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Leukocytoclastic Vasculitis Following Ceftriaxone Exposure

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Abstract

Leukocytoclastic vasculitis (LCV) is an immune-complex mediated inflammation of dermal capillaries and venules that can occur after infections, drugs, autoimmune disorders, neoplasms, or idiopathically. We present the case of a 59-year-old male who was treated with ceftriaxone for an abscess, *S. aureus* cellulitis, and osteomyelitis of his right second toe. Biopsy confirmed the diagnosis of LCV and symptoms resolved after ceftriaxone was discontinued and systemic corticosteroids were introduced.

Keywords

Leukocytoclastic Vasculitis, Immune-Complex, Ceftriaxone, LCV

1. Introduction

Leukocytoclastic vasculitis (LCV) is an immune-complex mediated inflammation of dermal capillaries and venules with complement system activation. It can occur after infections, drugs, autoimmune disorders, neoplasms, or idiopathically. It typically presents with benign palpable purpura and erythematous macules along the dependent areas of the body with 30 percent of individuals having extracutaneous involvements. The cutaneous manifestations occur about one to three weeks after triggers and palpable purpura is a strong indication of cutaneous manifestation of LCV. Lesions are often asymptomatic but have also been described as pruritic with stinging or burning pain [1] [2] [3] [4]. Systemic symptoms may include fever, weight loss, malaise, arthralgia and myalgia. Most cases of LCV are mild and self-limited, resolving within weeks to months after

the removal of the offending agent. A biopsy with direct immunofluorescence is the gold standard for diagnosis, along with clinical suspicion [5]. Treatment depends on the time of diagnosis and the severity of the disease. Supportive care, including compression stockings, leg elevation, and antihistamines can be given, along with a tapering dose of corticosteroids, if necessary [2] [6].

LCV affects about 10 - 30 persons per million persons per year and is reported to be more common in white versus other races. It is also reported that it affects males and females in equal proportion. However, some studies in Spain suggest that LCV may slightly be more common in men than in women. LCV is known to have a good prognosis, however, with systemic involvement, morbidity increases, and mortality can occur [3]. LCV is commonly caused by drugs and infective conditions including but not limited to Hepatitis B, C, and Human Immunodeficiency Virus (HIV) [7]. We present a case of ceftriaxone-induced vasculitis which improved with discontinuation of offending medication and administration of corticosteroids.

Case report: A 59-year-old male presented to the emergency department(ED) with a two-week history of worsening right second toe pain with associated fever and chills several days prior to ED visit. The patient had a medical history of coronary artery disease, hypertension, hyperlipidemia, COPD, and peripheral neuropathy and had no known drug allergies. On examination, the patient was tachycardic and febrile. His right second toe was erythematous, warm, and tender to palpation with purulent drainage. Laboratory studies revealed leukocytosis with neutrophil predominance and an elevated lactic acid of 3.2. The patient received one dose each of vancomycin and piperacillin-tazobactam empirically and was admitted for a right second toe abscess, sepsis, and concern for osteomyelitis (**Table 1**).

On hospital day two, antibiotics were switched to ceftriaxone 1 g IV daily. An MRI revealed osteomyelitis of the right second toe and subsequent wound cultures grew methicillin-sensitive *Staphylococcus aureus* (MSSA). Subsequently, a partial amputation of the right distal second toe was performed. On the patient's ninth day of ceftriaxone, he developed a painful, pruritic disseminated petechial rash of the bilateral lower extremities. On examination, there were areas of non-blanchable, palpable purpura that were tender to palpation from the ankles to the knees with more lesions observed around the ankles (**Figure 1**). Topical triamcinolone 0.1% cream twice daily was prescribed with minimal relief. The following day, ceftriaxone was discontinued and ertapenem 1 g IV daily was started. Additionally, oral prednisone 40 mg daily was prescribed.

