

# Levofloxacin – Induced Cutaneous Leukocytoclastic Vasculitis: Report of a Case in a Diabetic Man and Review of the Litterature

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**Abstract** Cutaneous leukocytoclastic vasculitis comprises a wide spectrum of etiologies including medications. Fluoroquinolones are rarely implicated in this disease. We report the case of a diabetic man who was referred to our hospital for purpuric rash and hyperglycemia. The cutaneous lesions appeared 3 days after the beginning of levofloxacin which was prescribed for a respiratory infection. Physical examination and laboratory evaluation findings ruled out renal, neurological, respiratory and gastrointestinal involvement. Skin biopsy confirmed the diagnosis of cutaneous leukocytoclastic vasculitis. Autoimmune investigations and infectious serologies were negative. Levofloxacin therapy was the most probable etiology. The patient was successfully treated by withdrawal of the offending antibiotic associated with topical steroids.

**Keywords:** fluoroquinolones, cutaneous leukocytoclastic vasculitis, levofloxacin, purpura

**Cite This Article:** Sahar El Aoud, Nadia Charfi, Nessrine Cheikhrouhou, Mariam Kesentini, Mouna Elleuch, Tahia Boudawara, and Mohamed Abid, "Levofloxacin – Induced Cutaneous Leukocytoclastic Vasculitis: Report of a Case in a Diabetic Man and Review of the Litterature." *American Journal of Epidemiology and Infectious Disease*, vol. 3, no. 4 (2015): 84-87. doi: 10.12691/ajeid-3-4-3.

## 1. Introduction

Fluoroquinolones (FQ) are one of the most widely used classes of antibiotics in clinical medicine because of a broad spectrum of activity. Levofloxacin, a third generation fluoroquinolone, is widely prescribed for skin, respiratory and genitourinary infections. It is generally well tolerated. Nevertheless, given such high prescription rate, clinicians are encountering more adverse events. In fact, this antibiotic had been rarely implicated as the cause of cutaneous leukocytoclastic vasculitis (CLV) [1].

We present a case of 63-year old diabetic man who had a levofloxacin-associated CLV and review the pertinent literature involving the association of FQ with CLV.

## 2. Case Report

A 63-year-old type 2 diabetic man presented for evaluation of a skin painful erythematous rash and hyperglycemia. The cutaneous lesions appeared three days after the beginning of levofloxacin which was prescribed at the dose of 500 mg twice daily for a respiratory infection. He had not hematuria neither abdominal pain. He had a history of a penicillin allergy. Medications included Metformin (1700 mg daily) and Glimperide (4mg daily) for four years.

The patient was febrile. He had a good state of hydration, a blood pressure of 115/75 mmHg, a pulse of 100 beats/min and a respiratory rate of 20 breaths/min.

Breath auscultation revealed inspiratory crackles. Cutaneous examination showed several confluent purpuric papules on his upper and lower members. There were coalesced plaques of palpable purpura of different diameter on the dorsum of the left hand, knee and ankles (Figure 1). On his abdomen, there were numerous scattered petechiae.

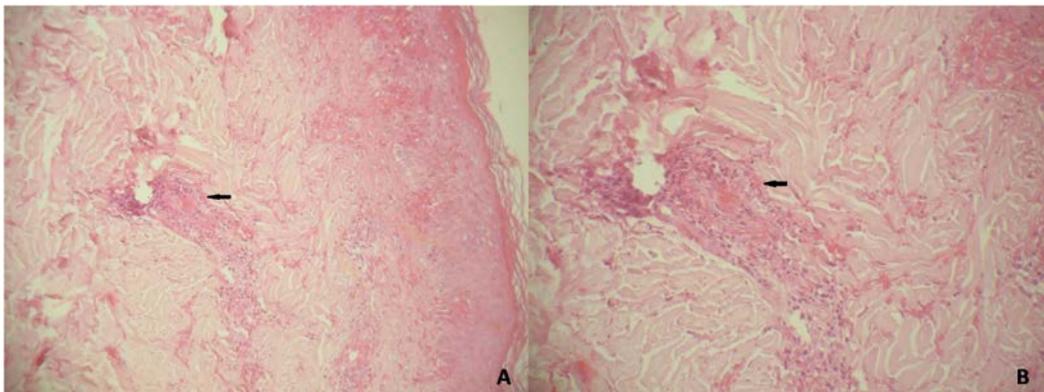
Laboratory analysis showed nonketotic hyperglycemic decompensation. A complete blood picture showed white blood cell: 7740 /  $\mu$ L, platelet: 381000 /  $\mu$ L, eosinophilic granulocyte: 40 /  $\mu$  L and hemoglobin: 12.8 g / dL. The erythrocyte sedimentation rate (ESR) was over 125 mm/hour and the C-reactive protein (CRP) was at 81 mg/l. His renal function and serum electrolytes were within normal limits. Urinalysis was unremarkable.

The admission chest radiograph demonstrated bilateral bronchitis.

A skin biopsy was performed showing infiltration of neutrophils and eosinophils leukocytoclasia and fibrinoid necrosis of the dermal superficial, small-vessel walls (Figure 2). Direct immune-fluorescence (DIF) showed the presence of IgG and C3 complement immune deposits in the skin. Therefore, the diagnosis of CLV was confirmed. Levofloxacin was suspended on admission and diagnostic testings were carried out to determine the etiology.



