Bilateral ankle pain and quinolone use: a case of tendon rupture secondary to quinolone use

Introduction

Tendonitis is a rare complication of fluoroquinolone use which was first described in 1983. It has been subsequently demonstrated in a range of case series and a large case control epidemiological study. If severe it can cause tendon rupture. This article describes a case where a patient presented with immobility and ankle pain after treatment with afloxacin.

Discussion

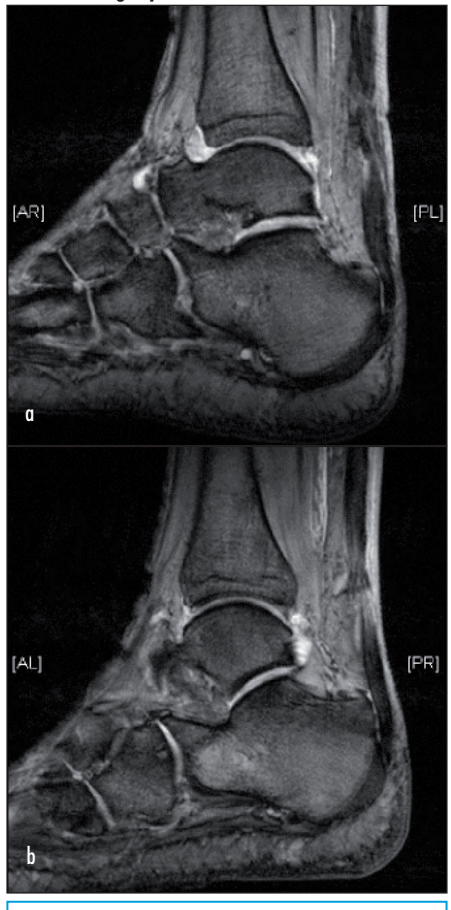
Tendonitis with norfloxacin was described by Bailey et al in 1983. However, the first case of tendon rupture following quinolone toxicity was not recorded until 1987. Public recognition of the complication came in the French Physicians Desk reference in 1992 (Zabraniecki et al, 1996). Since then there have been over 200 case reports describing the problem (Harrell, 1999). The risk of tendinopathy in the UK has been estimated at 3.2 per 1000 patient years (van der Linden et al, 2002), who looked at 46 776 patients taking fluoroquinolones. In those over 60 years of age the risk rose to 6.2 (3.0–12.8) when used in conjuction with corticosteroids. Ruptures are far less common, with worldwide surveillance data estimating levofloxacin-associated ruptures at less than 4 per million prescriptions (Kahn et al, 2001). French reports show the risk of tendon rupture varies with each fluoroquinolone: in descending order of association, pefloxacin, ofloxacin, norfloxacin and ciprofloxacin all cause this problem. The risk is estimated as 1 case per 23 130 treatment days for pefloxacin, and 1 per 779 600 treatment days for ciprofloxacin (Royer, 1996).

Presentation is characterized by sharp pain, sudden in onset, occurring on walking or palpation. Most cases occur after 2 weeks, but can occur after only a few hours or up to 6 months after treatment. The longer the duration of treatment the greater the severity of symptoms. Although the Achilles tendon is the most common site affected the shoulder and hand can be affected as well (Casparian et al, 2000). Examination typically reveals significant swelling, with a positive Simmonds test. The pain diminishes after rupture occurs.

Magnetic resonance imaging is the investigation of choice, as it can show both oedema associated with tendonitis, and rupture (Pierfitte et al, 1995; McGarvey et al, 1996; Harrell, 1999).

The key treatment is immediate discontinuation of quinolone therapy at the earliest suspicion of tendonitis (Gabutti et al, 1998). The natural course is for the tendons to heal slowly after cessation of fluoroquinolones. Weight bearing should be restricted for 2–6 weeks (Gold and Igra, 2003). However, the progress is typically slow, and one study has shown that at 1 month only 50% of patients with fluoroquinolone-induced tendonitis have recovered (Zabraniecki et al, 1996). Tendon rupture occurs in 30% of cases despite adequate intervention. Either surgical repair or conservative management can be

Figure 1. a and b. Magnetic resonance imaging demonstrating rupture of the Achilles tendons.



