Case Reports in Orthopedic Research

Case Rep Orthop Res 2022;5:51–56
DOI: 10.1159/000523950
Received: December 22, 2021
Accepted: February 18, 2022
Published online: March 28, 2022

Case Report

Delayed Fluoroquinolone-Induced Tibialis Anterior Rupture: Review and Case Report on Achilles and Tibialis Anterior Atraumatic Rupture with Operative Technique

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Keywords
Fluoroquinolone · Tendinopathy · Tibialis anterior · Achilles tendon · Rupture

Abstract
Tendinopathy is a well-defined adverse effect of fluoroquinolone (FQ) antibiotics with complete tendon rupture being the most serious consequence. The most described FQ-associated tendinopathies are of the Achilles tendon with an onset ranging between 2 h after initial FQ administration to 6 months after completing FQ treatment. We herein report the case of a 50-year-old diabetic woman who suffered from a right Achilles tendon rupture and contralateral nontraumatic tibialis anterior (TA) tendon rupture 11 and 25 months following FQ administration, respectively. Operative management of both injuries identified degenerative changes consistent with FQ treatment. This case is unusual in its involvement of an uncommon tendon in an atypical timeframe. Notably, only one other reported case of FQ-associated TA tendon rupture was identified.

Introduction

Quinolones were first introduced in 1967 with the approval of nalidixic acid. This evolved into fluoroquinolones (FQs) in the 1980s and became exceedingly popular among clinicians [1]. Ciprofloxacin, norfloxacin, and ofloxacin were the initial FQs used in urinary

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tract and respiratory infections for their inhibition of DNA gyrase in gram-negative microbes [2]. The development of newer agents such as levofloxacin and moxifloxacin allowed for greater bactericidal activity in respiratory infections to include topoisomerase IV inhibition of gram-positive microbes [3]. Currently, FQs are used in a wide variety of clinical situations due to their wide spectrum of coverage and are good candidates for bone and joint infections due to high levels of tissue penetration [4]. Despite evidence of adverse effects, there has been a 402% increase in the number of prescriptions from 1991 to 2015 [5, 6].

FQ-induced tendinopathy is one of the documented adverse effects which has high rates of long-term morbidity, especially among elderly populations [7]. An accumulation of various animal studies, case reports, and case-control studies led the FDA to issue warnings on FQ-associated "disabling and potentially permanent side effects of the tendons, joints, (and) nerves" in both 2008 and 2016 [8]. Incidence of FQ-induced tendinopathy has been cited as high as 10 cases per 10,000 patients, with tendon rupture being less common (2.9 cases per 10,000 patients). Certain groups are more at risk; the incidence of tendon rupture in patients greater than 60 years of age with concurrent oral corticosteroid therapies is 19.6 per 10,000 [9, 10]. Other known risk factors include renal dysfunction, history of tendinopathy, current athletic activity, rheumatic disease, diabetes mellitus, gout, and hyperparathyroidism. Of the FQs, ciprofloxacin and levofloxacin are the most commonly implicated [11].

FQs are thought to disrupt the tendon healing response, but their mechanism is not entirely well understood [7, 12]. Three potential mechanisms were described in a review by Tsai and Yang [7]: (1) downregulation of cyclin B, cyclin-dependent kinase 1, and check-point kinase 1 promoting decreased proliferation due to G2/M cell cycle arrest, (2) a decrease in the activity of focal adhesion kinase leading to decreased cell migration, and (3) increased expression of matrix metalloproteinase-2 causing amplified metabolism of type 1 collagen. There is also evidence that FQ consumption increases intracellular reactive oxygen species and, consequently, oxidative stress. Histologically, the tendons of rat models demonstrated severe edematous lesions with mononuclear infiltrate and abnormally deposited collagen following FQ ingestion [13].

Pain of sudden onset is the most common symptom of tendinopathy associated with FQ use, and while it may be generally mild in the case of tibialis anterior (TA) ruptures, there exists a clinical presentation triad [14–16]. Peterson et al. [17] describe a zone of avascularity 5–30 mm from the site of insertion, and this zone localizes the most common site of spontaneous TA ruptures [18]. The clinical presentation consists of a triad of anteromedial pseudotumor of the ankle, absent contour of the TA over the ankle, and use of the extensor hallucis longus and extensor digitorum to compensate with ankle dorsiflexion [15, 19, 20].

Sudden onset of pain and this triad of clinical symptoms allow for history and physical examination to be indicative of TA tendon rupture; however, magnetic resonance imaging is the modality of choice to determine the diagnosis when history and physical examination are not sufficient alone [14, 15, 18]. Onset of symptoms varies largely, from 2 h post-initial FQ administration to 6 months post-treatment termination. Researchers have reported 2 weeks to be the mean onset of symptoms, with approximately 50% cases exhibiting symptoms within 7 days of initial FQ administration [12, 17]. Our case report is unique in that it describes a nontraumatic rupture of the TA tendon 2 years after FQ treatment with a prior contralateral Achilles tendon rupture requiring operative repair. Due to the nontraumatic rupture and degenerative tissue, the healthy proximal tendon was attached to the medial cuneiform via an interference screw instead of direct end-to-end repair.

