A rare but a serious complication: gemifloxacin induced tendinopathy

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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

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...
have been proven, fluoroquinolones has been report-
ed 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 fluoroquino-
lones 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 spec-
trum 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 mus-
cle pain, tendonitis and tendon rupture have been
identified. Tendinitis associated with ofloxacin, nor-
floxacin 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 tendi-
nopathy 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 com-
plaints of cough and purulent sputum. She was pre-
scribed 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 examina-
tion, haemoglobin was 14 g/dL (normal range= 11-15
g/dL), platelet was 287 x 10^3/µL (normal range= 100-
400 x 10^3/µL), and her coagulation parameters pro-
thrombin 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 magnet-
ic 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 hemorrhagic 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.](image)
The patients were treated with nonsteroidal antiinflammatory 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.

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

AUTHORSHIP CONTRIBUTIONS
Concept/Design: AK, İM, NT
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Writing: AK, İM, NT
Critical Revision: AK, İM, NT
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