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OLGU SUNUMU
CASE REPORT

A rare but a serious complication: gemifloxacin induced tendinopathy

Asiye KANBAY¹(ID)
İrem MIHCIOĞLU²(ID)
Nilüfer TEKİN³(ID)

¹ Department of Chest Diseases, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

¹ İstanbul Medeniyet Üniversitesi Tıp Fakültesi, Göğüs Hastalıkları Anabilim Dalı, İstanbul, Türkiye

² Department of Family Medicine, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

² İstanbul Medeniyet Üniversitesi Tıp Fakültesi, Aile Hekimliği Anabilim Dalı, İstanbul, Türkiye

³ Department of Radiology, Faculty of Medicine, Istanbul Medeniyet University, Istanbul, Turkey

³ İstanbul Medeniyet Üniversitesi Tıp Fakültesi, Radyoloji Anabilim Dalı, İstanbul, Türkiye

ABSTRACT

A rare but a serious complication: gemifloxacin induced tendinopathy

We present a case of tendon rupture and subcutaneous bleeding after administration of gemifloxacin for the treatment of lower respiratory tract infection. Fluoroquinolone-induced tendinopathy is a rare but increasingly acknowledged adverse effect of this group of antibiotics. Most of the cases occur in the Achilles tendon and can lead to tendon rupture. Possible predisposing risk factors include steroid use, patients with renal failure or kidney transplantation, old age and being an athlete.

Key words: Gemifloxacin; tendon rupture; subcutaneous bleeding

ÖZ

Nadir ve ciddi bir komplikasyon: gemifloksasin kullanımı sonrası tendinopati

Bu yazıda, alt hava yolu enfeksiyonu nedeniyle gemifloksasin kullanımı sonrası alt ekstremitelerde tendon rüptürü ve subkütanöz kanama gelişen bir hasta sunulmuştur. Florokinolona bağlı tendinopati nadir olarak görülebilir ve daha çok aşıl tendon rüptürü gelişmektedir. Steroid kullananlarda, böbrek hastalığı olanlarda, yaşlılarda ve atletlerde florokinolon kullanımı sonrası tendon rüptürü daha fazla görülebilmektedir.

Anahtar kelimeler: Gemifloksasin; tendon rüptürü; subkütanöz kanama

INTRODUCTION

Fluoroquinolones have been used in many infections, especially in urinary tract infections, upper and lower respiratory tract infections since 1960 (1). Although their benefits as an antibiotic

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Yazışma Adresi (Address for Correspondence)

Dr. Asiye KANBAY
İstanbul Medeniyet Üniversitesi Tıp Fakültesi,
Göğüs Hastalıkları Anabilim Dalı,
İSTANBUL - TÜRKİYE
e-mail: kanbaydr@yahoo.com

have been proven, fluoroquinolones has been reported to be destructive to tendon tissue ranging from tendinopathy to rupture (2). These adverse effects are likely to occur within hours of the first treatment and can last up to six months after discontinuance of medications. Tendinopathy caused by fluoroquinolones was first reported in four cases in 1983, and since then more than 100 cases have been reported in the literature (3,4).

Gemifloxacin, one of the most recently developed fluoroquinolones, is a quinolone with a broad spectrum antibacterial activity that acts against both gram-negative and gram-positive pathogens. It has known side effects such as diarrhea, rash, nausea and headache. Its musculoskeletal side effects are minor but might be significant. Cases of arthralgia and muscle pain, tendonitis and tendon rupture have been identified. Tendinitis associated with ofloxacin, norfloxacin and enoxacin has also been reported but its incidence seems much lower than ciprofloxacin induced tendinitis (5).

The purpose of this case report is to show that tendinopathy such as tendon rupture and bleeding is a rare but important complication of gemifloxacin.

