Physiology and Pharmacology

Physiol Pharmacol 21 (2017) 172-174 **www.phypha.ir/ppj**

Letter to editor

A case of ciprofloxacin-associated Achilles tendinitis

Vahid Pirhajati Mahabadi[1], Somayyeh Nasiripour[2,3], Maryam Farasatinasab[3,4], Shabnam Nadjafi[5]*

1. Neuroscience Research Center, Iran University of Medical Sciences, Tehran, Iran
2. Colorectal Research Center, Iran University of Medical Sciences, Tehran, Iran
3. School of Pharmacy International Campus, Iran University of Medical Sciences, Tehran, Iran
4. Endocrine Research Center, Institute of Endocrinology and Metabolism, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran
5. Neuroscience Research Center, Iran University of Medical Sciences, Tehran, Iran

Abstract

Achilles tendinitis is a rare adverse effect of the fluoroquinolone antibiotics. Fluoroquinolone antibiotics have widespread usage for treatment of Gram-negative-related infections particularly urinary tract and respiratory infections. Due to the prevalent usage of this family of antibiotics, it is necessary to be careful about their side effects including Achilles tendinitis, which can ensue tendon rupture.

This case report introduces an 84-year-old man diagnosed with Achilles tendinitis due to consumption of ciprofloxacin for treatment of urethritis. The patient experienced pain on posterior region of the left ankle after three days of antibiotic therapy onset and the pain was alleviated within a week following ciprofloxacin cessation along with treatment with nonsteroidal anti-inflammatory drugs. The Naranjo score was determined seven for this patient; accordingly, ciprofloxacin was the probable cause of this reaction. Early diagnosis of fluoroquinolones-associated Achilles tendinitis and stopping the treatment may prevent tendon rupture.

Keywords:
Achilles Tendinitis;
Ciprofloxacin;
Fluoroquinolones

Received: 11 Mar 2017
Accepted: 26 Jul 2017

***Correspondence to:**
S. Nadjafi

Tel: +98-2186704529
Fax: +98-2188052248
Email:
najafi.sh@iums.ac.ir

Dear editor:

Fluoroquinolones including ciprofloxacin, the most widely used agent of this family of antibiotics, are the yields of structural changes on the basic quinolone structure (Kocsis et al., 2016). Each agent of quinolones and fluoroquinolones forms a ternary complex with a DNA molecule and gyrase and topoisomerase IV enzymes; therefore, bacterial DNA supercoiling is blocked and the result is inhibition of bacterial DNA synthesis (Kocsis et al., 2016).

Due to the structural changes, fluoroquinolones not only revealed improved pharmacokinetic parameters by enhanced tissue penetration that resulted in achieving therapeutic concentrations in kidney, lung and intestine, but also their activity spectrum was augmented, as they showed bactericidal effect against several pathogens including Gram-positives, Gram-negatives, aerobes and anaerobes (Kocsis et al., 2016).

Even though several fluoroquinolone agents have been produced in the last decades, just a few of them are marketed, and toxicity caused some of these agents became withdrawn or restricted (Kocsis et al., 2016).

Achilles tendon disorders consist of both traumatic and nontraumatic problems (Weinfeld, 2014). In this regard, some other factors including usage of oral steroids and fluoroquinolones besides metabolic disorders like diabetes, hyperuricaemia and hypercholesterolaemia are related to Achilles tendon pathology (Singh, 2015).

Amazingly, the simultaneous searching of the key words [based on MeSH (Medical Subject Headings)]:

"Fluoroquinolones", "Tendinopathy" and "Case Reports" in PubMed revealed that there are only 76 related articles from 1983 to 2016.

As the fluoroquinolone antibiotics are frequently used for treatment of urinary tract and respiratory infections (Wise et al., 2012), it can be practical to report this case of ciprofloxacin-related Achilles tendinitis.

An 84-year-old man, weighing 82 kg, presented with left ankle pain (at rest) to an outpatient clinic. The pain was local on posterior area of the left ankle and it would become more severe during walking. He had history of benign prostatic hypertrophy, diabetes, coronary artery disease and hypertension. His hypercholesterolemia had been controlled by medication, some years ago. He had no history of recent physical injury, intense physical activity, surgical intervention or admission at the hospital. Also, he had no change in his routine medications except recent consumption of ciprofloxacin. Ciprofloxacin 500 mg, per oral, twice daily had been started for treatment of his new onset urethritis from three days ago. In physical exam, there was a local tenderness on posterior area of the left ankle, the lower one-third of left Achilles tendon, with decreased range of motion. There was no swelling, warmth or skin color change on the painful region or around it. Other physical examinations were normal. Thus, ciprofloxacin-related Achilles tendinitis was purposed as the impression. The treatment with ciprofloxacin was stopped. We followed up the patient and he informed that the pain was alleviated within a week following ciprofloxacin cessation and treatment with oral and topical nonsteroidal anti-inflammatory drugs. We confirmed the pain decline by physical examination that revealed the reduction of local tenderness on the left ankle.