**Figure 1.** Purpuric lesions on the hand (A), knee (B) and ankles (C)



**Figure 2.** (A) Skin biopsy demonstrating a predominant neutrophilic infiltration, presence of eosinophils, leukocytoclasia and fibrinoid necrosis around the dermal superficial, vessel walls consistent with cutaneous leukocytoclastic vasculitis, (B) magnification 400x

All known causes of CLV were explored. Serology for hepatitis B and C, Epstein Barr virus, cytomegalovirus were negative. Autoimmune investigations such as rheumatoid factor, complement activation, antineutrophil cytoplasmic antibody (ANCA), antinuclear antibody and anticardiolipin antibody were also negative.

The patient was prescribed a 10-day course of doxycycline. Cefotaxim was associated during the first three days of treatment under close clinical monitoring. In addition, he was given topical steroids.

At follow up, two weeks after levofloxacin discontinuation, dermatological manifestations had completely resolved, his diabetes had been well-regulated with insulin therapy, inflammatory syndrome had regressed

FQ were avoided due to levofloxacin- induced vasculitis and a concern for a potential cross-reaction among other agents in the same drug class.

### 3. Discussion

CLV is an inflammatory process affecting the skin small-vessel wall. It frequently occurs as palpable purpura or infiltrated erythema [2,3].

Our patient presented a typical palpable purpura, so that the diagnosis of cutaneous vasculitis was strongly suspected. Physical examination and laboratory evaluation findings ruled out renal, neurological, respiratory and gastrointestinal involvement.

The diagnosis is based on histopathological findings. Early skin biopsy shows accumulation of neutrophils in the vessel wall. However, it reveals lymphocytes and macrophages within 18-24 h after the appearance of a lesion. Diagnosis confirmation is made by direct immunofluorescence (DIF) which identifies specific immunoglobulins [4]. Our patient had a skin biopsy consistent with CLV which was confirmed by DIF findings.

The etiology of CLV is diverse. It includes chronic or acute infections and autoimmune diseases. Drug-induced vasculitis are reported in 20% of cases [1]. Histopathological findings showing infiltration of eosinophils in the vessel walls is suggestive of a drug etiology as seen in the present case.

Various pharmacological classes of medications are implicated, but the anti-thyroid drugs are the most widely described [5]. However, FQ-associated cutaneous vasculitis have been rarely reported. There have been 20 published

cases of FQ- induced cutaneous vasculitis around the world until now [1,6]. All reported cases in the literature involve ciprofloxacin, ofloxacin, and levofloxacin [1,6-17].

Levofloxacin have been implicated in only 4 cases [1,7,8,9] ( Table 1).

**Table 1. Review of the literature of Levofloxacin-associated cutaneous vasculitis.**

Fluoroquinolones	Diabetic patient	Time to symptom onset	Skin manifestations	Biopsy proven	Final diagnosis	Treatment
Levofloxacin [1]	No	5 days	Purpuric papules, numerous petechiae	Skin biopsy	CLV	Withdrawal of FQ; prednisone
Levofloxacin [7]	No	3 days	palpable purpura	None	Nephrotoxicity and purpura	Withdrawal of FQ; prednisone
Levofloxacin [8]	No	5 days	Petechiae	None	Levofloxacin-induced interstitial nephritis and cutaneous vasculitis	Withdrawal of FQ; prednisone
Levofloxacin [9]	No	3 days	palpable purpura	Skin biopsy	Cutaneous vasculitis	Withdrawal of FQ
Our present case	Yes	3 days	purpuric papules	Skin biopsy	CLV	Withdrawal of FQ Topical steroids

FQ: Fluoroquinolone; CLV: Cutaneous leukocytoclastic vasculitis.

Additionally, adverse side effects of FQ may pose profound health threats such as glucose disturbances in diabetic patients [18,19].

In the present case, levofloxacin was probably implicated in the occurrence of nonketotic hyperglycemic decompensation. It was also the most probable cause of CLV which is rarely described.

The etiopathogenesis of FQ-induced vasculitis is poorly understood. Some suggested a non-immune mediated mechanism, others considered it to be IgE- or T cell-mediated reaction [20]. Our patient had a history of penicillin allergy which makes him prone to hypersensitivity events.

CLV may be the presenting manifestation of a FQ-induced systemic vasculitis syndrome with a life-threatening visceral involvement. Acute renal failure was reported in four cases [7,8,12,21] causing a worse prognosis. ANCA testing is generally negative as well as our present case [1,12].

Discontinuation of FQ usually induces a rapid improvement of cutaneous symptoms. Systemic corticosteroids are used for patients with haemorrhagic, extensive CLV [1,10,11] and severe renal involvement [7,8].

In this report, the vasculitis was limited to the skin with any severe organ involvement. Purpuric lesions improved two weeks after levofloxacin discontinuation and topical steroids. Levofloxacin was noted as an allergy in the patient's medical record in addition to penicillin therapy. The patient was well educated to avoid FQ and to be aware of hypersensitivity drug events in the future.

## 4. Conclusion

Levofloxacin –induced CLV is rarely reported. Therefore, we believe that clinicians should remain vigilant when prescribing fluoroquinolones, especially for patients who are prone to hypersensitivity events as the case of our patient.

## Conflict of Interest

The authors have no competing interests.

## List of Abbreviations

Fluoroquinolones (FQ)  
cutaneous leukocytoclastic vasculitis (CLV)  
erythrocyte sedimentation rate (ESR)  
C-reactive protein (CRP)  
Direct immune-fluorescence ( DIF)  
antineutrophil cytoplasmic antibody (ANCA).

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