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Statin Therapy and Tendon Rupture in High ASCVD Score Patient: A Comprehensive Case Report and Literature Review

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Abstract

Statin-induced tendon rupture is a rare clinical manifestation that warrants attention, especially in patients with a high 10-year atherosclerotic cardiovascular disease (ASCVD) risk score. This case report presents the unique scenario of a 58-year-old male with a history of ischemic heart disease and previous percutaneous coronary intervention who experienced tendon rupture following minor traumas while on long-term statin therapy. The patient underwent surgical intervention involving tendon repair to address the rupture.

Given the association between statins and tendon ruptures documented in the literature, we conducted a thorough review to identify reliable substitute medications for statins in high-risk patients with ASCVD. The literature review explored alternative treatment options that effectively manage cardiovascular risks while minimizing the potential risk of tendon rupture. The findings from this case report and literature review provide valuable insights into managing statin-induced tendon rupture and highlight the importance of considering alternative medications in patients with high 10-year ASCVD scores.

Introduction

The use of diagnostic biomarkers to diagnose common diseases is rising [1-3]. The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors or statins are used in the primary and secondary prevention of cardiovascular events [4,5].

Statins are usually well-tolerated and do not have many serious side effects. One of the side effects that can affect the decision to continue treatment with statins is musculoskeletal complications such as tendinopathy, which is most common with Atorvastatin and Simvastatin [6].

Statin-related musculoskeletal adverse effects (AE) vary from mild myalgia and muscle weakness to tendinopathy and rhabdomyolysis [1]. The probable risk factors are summarized in Table 1. Tendinopathy is usually presented with tendinitis and tendon rupture, especially of the Achilles, quadriceps, and distal biceps tendons, which mostly happen within the first year of initiation and improve after discontinuation [3].

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This case report describes a 58-year-old man who experienced tendon rupture as an adverse effect of statin use. Given the significance of this complication, it is crucial to explore alternative treatment options for high-risk patients, particularly those with a high ASCVD score. By examining the existing literature, we aim to identify a reliable substitute for statins in such patients, ensuring effective management of their atherosclerotic cardiovascular disease while minimizing the risk of tendon-related adverse events.

Case report

Patient presentation

A 58-year-old male, employed in a municipal position with a history of athletic experience, presented with two tendon ruptures in the rotator cuff, occurring in different shoulders after experiencing two minor traumas. His medical history included ischemic heart disease for which he underwent Percutaneous Coronary Intervention (PCI) four years ago. Additionally, he had a 10-year Atherosclerotic Cardiovascular Disease (ASCVD) risk score of 22.7% and had been diagnosed with benign prostatic hypertrophy, hypertension, and diabetes mellitus. The patient's prescribed medications consisted of 40 mg atorvastatin once daily, 0.4 mg tamsulosin once daily, 5 mg amlodipine once daily, dutasteride 0.5 mg once daily, metoprolol 12.5 mg every 12 hours, metformin 500 mg every 8 hours, pioglitazone 15 mg daily, and ASA 80 mg once daily. Notably, the patient did not consume alcohol and did not smoke.

Clinical course

Before the occurrence of these tendon ruptures, the patient reported experiencing shoulder pain following sports activities, such as soccer, which had not been a previous issue. The initial trauma occurred in 2020 while the patient was climbing a mountain with a slight slope. During this incident, he slipped on his left hand, experiencing mild pain at the moment. However, the pain was not severe enough to prompt him to seek medical attention, and similar occurrences in the past had resolved spontaneously. Subsequently, after some time (exact duration not recalled), the patient experienced a similar falling accident while participating in an indoor soccer game. This incident resulted in severe shoulder pain, leading him to consult a physician. The pain was intense, and he faced difficulties in lifting his hand.

Investigations and diagnosis

An MRI (Figure 1) revealed a full-thickness tear at the critical zone of the supraspinatus tendon, attributed to the initial mild trauma. Additionally, a partial tear of the right rotator cuff tendon was evident but remained undiagnosed and untreated at that time. After a two-year interval, the patient experienced another fall, causing the same severe, non-radiating pain that worsened during nighttime and hand abduction. A subsequent MRI (Figure 2) identified a complete rotator cuff tendon and joint effusion tear. As a result, the patient underwent a second arthroscopic tendon repair procedure.