In similar cases, the Naranjo score is used to determine the probability that the cause of an adverse reaction is a medication or the effect is the result of the other factors (Shimatsu et al., 2014). In brief, Naranjo algorithm consists of ten questions, which have been designed to clarify the relation between a drug and its adverse reaction (Shimatsu et al., 2014). The answer to each question should be one of these choices: “Yes”, “No” or “Do not know or not done” (Shimatsu et al., 2014). According to the type of each question, the “Yes” answer scores -1, +1 or +2; the “No” answer scores -2, -1, 0, +1 or +2, and the answer “Do not know or not done” always scores 0 (Shimatsu et al., 2014). Then, the sum of scoring determines the occurrence of adverse drug reaction (ADR): 9 = definite ADR, 5-8 = probable ADR, 1-4 = possible ADR, 0 = doubtful ADR (Shimatsu et al., 2014). The calculated Naranjo score for the presented patient was seven, suggesting the probable effect of ciprofloxacin.

On the other hand, there are some systemic diseases identified to cause an enthesopathy (such as inflammatory bowel disease, psoriasis, spondyloarthropathy or ankylosing spondylitis) (Haddow et al., 2003).

Particularly, Achilles tendinitis can be considered as a rare extraintestinal manifestation of ulcerative colitis (Zenda et al., 2016). Furthermore, it should be considered that there are other risk factors for tendinopathy including old age, steroid therapy, impaired renal function and chronic lung disease (Haddow et al., 2003). Although it is not a consistent finding, associated treatment with corticosteroids may be a predisposing factor for tendinitis (Haddow et al., 2003). Excluding the age factor, the introduced patient had no history on presence of the other causes of tendinopathy like the mentioned diseases or steroid utilization.

The pathological mechanism of fluoroquinolones-induced tendinitis is unknown even though the histological studies have recognized the similar features to those of overuse injuries (Haddow et al., 2003). It was known that occurrence of the fluoroquinolone-related tendinopathy symptoms can vary within hours of treatment initiation or up to six months later than ceasing the drug (Lewis and Cook, 2014), and in comparison with the other types of tendinopathy, the recovery of fluoroquinolone-associated tendinopathy can be slower and need a less aggressive approach early in rehabilitation (Lewis and Cook, 2014). Notably, fluoroquinolone-induced tendinopathy may be appeared even after topical administration as it was reported in a 58-year-old man after ofloxacin ear drops instillation (Grandvuillemin et al., 2015). In addition, it should be considered that fluoroquinolones-associated Achilles tendinopathy can lead to tendon rupture (Yu and Giuffre, 2005), especially in presence of the other related risk factors, such as steroid treatment or systemic diseases (Yu and Giuffre, 2005).

As mentioned before, some fluoroquinolone agents have been withdrawn or restricted because of their

serious toxic side effects (Kocsis et al., 2016). These toxicities had been affected different organs as hepatotoxicity due to trovafloxacin treatment; hemolysis was seen during temafloxacin administration and some other toxicities that were produced by some fluoroquinolones (Kocsis et al., 2016). It is interesting to know that the tendinitis after treatment with pefloxacin was the reason for withdrawal of this fluoroquinolone agent (Kocsis et al., 2016).

Overall, because of widespread usage of fluoroquinolone antibiotics, it is important to be vigilant about diagnosis of Achilles tendinitis. It seems that early diagnosis and stopping fluoroquinolones may prevent tendon rupture, which is a more severe complication. Accordingly, it is realized that the drug adverse effects may have various clinical presentations, which may be completely different from the expected pharmacological results. Thus, it is practical and critical that the physicians always consider the drug adverse effects in disease diagnostic approach.

Acknowledgments

A special acknowledgment is dedicated to the patient on whom the case report is based.

Conflict of interest

The authors declare that there are no conflicts of interest.

References

Grandvuillemin A, Contant E, Fedrizzi S, Gras V, Dautriche A. Tendinopathy after ofloxacin ear drops. Eur J Clin Pharmacol 2015; 71: 1407-1408.

Haddow LJ, Chandra Sekhar M, Hajela V, Gopal Rao G. Spontaneous Achilles tendon rupture in patients treated with levofloxacin. J Antimicrob Chemother 2003; 51: 747-748.

Kocsis B, Domokos J, Szabo D. Chemical structure and pharmacokinetics of novel quinolone agents represented by avarofloxacin, delafloxacin, finafloxacin, zabofloxacin and nemonoxacin. Ann Clin Microbiol Antimicrob 2016; 15: 34.

Lewis T, Cook J. Fluoroquinolones and tendinopathy: a guide for athletes and sports clinicians and a systematic review of the literature. J Athl Train 2014; 49: 422-427.

Shimatsu K, Subramaniam S, Sim H, Aronowitz P. Ciprofloxacin-induced tendinopathy of the gluteal tendons. J Gen Intern Med 2014; 29: 1559-1562.

Singh D. Cholesterol level in non-insertional Achilles tendonopathy. Foot (Edinb) 2015; 25: 228-231.

Weinfeld SB. Achilles tendon disorders. Med Clin North Am 2014; 98: 331-338.

Wise BL, Peloquin C, Choi H, Lane NE, Zhang Y. Impact of age, sex, obesity, and steroid use on quinolone-associated tendon disorders. Am J Med 2012; 125: 1228.e23-1228. e28.

Yu C, Giuffre B. Achilles tendinopathy after treatment with fluoroquinolone. Australas Radiol 2005; 49: 407-410.

Zenda T, Araki I, Nakamiya O, Tokuumi Y, Shimada Y, Komai K, et al. Achilles tendinitis as a rare extraintestinal manifestation of ulcerative colitis. Clin J Gastroenterol 2016; 9: 129-133.