Case Report

An 80-year-old man presented to the acute medical take in September 2007 with a mechanical fall at home. For the preceding 2 weeks he had developed progressive bilateral heel tenderness following a course of afloxacin prescribed by his GP for a chest infection. This spread to his calves, with the ankles giving way on weight-bearing. He had seen his GP after a week of symptoms, who had noted this as a possible rare side effect of the medication but continued the drug. He had started falling as a result of pain in the tendons, and had no history of trauma before developing these symptoms.

On examination both Achilles tendons were tender with associated bruising. The ankles were hot to touch with flexion confined to 20° because of the pain. It was not possible for the patient to weight bear because of the pain. Simmonds test showed that there was no continuity of the Achilles tendon. Blood tests revealed a C-reactive protein level of 269 mg/litre. The impression was that there was bilateral Achilles tendonitis secondary to the quinolone. Simple analgesia was given and the patient was advised to immobilize because of the significant risk of rupture of the tendons.

An orthopaedic opinion and magnetic resonance imaging was sought to confirm the diagnosis. This revealed bilateral rupture of Achilles tendons (*Figures 1a* and *b*), and repair was needed. A kersler suture repair and vicryl plication was performed.

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used. Surgical measures have a lower incidence of re-rupture and levels of functioning post-operation are often better. In either case casting and prolonged rest is required, with immobilization from 6 weeks to 6 months. Patients should not be rechallenged with quinolones (Harrell, 1999).

Previous cases have hypothesized that quinolones are involved in a cumulative risk of tendon rupture when present with other risk factors. One of the most important risk factors is thought to be concomitant use of steroidal therapy (Gold and Igra, 2003; Haddow et al, 2003; van der Linden et al, 2003). Other risk factors include advancing age, gout, rheumatoid arthritis, hypercholesterolaemia and renal failure (Szarfman, 1995).

There is little known about the pathological mechanisms responsible for quinolone-induced tendinopathy. Studies have implicated ischaemia and toxic matrix degrading processes (Gold and Igra, 2003). Animal studies have shown fluoroquinolones can damage juvenile weight-bearing joints, and most are contraindicated in pregnancy and lactation (Ribard and Kahn, 1991). Only a few histopathological studies have been performed in humans. Neovascularization with interstitial oedema and degenerative lesions were found, but no inflammatory cell infiltrate compatible with an ischaemic process (Ribard et al, 1992). This is similar to the pattern seen in overuse conditions in athletes, which gives credence to the premise that fluoroquinolones alter cellular function, causing an excess production of non-collagenous extracellular matrix (van der Linden et al, 2001).

In patients over 60 years of age, 2–6% of all Achilles tendon ruptures are thought to be attributed to quinolone therapy (van der Linden et al, 2003).

Conclusions

Fluoroquinolones are a rare cause of tendonitis and tendon rupture. In patients presenting with symptoms of tendonitis a clear drug history is required if tendon rupture is to be avoided. BJHM

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Elevated alkaline phosphatase: a diagnostic pearl for Paget's disease

A 96-year-old man presented with dizziness, falls, gradual onset of deafness and generalized joint pain. Clinically there was evidence of postural hypotension. All the blood tests were unremarkable except his alkaline phosphatase level which was 747 U/litre (normal range 38–126 U/litre). A skull X-ray (*Figure 1*) was subsequently requested which showed typical mosaic pattern of areas with increased sclerosis and lucency. After that a bone scan was performed which showed increased tracer accumulation in the calvarium and other parts of the body.

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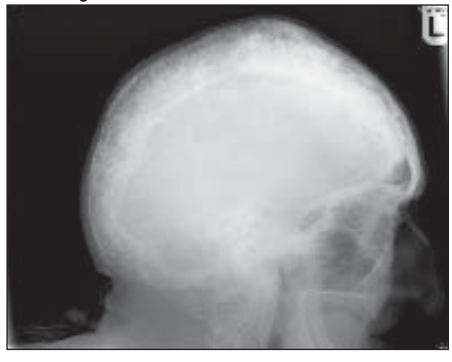
Figure 1. Skull X-ray showing disorder of bone modelling.



Paget's disease, although a localized disorder of bone modelling, typically begins with excessive bone resorption followed by compensatory bone formation. Common symptoms are bone pain, secondary arthritis, bony deformity and neurological complications caused by compressing neural tissue (e.g. deafness). Measuring the total alkaline phosphatase is useful in patients with otherwise normal liver function. Apart from radiographical and biochemical markers, bone biopsy may be necessary. BJHM