CASE REPORT

A 49-year-old female patient with a previous history of allergic rhinitis and asthma was admitted to the pulmonary medicine outpatient clinic with complaints of cough and purulent sputum. She was prescribed gemifloxacin 320 mg/day for 7 days with the diagnosis of pneumonia. On the 10th day of the treatment, she had difficulty in walking and noticed bruising and swelling on her right leg. There was no trauma history. In her admission laboratory examination, haemoglobin was 14 g/dL (normal range= 11-15 g/dL), platelet was $287 \times 10^3/\mu\text{L}$ (normal range= $100-400 \times 10^3/\mu\text{L}$), and her coagulation parameters prothrombin time and activated partial thromboplastin time were within normal ranges. A venous doppler imaging was performed on her right lower extremity did not show any finding of thrombosis. Her magnetic resonance imaging study revealed edema in fascial planes between right and left gastrocnemius and soleus muscles (Figure 1). A 13 cm cystic collection (possibly with blood contents) with dense content on vertical plane, edema in gastrocnemius lateral head, edema in soft tissues at the level of gastrocnemius myotendinous junction on the left and myotendinous myofascial injury was also found (Figure 2).

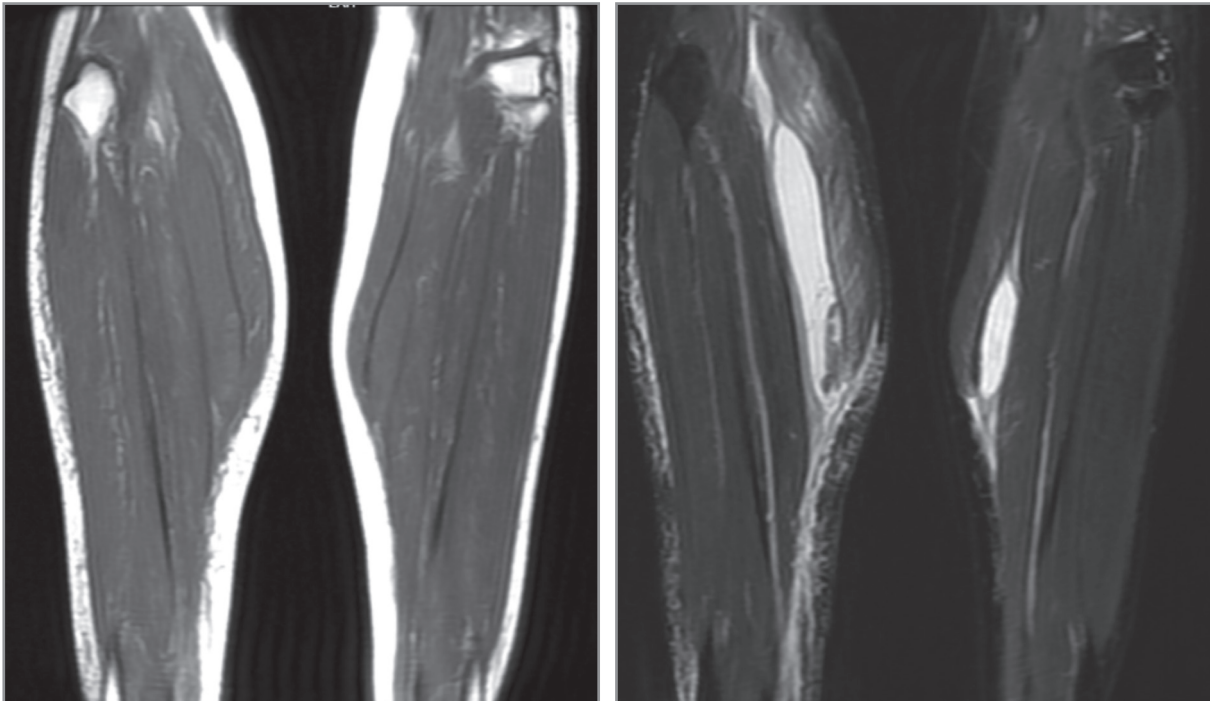


Figure 1. Coronal T1 and T2-weighted MR images showing a 13 cm measured hemoragic collection on the right side between gastrocnemius and soleus muscles with extensive peripheral fascial, muscular and subcutaneous fatty tissue edema. On the left side, on the same location a 6 cm measured pure cystic collection with mild peripheral edema are seen.

