

Cash Report

Quinolone induced tendon rupture: a case series

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ABSTRACT

Spontaneous rupture of tendons is a rare condition and mostly it is associated with fluoroquinolones or steroid use. Here we present three interesting cases of tendon ruptures [two cases of achilles tendon rupture and one case of long head of biceps tendon rupture] and investigated their etiologic factors. All the ruptures occurred after minimal stress on the tendons few days after initiation of quinolone therapy, leading to our diagnose of quinolone induced ruptures. Here we highlight the literature review showing association between this class of drug and tendon rupture and its possible mechanism.

Keywords: Fluoroquinolone, Tendoachilis, Biceps, Immobilization

INTRODUCTION

The fluoroquinolones are used to treat a wide range of infections because of its excellent gastrointestinal absorption, superior tissue penetration and broad-spectrum activity. Association of fluoroquinolones with tendon disruptions have been reported before. Achilles tendon is the most common tendon to rupture.¹⁻⁴ Other reported cases include rupture of extensor pollicis longus (lateral aspect of interosseous membrane), biceps long head, peroneus brevis, quadriceps and even rotator cuff.^{1,2} Average time to symptom onset is 2 weeks with range from 1 day to 3 months.¹⁻³ We report three cases of ciprofloxacin and ofloxacin induced achilles and biceps tendon rupture. Here we emphasize searching the potential cause for any spontaneous tendon rupture and importance of discontinuing the culprit drug even at the tendinitis stage.

CASE REPORT

Case one

A 35 year old lady software engineer by profession was having symptoms of urinary tract infection. She was put on ofloxacin for one week but she was continuing the same. After a fortnight of therapy while walking she had sudden, severe pain over right ankle followed by limping. Physical examination showed palpable gap over achilles area (Figure 1). Thompsons test was positive. MRI showed evidence of oedema, haemorrhage and fibre discontinuity confirming tendoachilis rupture (Figure 2). On taking history she had no other associated comorbidities and she had mild pain over retro calcaneal area 2 days before the rupture indicating the tendinitis stage. She subsequently undergone surgical repair of the rupture with uneventful post-operative follow up. Now she is 38 year and is doing well.

Case two

A 55 year old man chronic smoker was given levofloxacin [500 mg bid] for upper respiratory tract infection. 10 days after initiation of therapy he marked left anterior shoulder pain, with pain increased on weight bearing. Cessation of activity and conservative treatment did not relieve symptoms within 3 days of onset of symptoms of pain he felt a pop sound with giving away of anterior shoulder while lifting a bucket of water. Prominent bulge (Popeye muscle) over anterior of arm and USG showed long head of biceps tendon rupture (Figure 3 and 4). Patient was not keen on going under knife and a conservative approach followed. It has been 6 months since and patient is doing his daily activity with few degree of weakness around elbow and shoulder.



Figure 1: loosened tendo achillis depicting a full substance tear.

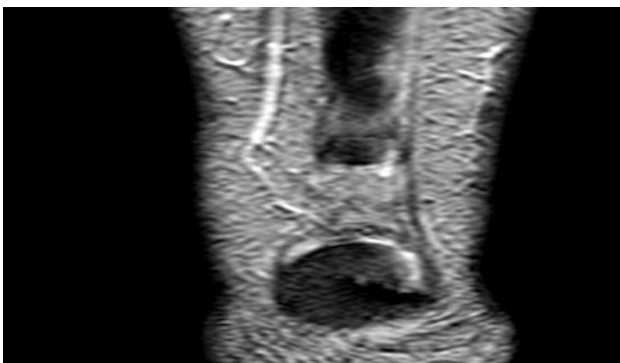


Figure 2: MRI picture showing tendo achillis discontinuity.

Case three

A 78 year old woman with history of hypothyroidism, osteoporosis and hypertension had a 3 week history of productive cough without any fever. She visited a general practitioner and was on levofloxacin thereafter. 5 days after starting the drugs she noticed pain and swelling over left retro calcaneal area after which she could not walk properly. She had no history of trauma or steroid intake. Physical examination revealed positive Thompsons sign, palpable depression over the tendon and USG proved it to

be a complete rupture of tendo achillis. Patient was operated with no post-operative complications (Figure 5).

