Case Report

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Nafcillin Implicated in A Case of Cutaneous and Gastrointestinal Leukocytoclastic Vasculitis

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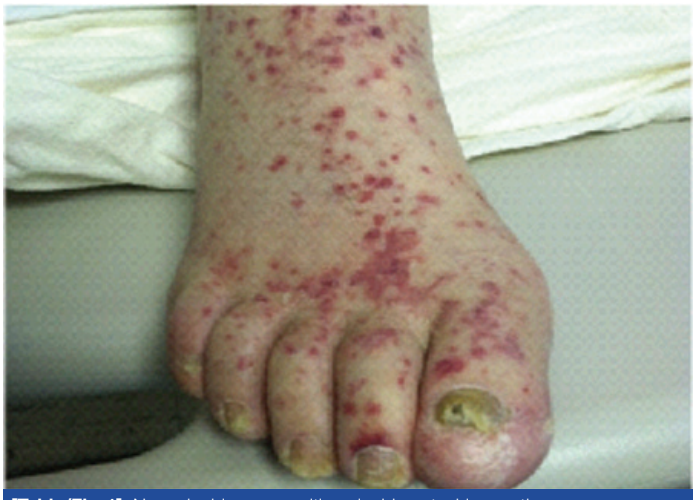
ABSTRACT

Leukocytoclastic vasculitis (LV) is a rare hypersensitive reaction involving the small vessels, which is usually mediated by drugs. Very few cases of nafcillin -associated LV have been reported. Here, we reported a case of LV with the presentation of skin rashes and gastrointestinal bleeding after receiving nafcillin, evidenced by endoscopy and skin biopsy. The symptoms resolved after withdrawal of nafcillin and the addition of prednisone treatment. LV should be considered in the differential diagnosis of erythematous rash, especially with gastrointestinal symptoms after the exposure.

Keywords: Biopsy, Endoscopy, Hypersensitive, Gastrointestinal

CASE REPORT

A 77-year-old man, who was on a six week nafcillin intravenous treatment for methicillin-sensitive *Staphylococcus aureus* (MSSA) septic arthritis, presented with increased swelling over his extremities and progressive rashes on the 19th day of treatment to Vidant Medical Center in July, 2013. The rashes began on his legs and feet and gradually extended to his proximal lower extremities and torso. Physical examination showed swelling in all limbs and multiple palpable purpuric lesions on the lower extremities [Table/Fig-1] and abdominal skin. He was found to be hemoccult positive. Shortly after admission, he suddenly developed nausea, bilious vomitus and frank hematochezia.

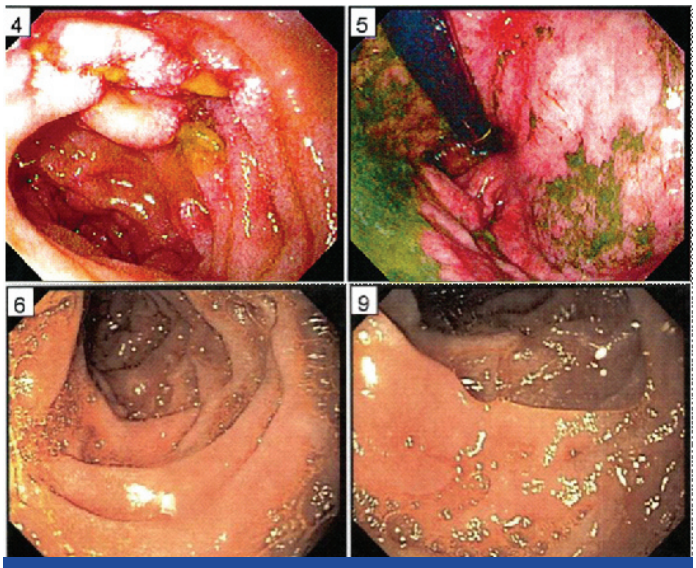


[Table/Fig-1]: Nonpalpable non-pruritic palpable petechia eruption

The blood tests showed: WBC 14.3 k/uL, Hemoglobin 9.2 g/dL, platelet count 295 k/uL, Lipase 24 U/L, ALP 51U/L, Total bilirubin 0.4 mg/dL, ALT 20U/L, AST 14 U/L, creatinine 2.2 mg/dL (baseline 1.7 mg/dL), ESR 23mm/hr, C-reactive protein 76.6 mg/l, lactate dehydrogenase 291U/L, Haptoglobin 124 mg/dL, trace cryoglobulin, Antinuclear antibody titer<40, Antineutorphil cytoplasmic antibody titer< 1:20, p-antineutorphil cytoplasmic antibody negative, C3/C4/CH50 within normal range, rheumatoid factor<10, RNP antibody negative, anti-Sm antibody negative, SS-A/Ro antibody and SS-B/La antibody negative, hepatitis C Antibody, hepatitis B surface antigen and HIV negative. Abdomen X-ray: mild gastric distention, non-obstructive bowel gall pattern, negative for pneumoperitoneum.