Implications and management

Following the occurrence of these two minor traumas, the possibility of atorvastatin side effects as the underlying cause was considered. Employing the Naranjo Adverse Drug Reaction (ADR) probability scale, the patient scored a 7, indicating a probable association between atorvastatin and tendon ruptures. Consequently, atorvastatin was discontinued, and an alternative drug was sought to manage the patient's high 10-year ASCVD risk.

Considering the necessity of reducing cardiovascular mortality while avoiding statins, evolocumab, a PCSK9 inhibitor, was selected as the suitable alternative after a comprehensive evaluation. The patient was prescribed a dose of 140 mg once every two weeks.

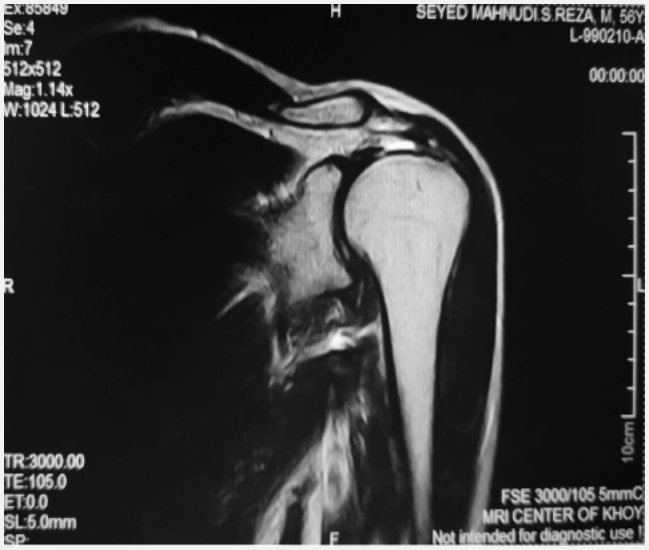

Figure 1: Full thickness tearing seen at critical zone of supraspinatus tendon.

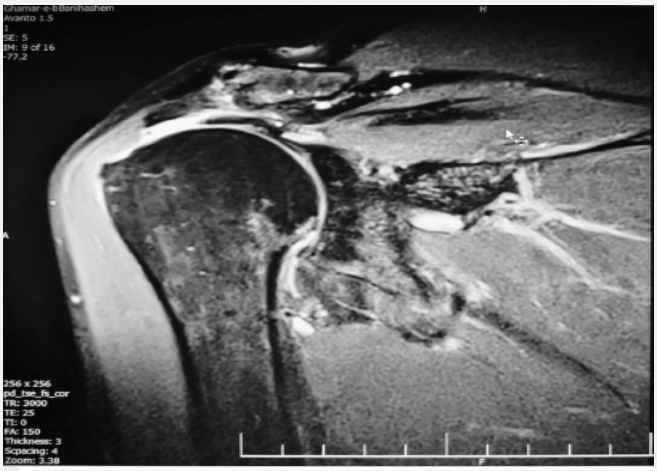

Figure 2: Complete tearing in the rotator cuff tendon.

Table 1: Major risk factors of statin-induced musculoskeletal injury.

Age>80 y/o
Female sex
Chronic kidney disease
Acute or chronic liver disease
Hypothyroidism
Recent major trauma or surgery
Drug interactions (ie. Fibrates, calcium channel blockers, amiodarone, pioglitazone and rosiglitazone, azole antifungals, protease inhibitors, etc.)

Discussion

The clinical benefits of statins in reducing mortality among patients with a history of cardiovascular events are attributed to their pleiotropic effects [7-9]. Several medications have been associated with an increased risk of tendon rupture. These include:

1. Fluoroquinolones, particularly ciprofloxacin and levofloxacin, have been associated with an increased risk of tendon rupture, especially in the Achilles tendon [10].
2. Corticosteroids such as prednisone and cortisone can weaken tendons and increase the risk of rupture [11].
3. Fluconazole: Also has been associated with an increased risk of Achilles tendon rupture [12].
4. Isotretinoin toxicity: Tendinopathy also have been reported in patients taking isotretinoin [13].
5. statins: Atorvastatin and simvastatin have also been linked to an increased risk of tendon ruptures.