DISCUSSION

Quinolones were first introduced to the international market in early 1980s within 2/3 years of introduction first case of quinolone induced tendinopathy was reported by bailey et al in 1983 in a patient on norfloxacin.⁵ The first case of tendon rupture was reported in 1987 and the patient was on ciprofloxacin.⁶ A pefloxacin induced tendon rupture in 1991 led to recognition of this complication in French PDR.¹ In 1996 USFDA revised the class levelling for quinolones to include tendinitis/tendinopathy/tendo rupture as possible adverse effect.² Physicians do not appear to be familiar with these adverse effects.



Figure 3: Bulge of anterior arm muscle showing biceps rupture.

Exact mechanism of rupture still remains obscure. There are various proposed theories like ischaemic, toxic, matrix degradative and in vitro studies to support the mechanism of tendon rupture. Quinolones act by inhibiting DNA gyrase (topoisomerase II).¹ Quinolones have metal ion chelating properties and it cause direct toxicity to type 1 collagen synthesis and promote collagen degradation.⁷ This group of antibiotics affect fibroblast metabolism in tendon structures by increasing extracellular matrix degradation. There are evidences about fluoroquinolones induced apoptosis in human tenocytes.⁹ Quinolone induced ruptures occur in less vascularized area, which support the ischaemic theory as well.⁸ Histologically interstitial oedema and severe degenerative changes with absence of inflammatory infiltrates are seen in quinolone induced tendinopathy findings similar in overuse ruptures in athletes.¹¹

The risk factors include concomitant steroid use, age > 60, haemodialysis, renal impairment, renal transplant recipients, diabetes, athletes, female sex, rheumatism etc. Quinolone induced tendinitis are characterized by spontaneous onset and sharp pain that follows walking or palpation on examination marked tendon swelling is present, may mimic cellulitis.² Palpable depression or gap is felt. Thompsons sign (absence of plant flexion of foot

on squeezing of calf) is positive. Clinical diagnoses are confirmed by USG or MRI.



Figure 4: Bulge of anterior arm muscle comparative to the contralateral muscle.

The injury may be unilateral or bilateral, partial or total and in case of achilis tendon located nearly 4 to 5 cm above calcaneal insertion. Though average time to onset of symptoms is 2 weeks with range from day 1 to 3 months. Reports of tendinitis occurring hours after single dose have been reported.^{2,3,12} Quinolone induced tendinopathy occur at normal dose and treatment duration.¹ However a direct relation exist between duration of treatment and severity of rupture.³

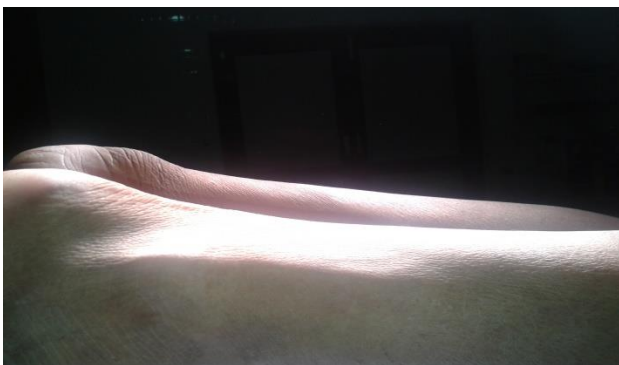


Figure 5: Unilateral tendo achilis discontinuity.

Treatment consists of immediate discontinuation of therapy at the earliest suspicion at the tendinitis stage weight bearing restriction, activity modification for 2-6 weeks needed.¹³ Tendon rupture may be treated conservatively or surgically and need prolonged cast therapy. Prevention is also important. Fluoroquinolone should be used when necessary. As quinolone is a second line antitubercular drugs, its use should be restricted to keep its spectrum sensitive. Co-prescription with steroids should be made cautiously. Thirty percent of patients proceed to tendon rupture despite adequate intervention.¹⁴ Once quinolone induced tendinitis suspected further challenge should be avoided. It is difficult to quantify the risk of tendon ruptures as there may be bias in over reporting. Thus association involving cases that might have occurred spontaneously without medication on the

other hand association may be unrecognized and therefore may be underreported.

CONCLUSION

Since the documentation of this atypical side effects of the quinolone group, the incidence of tendon ruptures have been increased. As the use of quinolones is expanding, more number of patients of tendinitis or tendinopathies is expected. Patients presenting with complain of tendinitis especially those in a risk category should be questioned about history of quinolone use in last 90 days.¹⁰ Prescribers should be well aware of this side effects and should avoid combination of quinolones and steroid unless absolutely needed. Even the patients should know of these side effects and patients of concomitant users of both quinolones and steroid should be advised to do regular physical exercises to reduce the rupture risk.

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