An upper gastrointestinal (GI) endoscopy, which showed multiple ulcers scattered throughout the 2nd and 3rd segments of duodenum consistent with vasculitis [Table/Fig-2 upper panel]. The skin biopsies revealed leukocytoclastic vasculitis (LV) with significant number of eosinophil being present within the infiltrate, consistent with LV induced by drug reaction [Table/Fig-3].

Nafcillin was switched to cefazolin. Prednisone and proton pump inhibitor were started. Clinical improvement was noted with resolution of GI symptoms. During the follow up of one month, patient's skin purpuric lesions resolved completely. The duodenum ulcers healed, evidenced by repeat endoscopy four months later [Table/Fig-2 lower panel].



[Table/Fig-2]: Endoscopy showed multiple ulcers scattered throughout 2nd and 3rd parts of duodenum consistent with vasculitis before treatment (upper) and healed ulcers after treatment (lower) (From GI lab of Vidant Medical Center)

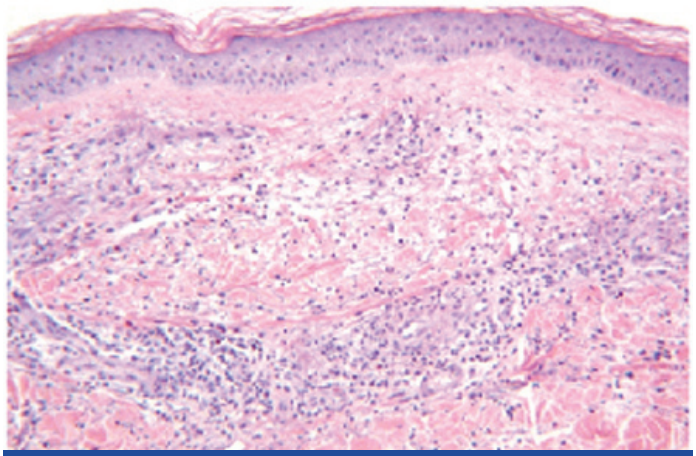
DISCUSSION

LV is a type III hypersensitive reaction involving the small vessels. This disorder is usually mediated by drugs and the resultant inflammatory response leads to leukocyte infiltration, necrosis and fibrin deposition and subsequently, the destruction of small vessels [1].

Many medications can mediate the onset of LV, including NSAIDs, antibiotics, sulfonamides, warfarin and adjuvant hormonal therapy.

Certain infections, such as *Staphylococcus aureus*, hepatitis B and C and HIV, may be associated with this disorder [2-5]. Some diseases, such as malignancies [6] and collagen vascular diseases [7], may also have this presentation on the skin. Few cases of nafcillin-associated LV have been reported and we reported this case on the 28th Annual Yash P. Kataria Internal Medicine Research Day in Vidant Medical Center of North Carolina, USA. Though *Staphylococcus aureus* is able to trigger LV, the clinical features and pattern of recovery after discontinuation of nafcillin of this case were considered as most suggestive of nafcillin-induced LV. Other infectious and rheumatologic causes of LV were excluded in this patient.

LV usually presents with non-blanching, palpable petechia or purpura on the lower extremities and other dependent areas [8]. Biopsy of these skin lesions typically exhibits inflammation of the small blood vessels with soft tissue swelling. The clinical diagnosis of LV is confirmed by skin biopsy. In this case, the timing of the purpura onset, approximately 19 d after the start of nafcillin, is within the reported range of onset timing of 7–21d after exposure [1]. Consistent with the majority of published cases, this patient had purpura and petechia, initially appearing on a lower extremity, and supported by the results of skin biopsy [Table/Fig-3].



[Table/Fig-3]: Skin biopsy revealed perivascular and eosinophil infiltrates and tissue swelling consistent with leukocytoclastic vasculitis. There was fibrin deposition and vessel wall damage. (From Path lab of Vidant Medical Center)

In addition to the skin lesions, patients may develop systemic symptoms and signs, such as fever, malaise, myalgia, lymphadenopathy, arthritis and abdominal pain, etc [9]. The involvement of other organs is not rare but may be severe. Our case only had mild elevated creatinine and resolved after nafcillin stopped. GI tract involvement manifested as bright red bloody per rectum after purpura occurred for two days. Endoscopy found multiple ulcers, which were consistent with LV and biopsy only showed fibrino-purulent exudate and destruction of tissues.

The course of LV is variable with most of cases is acute and resolves once the antigen has been cleared. The prognosis depends on the severity of internal organ involvement. Most presentation on the skin will usually subside after discontinuation of the offending medication within a period of days to a few weeks. Mild forms of disease may require no specific treatment. For the critically ill patients with renal disease or rapidly progressing course, systemic corticosteroid therapy may produce rapid resolution of symptoms [10]. In patients with more severe or persistent cutaneous disease not due to infection, drugs such as colchicine [9], and dapsone [11] have been used with certain degree of success. Plasma exchange was reported in the management of patients with refractory and fulminant vasculitis [12]. In our case, patient received prednisone and nafcillin was switched to cefazolin, purpura resolved by one month and GI lesions healed in four months [Table/Fig-2 lower panel].

CONCLUSION

It is notable that nafcillin can cause Leukocytoclastic vasculitis with the presentation on the skin and GI tract, which should be considered in the differential diagnosis of erythematous rash, especially with GI symptoms.

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