A 4-mm punch biopsy was performed due to worsening of the patient's rash and symptoms. The pathology report confirmed a diagnosis of leukocytoclastic vasculitis, revealing superficial and mid-dermal perivascular and interstitial mixed inflammatory cell infiltrate with eosin (from Hematoxylin and Eosin) giving it a bluish appearance (**Figure 2**), and evidence of nuclear dust from polymorphonuclear cells within the inflamed dermal vessels and crowded pool of extravasated erythrocytes with hematoxylin (from Hematoxylin and Eosin)

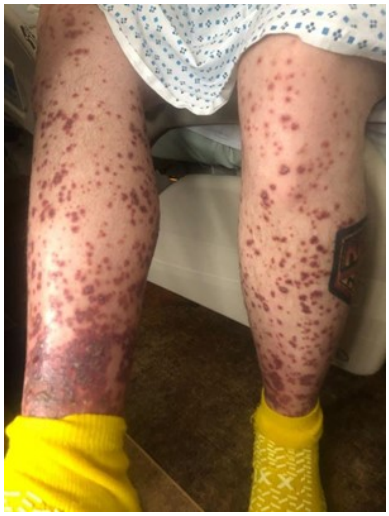

Figure 1. Initial presentation of non-blanchable, palpable purpura on the lower extremities.

Table 1. Summary of laboratory results.

Test	Result	Reference
ESR	30	0 - 20
CRP	4.9	0.00 - 0.3
CH50	36	>41
c-ANCA	<1.20	<1.20
Atypical p-ANCA	<1.20	<1.20
p-ANCA	<1.20	<1.20
Proteinase 3	<3.5	0.0 - 3.5
Myeloperoxidase Anbidody	<9.0	0.0 - 9.0
C3	157	82 - 167
C4	36	12 - 38
Cryoglobulin	none detected	none detected
Hepatitis B surface Antigen	negative	negative
Hepatitis B surface Antibody	non-reactive	non-reactive
Hepatitis Bs Antibody	negative	negative
Hepatitis B Total core Antibody	negative	negative
Hepatitis B core IgM Antibody	negative	negative
Hepatitis B effectivity Antibody	negative	negative
Hepatitis B effectivity Antigen	negative	negative
Rapid Plasma Reagent Titre	nonreactive	nonreactive
Hepatitis C Studies	unattainable due to insufficient sample	

giving it a light pink appearance (Figure 3). Prednisone 40 mg was increased to twice daily, with gradual improvement shortly thereafter. The patient was discharged on day seventeen with a one-week prescription of oral prednisone 40 mg twice daily. On a two-week follow-up, there was significant improvement in the appearance and symptoms of his rash.

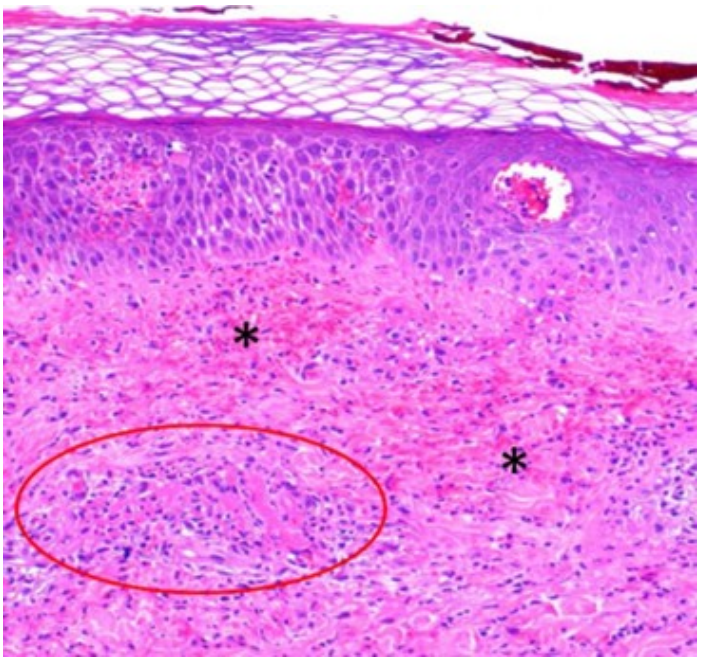

Figure 2. Superficial and mid dermal perivascular and interstitial mixed inflammatory cell infiltrate composed of lymphocytes, histiocytes, eosinophils, and numerous neutrophils, H & E. *Courtesy of Dr. Maria Laureana Santos-Zabala M.D.* ◯ (Red Circle): Inflamed dermal vessels.