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Case Report/Case Presentation

A 50-year-old diabetic female treated with metformin presented with difficulty ambulating after feeling a pop in her right foot while walking. The patient's medical history includes presenting to an outside institution 11 months prior with cellulitis of the left 5th toe following a spider (brown recluse) bite. Debridement and amputation of the toe were performed, and the patient was started on Zyvox/Zosyn but was later transitioned to Levaquin/Zyvox after the causative agent was identified (Stenotrophomonas) for a combined duration of 1 month. Simultaneously, the patient's management included weekly debridement of the affected area and negative pressure wound therapy for 3 months. Physical examination was notable for difficulty with resisted plantar flexion and a palpable lump 4–6 cm above insertion of the Achilles tendon. MRI demonstrated a complete rupture of the Achilles tendon with associated edema and tendinosis; however, chronicity to the tear was unable to be determined from imaging. A flexor hallucis tendon transfer was performed 3 weeks from her presentation, and the patient was weight-bearing as tolerated 6 weeks later. At 6 months postoperative, the patient was managed for osteomyelitis of her right calcaneus with a 6-week course of parenteral ceftriaxone and daptomycin, followed by a 4-week course of Augmentin.

The patient returned 13 months after Achilles tendon repair and 25 months after Levaquin therapy for acute onset of left ankle pain after feeling a pop on the anterior aspect of her ankle. Examination was notable for inability to dorsiflex the foot in an inverted position and lack of a palpable TA. MRI demonstrated a complete tear of the TA tendon with a majority of the fibers retracted to the level of the tibiotalar joint, a bone marrow contusion to the medial cuneiform, and fusiform thickening to the distal Achilles tendon with surrounding edema.

Operatively, degenerative changes consistent with FQ-associated tendinopathy were observed at the proximal end of the TA tendon rupture and the frayed, and proximal ends of the aforementioned tendon were determined to be inadequate for direct end-to-end repair. The distal 6 cm of the anterior segment of frayed tendon was whipstitched to form a single tubular structure and directly attached to the medial cuneiform using a 6 mm Arthrex interference screw. The Achilles tendon was percutaneously lengthened to release the significant equinus contracture observed and prevent it from compromising the TA tendon repair. The patient's 1-week postoperative plan included weight-bearing as tolerated in a controlled ankle movement boot along with active range of motion exercises. At 4 months postoperative, the patient had active TA dorsiflexion with good strength.

Discussion

FQs seem to have the greatest effect on the Achilles tendon. A 2003 analysis of 98 cases found that 89.8% involved the Achilles tendon, with the other cases involving the triceps epicondyle, flexor tendon sheath, thumb, patella, supraspinal tendon, quadriceps, subscapularis terra, and rotator cuff [9, 12]. FQ-associated TA tendinopathy has been previously described in the literature, but only 1 case of tendon rupture has been reported to the authors' knowledge [14]. Ruptures of the TA tendon are exceedingly uncommon and are more commonly associated with traumatic events such as lacerations or sudden forces [14, 15]. Nontraumatic events, which are the more uncommon of the two event types, have been described as spontaneous tears of degenerative nature typically affecting males in their sixties to seventies [14]. These have been reported in the literature in case reports of a patient

with psoriasis using a corticosteroid cream and a patient with a gouty tophaceous deposit within the tendon [21, 22].

The preferred treatment for young and physically active patients is surgical repair with early surgical treatment favored over a delayed intervention [19, 23]. Uncorrected TA rupture can produce Achilles tendon contracture and a slap foot gait characterized by significant foot drop and clawing of the toes [24]. For older and less active patient populations, it is possible to opt for conservative treatment with an ankle-foot orthosis. In operative management, it is common for the Achilles tendon to be lengthened to eliminate equinus contracture [19, 24].

Most TA ruptures are caused by traumatic laceration and therefore can be corrected with end-to-end direct repair due to the presence of well-defined edges. Direct repair is often unviable in nontraumatic ruptures because of less clear margins secondary to degenerative changes. As is performed in this case, a possible solution is the attachment of the proximal tendon directly to the medial cuneiform using an interference screw. Other techniques include hallucis longus or extensor digitorum longus tendon transfer, auto- and allografts, and repair to a nonanatomic site [24]. Since the examination of surgical techniques for nontraumatic TA rupture is largely limited to case reports, there is no consensus nor criteria on which affords the best outcomes [19, 23, 24]. However, surgical management as a whole has been demonstrated to lead to a statistically significant improvement of the Foot and Ankle Outcome Score (FAOS) as compared to conservative approaches [24].

Conclusion

Our case presents three unique aspects for FQ-induced tendinopathies and ruptures: (1) atypical tendon involvement; (2) onset exceeding 6 months post-FQ treatment; and (3) surgical tendon attachment to the medial cuneiform via an interference screw. FQ-associated TA tendinopathy and subsequent tendon rupture are uncommon clinical presentations more often described for the Achilles tendon. Pain of sudden onset occurring at an average of 2 weeks post-FQ treatment and a triad of clinical symptoms typically allow for a diagnosis to be made with a history and physical examination alone. While no clear surgical technique criteria to optimize patient outcomes currently exist, ruptures most commonly occur from a traumatic laceration and guide for an end-to-end tendon repair. The decision for surgical management can vary depending on patient age and physical activity goals; however, an unmanaged TA tendon rupture can result in Achilles tendon contracture and subsequent gait abnormalities.

Statement of Ethics

This case report did not meet the regulatory definition of Humans Subject Research as defined by the Augusta University Institutional Review Board and thus does not necessitate an IRB review process. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

No funding supported this article.

Author Contributions

All four authors (Matthew Prevost, MD; Edward Szabo, DPM; Mario Ramirez, BS; and Matthew Heiken, BS) helped with concept, research, writing, and reviewing the article.

Data Availability Statement

The data that support the findings of this study cannot be shared due to the patients' right to protected health information. Queries regarding the data in this article should be addressed to Matthew Prevost, MD, at mprevost@augusta.edu.

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