CLINICAL VIGNETTE

Tendinopathy and Fluoroquinolones

By Brian S. Morris, MD

Case Report

The patient is an 81-year-old white male with a history of hypertension, paroxysmal atrial fibrillation, and metastatic esophageal cancer who presented with leg discomfort for 3 days. He had seen another physician 5 days prior for dysuria and nocturia and was started on levofloxacin. The discomfort in his calves began 2-3 days after starting the levofloxacin. He had no fevers, chills, or sweats. He had no arthralgias, rash, or GI complaints and his urinary symptoms resolved.

Past Medical History was significant for hyperlipidemia. Current Medications included omeprazole, dabigatran, atorvastatin, and olmesartan.

He has no medication allergies, does not smoke and drinks 1-2 alcoholic beverages per night.

Physical examination included normal vital signs. There was tenderness over the distal Achilles tendons bilaterally, without swelling or skin changes. Motor, sensory, and reflex exams were normal. Laboratory evaluation revealed a normal CBC, chemistries, ESR, TSH, and urinalysis.

General Discussion and Epidemiology

Fluroquinolone tendinopathy was first reported in 1983 in patients taking norfloxacin[1] In 1987, case reports showed ciprofloxacin was also linked to similar problems[2]. By October of 1998, the FDA had received information on over 200 affected patients and they issued a warning to practicing physicians[3]. The PDR added tendinopathy as a fluoroquinolone side effect noting that the elderly and those with renal insuffiency are at highest risk[4]. The tendinopathy can be noted in patients of any age with a mean age of 60 years with males being at greater risk than females[5]. The risk of fluoroquinolone tendinopathy is 0.1-0.4% but can be more common in high-risk groups such as renal transplant patients or elderly patients with renal insufficiency[5].

Etiology and Pathophysiology

The pathophysiology of the tendinopathy appears to be multifactorial resulting in ischemia and degradation of the tendon matrix with interstitial edema and necrosis[6]. Fibroblast proliferation, altered collagen synthesis, a decrease in proteoglycan synthesis, and an increase in proteolytic activity are also noted[7,8].

Clinical Features

Tendinopathy associated with fluoroquinolones usually presents with the acute onset of sharp pain on ambulation or palpation of the affected tendons with about half of affected patients with bilateral symptoms[9]. Rupture occurs in 25% of affected patients[9]. Symptoms begin days to weeks after the first dose of the medication, but have ranged from after one dose to 6 months after discontinuation of the medication[10]. The risk of tendinopathy appears to be directly related to how long the patient takes the medication and the dose prescribed[11]. The calf, the rotator cuff, the quadriceps, the biceps, and the hand tendons appear to be the most vulnerable[11]. Swelling is typically noted and a DVT or cellulitis is often suspected by the clinician[10]. A positive Thompson sign may be present with absence of plantar flexion on palpating the calf muscles in the prone position[12]. Tendon rupture often relieves the pain in the affected tendon[12]. The most common risk factors include age, renal insufficiency, prior tendon injury, diabetes, peripheral vascular disease, strenuous physical activity, and steroid usage[13]. Reduced renal clearance of the medication significantly increases the risk of tendinopathy so careful attention to renal dosing is critical in this population[13].

Diagnosis and Testing

The diagnosis of fluoroquinolone-induced tendinopathy can be confirmed by ultrasound or more definitively by MRI. An MRI is particularly useful if a rupture is suspected as evidence of edema and hemorrhage can be noted[13]. Findings on MRI can vary from a mild focal defect to full thickness inflammation to complete tendon rupture[14]. Granulomatous changes, degenerative changes, hyaline degradation products, collage proliferation, vascular proliferation, and fibrocystic proliferation are typical findings[14].

Treatment

Patients who present with tenderness or swelling of the lower extremities, especially high-risk patients, should be questioned about use of fluoroquinolones over the last six months[10]. If the patient is still taking the fluoroquinolone, immediate discontinuation of the medication is paramount[9]. Preventive measures include avoiding indiscriminate use of quinolones (especially if safer equivalent antibiotics exist), recognition of patient risk factors, and adherence to proper renal dosing[9]. Also, patients should avoid strenuous lower extremity exercises while on the medication[9]. Patients with mild tendinopathy are instructed to avoid weight bearing for 4-6 weeks after discontinuation of the medication[5]. Patient education may help reduce the musculoskeletal risks associated with this class of medications[9]. Tendon rupture requires a much longer period of treatment with immobilization from six weeks to six months depending on the severity of the rupture[3]. Twenty-five % of patients with fluoroquinolone-induced tendinopathy may eventually suffer rupture so these patients should generally avoid fluoroquinolones in the future[3]. The recovery is slow with a mean of 15-30 days with some patients requiring many months to reach full healing[5]. High-impact sports should be avoided for at least a few months[15].

Prognosis

The prognosis varies widely with elderly patients with renal insufficiency being at particularly high risk for rupture and poor outcomes[3]. Peripheral vascular disease increases the risk in these patients[3]. The quinolone should be discontinued as soon as this side effect is suspected[3]. Healing can take considerable time with studies showing that only 50% of patients are fully healed by one month and 75% are fully healed by 2 months[9,12]. Abnormal biopsy findings suggestive of cystic degeneration of the tendons with increased glycosaminoglycans suggest poor healing and higher risk for tendon rupture[16].

Clinical Course and Follow-Up

The patient was seen and the antibiotic was immediately discontinued. He avoided weight-bearing activities and was fully recovered by three weeks.

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Submitted on June 1, 2014