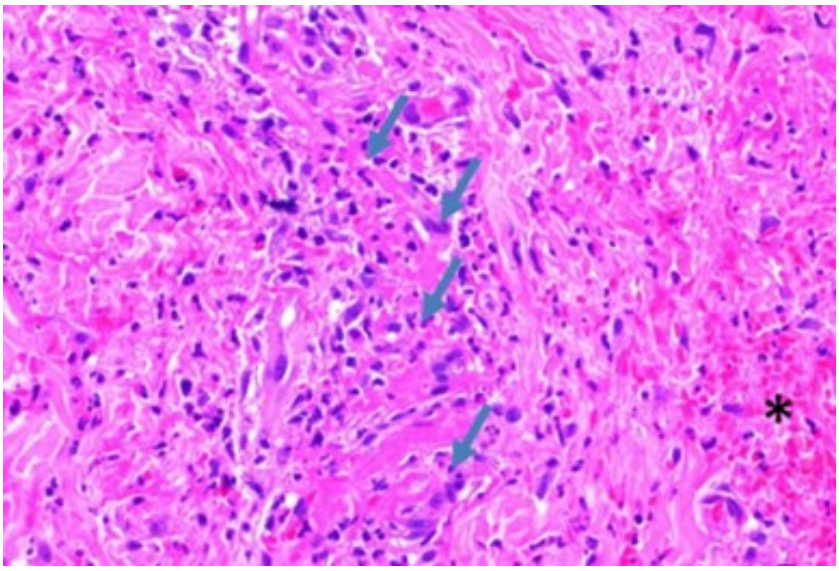

Figure 3. Nuclear dust, fibrin within dermal vessels, and extravasated erythrocytes, H & E. *Courtesy of Dr. Maria Laureana Santos-Zabala M.D.* ✱ (Black Asterisk): Extravasated erythrocytes. ↓ (Blue Arrow): Nuclear dust and fibrin within dermal vessels.

2. Discussion

Leukocytoclastic vasculitis occurs in approximately 45 million individuals each year.

Common secondary causes of LCV include beta-lactam antibiotics, however, there are only a few reported cases of ceftriaxone-induced LCV [6].

Ceftriaxone, a beta-lactam, third-generation cephalosporin antibiotic has been shown to be effective in the treatment for MSSA osteoarticular infections. It is one of the favorites for treatment of MSSA due to its once-daily dosing, low cost, and well tolerability [6]. In a retrospective, single-center matched cohort study of patients treated with ≥2 doses of ceftriaxone for infections including osteomyelitis, blood-stream infections, and acute bacterial skin infections at the VA St. Louis Health Care System between October 2010-March 2017, an adverse drug reaction occurred in 20% of patients. Of the 26,172 people who reported adverse effects of ceftriaxone on eHealthMe, which regularly updates drug side effects reported to the FDA, only 24 (0.09%) reported leukocytoclastic vasculitis after receiving ceftriaxone. The most common adverse reactions were eosinophilia (6%), followed by thrombocytopenia (4%), AKI (4%), transaminitis (2%), neutropenia (2%), and rash (2%). Only one patient required premature withdrawal of treatment due to an adverse reaction of neutropenia [8]. Of these patients, all experienced the onset of LCV within a month of drug use, 59% were male, and 65% of patients were over 50 years old [9]. Most cases of LCV vasculitis have a good prognosis and resolve with discontinuation of the offending agent. However, with systemic involvement, morbidity increases, and mortality can occur [3]

