient with bacteremia-triggered leukocytoclastic vasculitis, which presented clinically with focal areas of flagellate purpura. Furthermore, we compare the reported clinical, etiologic, and histopathologic features of flagellate purpura and flagellate erythema.

Case Synopsis

A 76-year-old woman presented with a one-week history of fever, cough, shortness of breath, malaise, and a pruritic rash on the trunk and bilateral upper and lower limbs. She denied recent ingestion of mushrooms, initiation of new medications in the prior three months, or contact with new products or plants. Past medical history included congestive heart failure, atrial fibrillation, chronic kidney disease, and hepatic cirrhosis. Medications included bisoprolol, spironolactone, and furosemide. Examination revealed whip-like curvilinear purpuric plaques on the upper limbs, abdomen, and back, along with purpuric papules and plaques on the lower limbs (**Figure 1**). There was facial sparing. Systemic examination showed crackles on the left lower lung but was otherwise unremarkable.

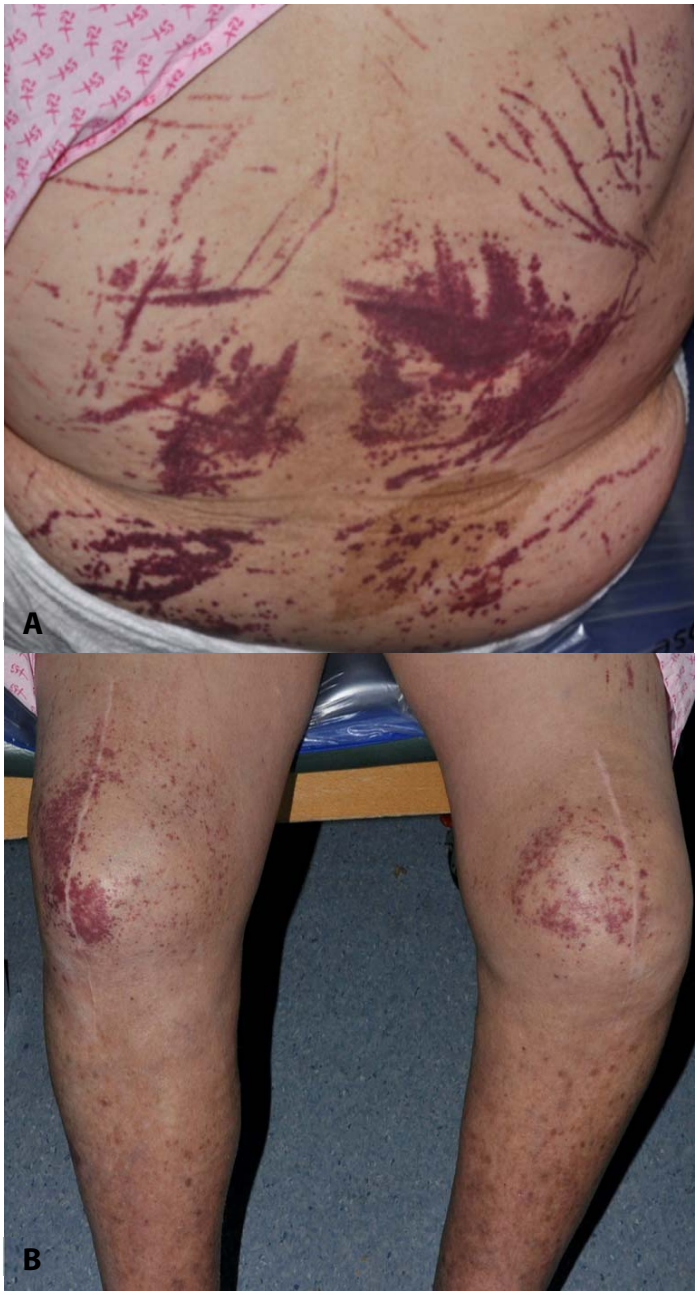

Figure 1. ***A)*** *Whip-like curvilinear purpuric papules plaques on the back.* ***B)*** *Purpuric papules and plaques on the lower limbs.*

