Tendons in a Patient Undergoing Statin Therapy: A Case Report

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Abstract

In treating cholesterol-related cardiovascular diseases, statins are commonly used as preventative medication and are associated with few side effects. However, recent studies have described a connection between statins and development of tendinopathy. Similar research has noted bilateral rupture of the Achilles tendon, a rare injury, in patients undergoing statin therapy. We describe a 74-yearold man undergoing statin (ie, simvastatin) therapy who presented with pain and swelling in the right ankle after exertional-type activity. Magnetic resonance imaging confirmed a rupture of the Achilles tendon, with rupture of the left Achilles tendon identified 5 weeks later without any obvious trauma-related event. Nonoperative treatment included nonweight bearing in short-leg casts, physical therapy, and eventual temporary discontinuation of simvastatin therapy, which resulted in full return to previous levels of activity by 6-month follow-up. Orthopaedic surgeons should be aware of potential musculoskeletalrelated side effects in patients undergoing statin therapy.

Introduction

Rupture of the Achilles tendon is common and generally occurs in weakened tendons and after high-impact force, particularly in men aged 30 to 50 years who play exertional-type sports intermittently.¹ On the other hand, bilateral tendon rupture is rare and may indicate systemicrelated causes.² These injuries have been associated with renal transplantation,³ systemic lupus erythematosus,⁴ rheumatoid arthritis,⁵ fluoroquinolone use,² and systemic or locally injected steroid.^{6,7}

Recent case reports and retrospective analyses have also noted statin therapy as a possible cause of tendon rupture, specifically in the Achilles tendon.⁸ Statins are commonly administered as preventative treatment of cholesterol-related cardiovascular disease.⁹ Although statin therapy has generally been considered safe with few side effects, musculoskeletal toxicity and myopathy have been reported.¹⁰ We present a 74-year-old man undergoing statin therapy with ruptures of both Achilles tendons, in whom no traditional risk factor for tendinopathy was noted. By 6-month follow-up, the patient returned to previous levels of activity after undergoing nonoperative treatment such as nonweight-bearing short-leg casts and physical therapy.

Case Report

A 74-year-old man presented to our clinic with pain in the right ankle and a soft ankle brace, having injured his Achilles tendon 9 days earlier after lunging forward in a game of pickle ball. He described the resultant feeling as if he "was hit in the back of the ankle with a two-byfour." He did not have history of autoimmune disease, had not undergone an organ transplant, and did not recently undergo steroid or fluoroquinolone therapy. The patient was undergoing simvastatin therapy, with doses of 20 mg per day for treating hyperlipidemia.

No palpable gap was noted in the Achilles tendon with the patient in prone position, but swelling was observed in the region. Results of the Thompson test were positive for a torn tendon. Notably, the results of the Thompson test were negative for tears in the left Achilles tendon and the patient had no complaints of left-sided pain. Magnetic resonance imaging (MRI) revealed a ruptured Achilles tendon without retraction (Figure 1A). After discussing risks and benefits

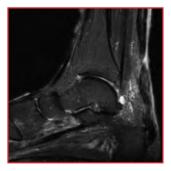


Figure 1A. Magnetic resonance imaging of the right ankle at 9 days after initial injury, showing rupture of the right Achilles tendon.

between nonoperative and operative treatment methods, the patient elected to use nonoperative techniques. His right ankle was placed into a nonweight-bearing short-leg cast in slight equinus position.

At 3 weeks after initial injury, the patient begun to develop pain in his left Achilles tendon. He suspected the pain resulted from overuse owing to the nonweight-bearing status of his right lower extremity. Increased strength of the right lower extremity was observed during right ankle plantarflexion, and use of a short-leg cast was continued.

At 4 weeks after the initial injury, the right Achilles tendon had improved union without any particular swelling on physical examination, and plantar flexion of the ankle against resistance could be performed comfortably with moderate strength. In the left lower extremity, mild swelling was noted, with tenderness around the posterior ankle and Achilles tendon. The tendon seemed to be intact with palpation, with improved strength in plantarflexion. Owing to concern for possible rupture, an MRI was ordered. Until the MRI was obtained, both lower extremities were placed into walking boots with heel lifts.

At 5-week follow-up, findings of the MRI indicated an Achilles tendon rupture of the left ankle (Figure 1B). A short-leg cast was placed on the left lower extremity, whereas the right lower extremity was transitioned into weight bearing with passive range of motion exercises. The concern of statin therapy associated with tendinopathy was discussed with the patient and relayed to his primary care physician. The patient decided to temporarily discontinue statin therapy while the Achilles tendons healed.

At 3 and 2 months after right and left Achilles tendon ruptures, respectively, the patient stopped using walking boots and transitioned into lace-up ankle braces for comfort. Physical therapy was initiated for gait training and progressive strengthening of both lower extremities.



Figure 1B. Magnetic resonance imaging of the left ankle at 5 weeks after initial injury, showing rupture of the left Achilles tendon.

At 6 months after his initial right-sided injury, the patient walked similarly to before the injury and returned to previous levels of daily activity, without use of the brace or other nonweight-bearing devices.