In our patient, we present a rare manifestation of ceftriaxone hypersensitivity. A case of Leukocytoclastic Vasculitis occurring on the ninth day of treatment with ceftriaxone and presenting with painful, pruritic disseminated petechial rash of bilateral lower extremities extending from the ankles to the knees. The patient's presentation, histological findings and other common differentials ruled out aligned with a diagnosis of LCV. While alternate causes were investigated, the patient did not have any evidence of any other viral infection, autoimmune disease, or malignancy as represented in. The patient did not have any systemic symptoms, immunological workup was negative, so systemic vasculitis was ruled out. The one-time doses of vancomycin and piperacillin-tazobactam he received in the ED seemed to be unlikely offenders as he received only one dose of each antibiotic more than one week prior to rash onset. With absence of systemic symptoms, negative immunological and serological studies, systemic vasculitis and infection-induced vasculitis was ruled out. In our patient, the vasculitis was assumed to be ceftriaxone-induced in the absence of other obvious causes as the lesions regressed after withdrawal of ceftriaxone and the use of corticosteroids.

3. Conclusion

This was a case of LCV after exposure to ceftriaxone. This case highlights the importance of clinicians' vigilance when prescribing medications such as cef-

triaxone, and considering all rare side effects that have been implicated in the literature. In our patients, we were able to identify the skin lesions in a timely manner and after all possible diagnoses were ruled out clinically and immunologically, we were able to conclude that his LCV was ceftriaxone induced. It is important to identify drug-induced vasculitis promptly as early detection and withdrawal of offending medication as well as treatment with corticosteroids in many cases lead to resolution of symptoms.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Einhorn, J. and Levis, J.T. (2015) Dermatologic Diagnosis: Leukocytoclastic Vasculitis. *The Permanente Journal*, **19**, 77-78. https://doi.org/10.7812/TPP/15-001

[2] Baigrie, D., Goyal, A. and Crane, J.S. (2018) Leukocytoclastic Vasculitis. StatPearls Publishing, Treasure Island.

[3] Turda, C., Dumnici, O.O. and Huplea, V. (2019) Case Report: Cytomegalovirus Reinfection in a Patient with Chronic Hepatitis C. http://protmed.uoradea.ro/facultate/publicatii/ecotox_zooteh_ind_alim/2019A/Varia/2%20Turda.pdf

[4] Merkel, P.A. (2021) Overview of and Approach to the Vasculitides in Adults. UpToDate. https://www.uptodate.com/contents/overview-of-and-approach-to-the-vasculitides-in-adults

[5] Sunderkötter, C., Bonsmann, G., Sindrilaru, A. and Luger, T. (2005) Management of Leukocytoclastic Vasculitis. *Journal of Dermatological Treatment*, **16**,193-206. https://doi.org/10.1080/09546630500277971

[6] Baigrie, D., Goyal, A. and Crane, J.S. (2021) Leukocytoclastic Vasculitis. StatPearls Publishing, Treasure Island.

[7] Haehn, D.A., Patel, A., Youngberg, G. and Gonzalez-Estrada, A. (2019) Ceftriaxone-Induced Leucocytoclastic Vasculitis. *BMJ Case Reports*, **12**, e229411. https://doi.org/10.1136/bcr-2019-229411

[8] Jansen, J.W., Linneman, T.W., Tan, X. and Moenster, R.P. (2019) Comparison of Adverse Drug Reactions between Patients Treated with Ceftaroline or Ceftriaxone: A Single-Center, Matched Cohort Study. *Open Forum Infectious Diseases*, **6**, ofz279. https://doi.org/10.1093/ofid/ofz279

[9] Ceftriaxone and Leukocytoclastic Vasculitis, a Phase IV … eHealthMe. https://www.ehealthme.com/ds/ceftriaxone/leukocytoclastic-vasculitis/