Laboratory investigations showed anemia, leukocytosis, and raised inflammatory markers. Three sets of blood cultures were positive for *Streptococcus gallolyticus*. Respiratory viral panel, viral serology, serum antinuclear antibody (ANA), extractable nuclear antigen (ENA) panel, antineutrophil cytoplasmic antibody (ANCA), and dermatomyositis antibody panel were negative. Creatine kinase and tumor markers were normal. Computerized tomography (CT) of the chest, abdomen, and pelvis showed infective consolidation in the left lower lobe of the lung but no ascites or malignancy. Echocardiogram, colonoscopy, and liver and transvaginal ultrasounds showed no acute pathology or malignancy.

Punch biopsies revealed a dense neutrophilic infiltrate in the dermis with leukocytoclasis, focal fibrinoid necrosis, and red cell extravasation in small-sized vessels, consistent with leukocytoclastic vasculitis (**Figure 2**). Immunofluorescence studies revealed deposition of IgA, IgG, and fibrinogen in the superficial vessel walls. Therefore, she was diagnosed with leukocytoclastic vasculitis presenting clinically with focal areas of flagellate purpura. She was treated with intravenous ceftriaxone, oral azithromycin, and mometasone furoate 0.1% ointment for one week, which resulted in marked clinical improvement with complete resolution of the rash, normalization of inflammatory markers, and negative repeat blood cultures.

Case Discussion

Herein, we report flagellate purpura as a possible clinical manifestation of leukocytoclastic vasculitis. Leukocytoclastic vasculitis results from the disruption of small vessel walls by deposition of immune complexes and activation of the complement cascade [2]. On histology, this is seen as

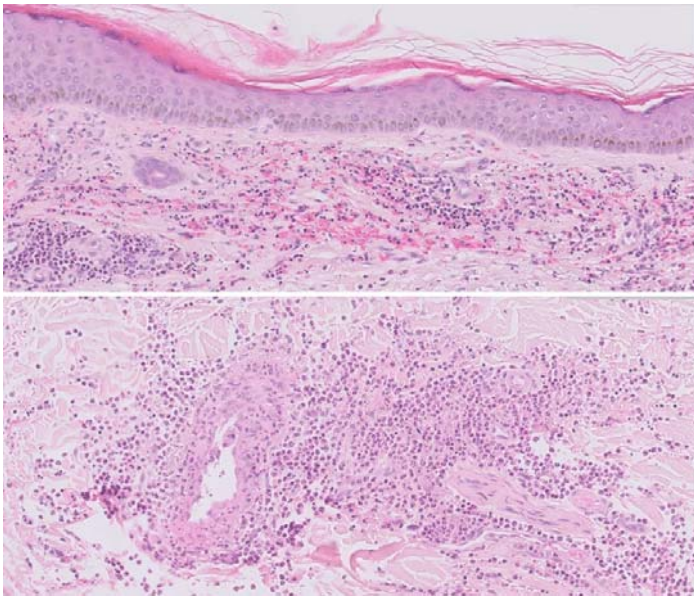

Figure 2. *H&E stain of a punch biopsy from the mid back, showing superficial dermis with a predominantly perivascular neutrophilic infiltrate and associated red blood cell extravasation, 20×.*

Table 1. *Comparison of the etiologic, clinical, and histopathologic features of flagellate purpura and flagellate erythema.*

