

Levofloxacin-Induced Achilles Tendinitis in a Young Adult in the Absence of Predisposing Conditions

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Fluoroquinolones (FQs) represent a major class of antimicrobials that have a high potential as therapeutic agents. Although FQs are generally safe for the use as antimicrobials, they may induce tendinopathic complications such as tendinitis and tendon rupture. A number of factors have been suggested to further predispose a patient to such injuries. Hitherto, a few published cases on tendon disorders have implicated levofloxacin, a more recently introduced FQ. Here, we report a patient with levofloxacin-induced Achilles tendinitis, who exhibited no known predisposing factors. A 20-year-old man without any history of disease or medication presented with community-acquired pneumonia. Levofloxacin was administered and 3 days later, he complained of pain in the left Achilles tendon and revealed redness and swelling in the area. On suspecting Achilles tendinitis, levofloxacin treatment was discontinued, and the tendinitis subsequently improved. To our knowledge, this is the first case report on FQ-induced Achilles tendinitis in Korea.

Key Words : Fluoroquinolones, tendinopathy, Achilles tendinitis, adverse reaction

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INTRODUCTION

Fluoroquinolones (FQs) are potent broad-spectrum antimicrobial agents. Since the introduction of nalidixic acid in the 1960s, FQs have undergone extensive synthetic and clinical development.¹ In particular, the newer generation agents are demonstrated to be highly effective in the treatment of upper and lower respiratory tract infections.^{2,3} Among the newer FQs, levofloxacin appears to be safe and extremely well tolerated. It exhibits a low incidence of gastrointestinal and central nervous system adverse events, extremely low phototoxicity, and no cardiotoxicity.⁴ Recently, the possibility of tendinitis and tendon rupture associated with FQ treatment has been raised.^{5,6} A number of factors have been suggested to further predispose a patient to tendon injury. The proposed factors include age over 60, renal failure, diabetes mellitus, renal transplantation, hyperparathyroidism, rheumatic disease, trauma, and corticosteroid treatment.⁷⁻¹⁰ The incidence of FQ-induced tendinopathy in a healthy population is not entirely clear but is assumed to be low.^{11,12}

We present the case of a young healthy man lacking any predisposing conditions who developed Achilles tendinitis following levofloxacin administration for the treatment of community-acquired pneumonia.

CASE REPORT

A 20-year-old man presenting with a 5-day history of fever, cough, and right

pleuritic chest pain was brought to the emergency department. He had no past medical history of asthma, diabetes, renal failure, or rheumatic disease and was not under any medication including steroids. He was a butcher by profession and lacked any history of trauma or tendon injury prior to admission. A physical examination revealed a body temperature of 38.2°C, and inspiratory crackles were heard over the right lung field. Blood cultures were performed and expectorated sputum specimens were collected for gram staining and culture. The laboratory findings were as follows: white blood cells, 20,000/L (90% neutrophils); C-reactive protein, 30.34 mg/dL (reference range, 0.00-0.30 mg/dL); blood urea nitrogen, 8.7 mg/dL; and creatinine, 1.0 mg/dL. Arterial blood gas values were pH, 7.42; pCO₂, 38 mmHg; pO₂, 57 mmHg; HCO₃, 24 mmol/L; and arterial oxygen saturation, 89%. The results of the serum electrolyte investigations and the liver function tests were normal. The serological test for HIV was negative. Simple chest radiography revealed increased opacity in the right middle and lower lobe along with parapneumonic effusion. The patient was hospitalized with a diagnosis of community-acquired pneumonia and intravenous cefminox (1 g, three times a day) and oxygen supplements were initiated. However, subjective and objective parameters including respiratory symptoms, fever, partial pressure of oxygen, and peripheral leukocyte count showed no improvement after 2.5 days of treatment and it was decided to change the treatment to intravenous levofloxacin (750 mg, once a day).

The patient developed sudden pain in the left ankle 3 days after the initial dose of levofloxacin was administered. The pain was located 2-3 cm proximal to the insertion of the left Achilles tendon at the back of the heel. Swelling of the skin over the tendon was noted, associated with warmth and redness (Fig. 1). Examination revealed marked tenderness with mild palpation of the Achilles tendon and difficulty in moving the ankle, particularly when pushing off with the toes. No swelling or tenderness was observed in the other joints, particularly the shoulder or hand. We suspected levofloxacin-induced Achilles tendinitis and decided to discontinue levofloxacin treatment and ease the strain to the tendon. Levofloxacin was substituted with 2 g ceftriaxone administered intravenously once a day. The symptoms of the left Achilles tendon improved within a few days after levofloxacin treatment was discontinued. Complete recovery ensued 1 month later without any sequelae of tendinopathy.

DISCUSSION

Due to extensive developments in the synthesis and clinical use of FQs, they now exhibit improved antimicrobial acti-



Fig. 1. Close-up photograph of the left ankle. Redness and swelling of the skin over the Achilles tendon was noted; this finding was consistent with acute Achilles tendinitis.

city, pharmacokinetic features, and toxicity profiles.¹ Over time, several structure-side effect relationships have been established, and it has become standard practice to label adverse reactions to drugs based on either their class or individual idiosyncratic effects. Some FQ-induced side effects are class effects and cannot be modulated by molecular variation. These include GI symptoms, arthropathy, and interactions with metal ions. However, crystalluria, CNS effects, drug interactions, phototoxicity, and potential genotoxicity are very sensitive to chemical modifications.¹³

The first case of FQ-associated tendinopathy was reported in 1983.¹⁴ Since then, there has been a marked increase in the number of spontaneous reports on FQ-induced tendinopathy; however, the incidence of this condition remains unclear. In a recent study, the overall excess risk was 3.2 cases per 1,000 patient-years.¹⁵

Among newer FQ agents such as gatifloxacin, moxifloxacin, and gemifloxacin, levofloxacin appears to be relatively safe and very well tolerated. However, reports on levofloxacin-induced tendinopathy are now emerging.^{5,6} A few cases of levofloxacin-associated tendon disorders have been published, and Fleisch, et al.¹⁶ suggested that levofloxacin may have a higher incidence of drug-induced tendinopathy among newer FQs than previously expected. There have been no reports on FQ-induced Achilles tendinopathy in Korea. This may be due to the physician's unawareness of the complications involved, underreporting, or racial differences in the prevalence of FQ-induced Achilles tendinopathy. Further studies on the prevalence of FQ-induced tendinopathy in Korea should be conducted.

It is essential to discontinue antibiotic treatment on the first signs of symptoms and to ease the strain to the tendon. MRI may be useful for the early detection and monitoring

of tendinitis or tendon degeneration.¹⁷ Moreover, once FQ-induced tendinopathy is suspected, a patient should not be rechallenged by quinolone treatment.¹⁸ Considering the potential for severe disabilities arising from tendon rupture, physicians should be aware of the possibility of FQ-induced tendon injury and should carefully assess the risks of FQ treatment. The risk of tendinopathy appears to be a class effect that is not easily ameliorated by chemical modification¹⁹ and it is noteworthy that up to 50% of tendon ruptures occur without any warning signs.^{7,9}

In summary, we report a patient with levofloxacin-associated Achilles tendinitis. The symptoms arose 3 days after levofloxacin was administered, and they improved within a few days after the treatment was discontinued. The present case emphasizes the fact that FQ-induced tendinopathy may occur even in the absence of predisposing factors, particularly with the newer generation agent levofloxacin. To our knowledge, this is the first case report of FQ-associated tendinopathy in Korea.

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