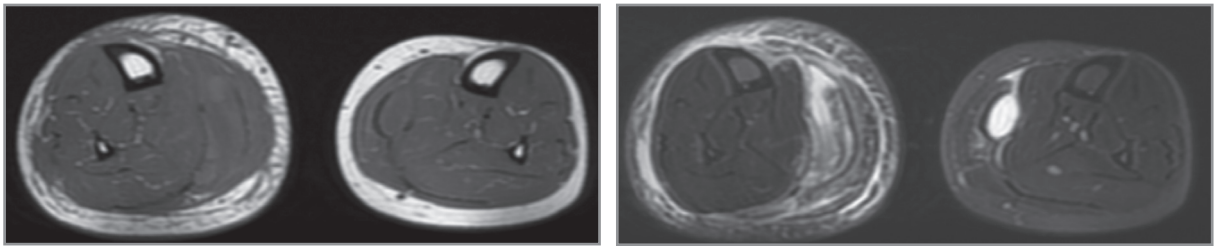


Figure 2. Axial T1 spin fast echo (FSE) and T2 weighted fat sat (FS) magnetic resonance images of the same pathologies mentioned for the coronal images.

The patients were treated with nonsteroidal anti-inflammatory agent and cold compression to her right leg swelling region. Her complaints were progressively improved and resolved within six weeks.

DISCUSSION

Fluoroquinolones are broad spectrum antibiotics and therefore, they are commonly used in the management of community acquired pneumonia. Gemifloxacin is prescribed as a once daily treatment for seven days in patients with community acquired pneumonia.

The most common side effects produced by fluoroquinolones are gastrointestinal (1%-5%), skin changes (maculopapular reactions or skin rash), photosensitivity (less than 2.5%), and neurological effects (1%-2% headache and dizziness) (2,3). Tendinopathy can be seen as a complication of treatment with fluoroquinolones and is often associated with one or more risk factors. The incidence of fluoroquinolone induced tendinopathy is very rare, typically classified as tendinitis (inflammatory) or tendinosis (microtear), is 2.4 in per 10.000 patients. Partial Achilles tendon rupture is rarer as 1.2 patients in per 10.000 (3).

The most commonly reported fluoroquinolones, causing Achilles tendinopathy are ciprofloxacin and pefloxacin. However, all commonly used fluoroquinolones, such as levofloxacin, ofloxacin and norfloxacin, were also been reported (4). Due to the different chemical structure of the new fluoroquinolones (levofloxacin, ofloxacin, gemifloxacin and pefloxacin) is believed to make them more toxic on cartilage and tendons than the former fluoroquinolones (norfloxacin, ciprofloxacin and enoxacin) (6). To the best of our knowledge, this is the first reported case of gastrocnemius myotendinous tendon rupture with bleeding after gemifloxacin therapy.

Risk factors for tendinopathy include old age, long-term history of lung disease, steroid therapy, and

impaired kidney function. In addition, previous studies showed that men are more likely to develop this side effect (4,6). Interesting, none of the risk factors were present in our case other than gemifloxacin.

The underlying pathophysiology of fluoroquinolones-induced tendinopathy is not fully known, but it appears to be multifactorial. The postulated mechanisms are ischemic, toxic, and matrix decomposition processes of the drugs. The clamping properties of fluoroquinolones may also impair the integrity of the tendon (4). Lastly, animal studies have shown that fluoroquinolones has toxic effects on collagen due to chelation of magnesium and free radical formation with subsequent oxidative stress (1,3).

Tendinopathies generally occur within the range of therapeutic doses of fluoroquinolones. However, the severity of tendinopathy seems to be proportional to the duration of treatment (1). In patients with fluoroquinolones-induced tendinopathy/rupture, treatment is based on immediate cessation of fluoroquinolones and pain control (2,3). With mild tendinopathy, non-weight-bearing activity for 2 to 6 weeks may be sufficient. In case of tendon rupture, the patient should be referred to an expert orthopedist. The average recovery time for tendinopathy ranges from 3 weeks to 6 months (3,6).

Gemifloxacin-induced tendinopathy and/or rupture is a rare complication, but it should be kept in mind in the differential diagnosis. Considering these complications, fluoroquinolones should be avoided in patients with risk factors especially in patients with history of tendinopathy. We should also avoid to prescribe fluoroquinolones in patients using steroids. Our patient was under inhaled steroid therapy. If there is no better alternative, patients should be warned about this potential adverse effect, and if there are symptoms suggestive of tendinopathy, they should be advised to stop the medication.

CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: AK, İM, NT

Analysis/Interpretation: AK, İM, NT

Data Acquisition: AK, İM, NT

Writting: AK, İM, NT

Critical Revision: AK, İM, NT

Final Approval: AK, İM, NT

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