	Flagellate purpura	Flagellate erythema
Clinical presentation	- Whip-like linear or curvilinear purplish streaks	- Whip-like linear or curvilinear pink or red streaks - May present with darker pigmentation in skin of color
Reported etiologies	- Leukocytoclastic vasculitis - ChAdOx1-S COVID-19 vaccination	- Antineoplastics (bleomycin, peplomycin, bendamustine, trastuzumab) - Shiitake mushrooms - Dermatomyositis - Adult-onset Still disease - Systemic sclerosis - Chikungunya fever - Parvovirus B19 - *Mycoplasma pneumoniae*
Reported histopathologic features	- Leukocytoclastic vasculitis: perivascular neutrophilic infiltrate, fragmented neutrophilic nuclei, fibrinoid necrosis of vessel walls, red blood cell extravasation - ChAdOX1-S COVID-19 vaccination: perivascular lymphocytic infiltrate with red blood cell extravasation and perifollicular fibrosis	- Subtle spongiosis and/or interface dermatitis - Dermal lymphocytic infiltrate with increased numbers of eosinophils - Lymphocytic vasculopathy seen in a subset of cases
Evaluation and management	- Obtain history of recent vaccination - If suggestive of systemic vasculitis, obtain CBC, CMP, ESR or CRP, ANA, complement, ANCA, viral hepatitis serology, urinalysis with urinary sediment, and blood cultures to exclude infection - Manage underlying condition	- Obtain history of shiitake mushrooms ingestion or antineoplastics - If suggestive symptoms and signs, investigate for associated connective tissue disease or infection - Manage underlying condition

ANA, antinuclear antibody; ANCA, antineutrophil cytoplasmic antibodies; CBC, complete blood count; CMP, comprehensive metabolic panel; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

a predominantly neutrophilic perivascular infiltrate, nuclear debris, and deposition of fibrin within the lumen of small vessels [1]. The management of skin-limited leukocytoclastic vasculitis is primarily supportive and consists of removal of inciting causes, leg elevation, and compression [5]. However, a short taper of prednisone or other immunosuppressants may be required for severe, widespread, or ulcerative or necrotic disease [5].

Flagellate purpura has also been described in association with other etiologies, including the AstraZeneca (ChAdOx1-S) COVID-19 vaccine [6], (**Table 1**). In contrast with our case, the onset of flagellate purpura was more acute in this patient, presenting four hours after the first dose of COVID-19 vaccine. Furthermore, histopathology revealed a perivascular lymphocytic infiltrate with red blood cell extravasation, but no evidence of vasculitis per se.

On the other hand, flagellate erythema is a rare eruption that presents with highly distinctive "whip-like" erythematous linear streaks. Although classically associated with bleomycin and shiitake mushroom consumption, it has since been reported in association with other antineoplastic agents [7,8], dermatomyositis [9], adult-onset Still disease [10], systemic sclerosis [11], chikungunya fever [12,13], parvovirus B19 infection [14], and *Mycoplasma pneumoniae* infection [15], (**Table 1**). The pathogenesis of flagellate erythema remains under debate. In the case of bleomycin-induced flagellate dermatitis, the characteristic linear markings are believed to relate to local vasodilation due to scratching, leading to subsequent aggregation of toxic metabolites and an accompanying inflammatory response [16,17]. The histopatho-logical features of flagellate erythema are variable,

but the most commonly reported findings include mild spongiosis, interface dermatitis, and a lymphocytic and eosinophilic perivascular infiltrate [3]. Flagellate erythema can be diagnosed by its distinct appearance along with a compatible history. Although the clinical appearance of flagellate erythema is characteristic, minor trauma, dermatographic urticaria, contact or photo-induced dermatitis, and Koebnerization can be considered in the differential diagnosis [4,18]. Similar to presentations of flagellate purpura, the underlying cause should be identified and treated if possible.

Conclusion

This report illustrates the heterogeneous clinical presentation of leukocytoclastic vasculitis, which includes flagellate purpura. In these cases, it is important to differentiate flagellate purpura from flagellate erythema, as these conditions have been reported in association with distinct etiologies and histopathological features in the literature.

Potential conflicts of interest

The authors declare no conflicts of interest

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