Discussion

To date, no precise mechanism for bilateral rupture of the Achilles tendon has been identified, and the causal relationship between statin therapy and tendinopathy is still in question. A postmarket analysis⁸ reported statinassociated tendinopathy (with the Achilles tendon being the most affected) in a small proportion of patients (2.1%) administered low-density lipoprotein. Furthermore, results of another retrospective study¹¹ indicated no significant increase in tendinopathy among patients undergoing statin therapy compared with age-matched control groups. However, biochemical studies on rodents have reported definite change in the chemical makeup of tendons exposed to prolonged use of statin.¹²

Multiple theories have been suggested for explaining statin-related tendon toxicity, including decreased angiogenesis and vascularization,¹³ reduced cholesterol content of cell membranes,¹¹ and imbalance of matrix metalloproteinases and eicosanoids.¹⁴ To our knowledge, one case report¹⁵ has described bilateral Achilles tendon rupture and attributed the injury to statin therapy because no other risk factors were identified. Two studies have reported more generally on bilateral quadriceps tendon rupture indirectly associated with statin therapy.^{16,17} Notably, in the current study, the rare occurrence of metasynchronous bilateral Achilles tendon rupture indirectly associated with statin therapy.^{16,17} Notably, in the current study, the rare occurrence of metasynchronous bilateral Achilles tendon rupture was noted without identifiable systemic risk factors, and the second rupture involved no apparent trauma-related event.

Although the relationship between statin therapy and tendinous injury remains unclear, orthopaedic surgeons and primary care physicians should consider potential risk for musculoskeletal side effects in patients undergoing statin therapy. In avoiding tendon-type injuries, caution should be taken in prescribing statin for patients with higher risks for tendinous disorders (ie, patients with concomitant fluoroquinolone therapy, high-intensity muscular activity, and healing tendinous injuries).

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Conflict of Interest

The authors report no conflicts of interest.

Informed Consent

The patient was informed that the data concerning the case would be submitted for publication, and he provided verbal consent.

References

1. Hayes T, McClelland D, Maffulli N. Metasynchronous bilateral Achilles tendon rupture. Bull Hosp Jt Dis 2003;61(3-4):140-4.

2. Stinner DJ, Orr JD, Hsu JR. Fluoroquinolone-associated bilateral patellar tendon rupture: a case report and review of the literature. Mil Med 2010;175(6):457-9.

3. Hestin D, Mainard D, Pere P, et al. Spontaneous bilateral rupture of the Achilles tendons in a renal transplant recipient. Nephron 1993;65(3):491-2.

4. Formiga F, Moga I, Pac M, Valverde J, Fiter J, Palom X. Spontaneous tendinous rupture in systemic lupus erythematosus: presentation of 2 cases [In Spanish]. Rev Clin Esp 1993;192(4):175-7.

5. Rask MR. Achilles tendon rupture owing to rheumatoid disease: case report with a nine-year follow-up. JAMA 1978;239(5):435-6.

6. Kotnis RA, Halstead JC, Hormbrey PJ. Atraumatic bilateral Achilles tendon rupture: an association of systemic steroid treatment. J Accid Emerg Med 1999;16(5):378-9.

7. Unverferth LJ, Olix ML. The effect of local steroid injections on tendon. J Sports Med 1973;1(4):31-7.

8. Marie I, Delafenêtre H, Massy N, Thuillez C, Noblet C; Network of the French Pharmacovigilance Centers. Tendinous disorders attributed to statins: a study on ninetysix spontaneous reports in the period 1990-2005 and review of the literature. Arthritis Rheum 2008;59(3):367-72.

9. Choudhry NK, Dugani S, Shrank WH, et al. Despite increased use and sales of statins in India, per capita prescription rates remain far below high-income countries. Health Aff (Millwood) 2014;33(2):273-82.

10. Finegold JA, Manisty CH, Goldacre B, Barron AJ, Francis DP. What proportion of symptomatic side effects in patients taking statins are genuinely caused by the drug? Systematic review of randomized placebo-controlled trials to aid individual patient choice. Eur J Prev Cardiol 2014;21(4):464-74.

11. Contractor T, Beri A, Gardiner JC, Tang X, Dwamena FC. Is statin use associated with tendon rupture: a population-based retrospective cohort analysis. Am J Ther 2015;22(5):377-81.

12. de Oliveira LP, Vieira CP, Da Ré Guerra F, de Almeida Mdos S, Pimentel ER. Statins induce biochemical changes in the Achilles tendon after chronic treatment. Toxicology 2013;311(3):162-8.

Esenkaya I, Sakarya B, Unay K, Elmali N, Aydin NE. The influence of atorvastatin on tendon healing: an experimental study on rabbits. Orthopedics 2010;33(6):398.
Gómez-Hernández A, Sánchez-Galán E, Ortego M, et al. Effect of intensive atorvastatin therapy on prostaglandin E2 levels and metalloproteinase-9 activity in the plasma of patients with non-ST-elevation acute coronary syndrome. Am J Cardiol 2008;102(1):12-8.

15. Carmont MR, Highland AM, Blundell CM, Davies MB. Simultaneous bilateral Achilles tendon ruptures associated with statin medication despite regular rock climbing exercise. Phys Ther Sport 2009;10(4):150-2.

16. Rubin G, Haddad E, Ben-Haim T, Elmalach I, Rozen N. Bilateral, simultaneous rupture of the quadriceps tendon associated with simvastatin. Isr Med Assoc J 2011;13(3):185-6. 17. Nesselroade RD, Nickels LC. Ultrasound diagnosis of bilateral quadriceps tendon rupture after statin use. West J Emerg Med 2010;11(4):306-9.