Although statins have been associated with an increased risk of Achilles tendon rupture, the risk is relatively low. Recent studies found that the risk of tendon rupture in statin users was 0.4%, compared with 0.2% in nonusers. The studies also found that the risk was highest in those who took high doses of statins over a long period [14]. But in addition to statin use, other risk factors, as mentioned in Table 1, may also increase the likelihood of tendon rupture, and in patients, such as those discussed in our case report, who do not have any of the risk factors listed in the table, we should consider the higher likelihood of tendon rupture due to statins [15-19].

The clinical effect of statins in reducing mortality in patients with a history of cardiovascular events is related to their pleiotropic effects, which means that, in addition to the cholesterol-lowering effect, they have additional effects that are responsible for the clinical benefits in patients with CVD. These effects include improvement of myocardial perfusion and reduction of recurrent anginal episodes after acute chronic events through modulation of endothelial function, plaque stabilization, neovascularization, attenuation of atherogenesis, improvement of neurohormonal imbalance, reduction of oxidative stress, vascular inflammation, and antithrombotic effects action [7,20,21].

Suggesting an alternative drug in patients requiring secondary prophylaxis for cardiovascular events is considered a serious challenge, especially in the case of adverse events such as recurrent tendinopathy requiring discontinuation of the statin.

Proprotein convertase subtilisin/kexin type 9 inhibitors (PCSK9 inhibitors) are one of the hypolipidemic classes approved by the Food and Drug Administration (FDA) for treating autosomal familial hypercholesterolemia. Evolocumab, alirocumab, and cocizumab are known PCSK9 inhibitors. Their main mechanism of action is to increase LDL receptors on hepatocytes by inhibiting PCSK9, a protein responsible for suppressing LDL receptor activity [22,23].

The pleiotropic effects of this family include lipid-lowering effects, inhibition of atherogenesis, stabilization of atherosclerotic plaque, anti-inflammatory effects by increasing the concentration of interleukin 10 (IL -10) and decreasing the concentration of interleukin-1α (IL -1α), interleukin-6 (IL -6) and tumor necrosis factor α (TNF-α) [24,25], anti-aggregation and anticoagulant properties [22,26,27].

Because of its effect on reducing cardiovascular events and all-cause mortality in patients at very high risk for atherosclerotic cardiovascular disease (ASCVD) [28,29], they can be considered as a suitable alternative in patients with statin intolerance.

There are few studies on the association between PCSK9 inhibitors and tendon rupture. However, some studies suggest that PCSK9 inhibitors may negatively affect tendon health and increase the risk of tendon rupture. This is because PCSK9 inhibitors can cause a decrease in cholesterol levels, which can affect tendon structure and function [30,31].

In cases of rare but urgent conditions similar to the occurrence of statin-induced tendon rupture in patients on long-term statin therapy, it is crucial to consider alternative treatment options and prioritize anticipatory care planning and follow-up to potentially restore normal tissue function and preserve organ integrity [32-34].

Conclusion

This case highlights the significance of vigilance regarding rare yet severe adverse effects of medications, such as tendon ruptures in patients receiving statin therapy. Additionally, it underscores the importance of considering alternative treatment options, like PCSK9 inhibitors, to effectively manage cardiovascular risks in individuals with a high 10-year ASCVD score. Further research is warranted to better understand and mitigate such uncommon side effects associated with statins.

It is important to note that the risk of tendon rupture with statins is relatively low and that its benefits often outweigh the risks. However, if your patient is taking one of these medications and experiences sudden pain or weakness in a tendon, you should consider the possibility of tendon rupture, and we recommend (PCSK9) inhibitors as an alternative choice for these patients.

Declarations

1. **Funding:** Not applicable
2. **Conflicts of interest/Competing interests:** The authors declare that there is no conflict of interest to declare.
3. **Ethics approval:** No additional costs and procedures were imposed on the patient's family members in this study. We reported the retrograde standard treatment process of the patient. We maintained the patient's privacy
4. **Consent to participate:** The patient has consented to participate in this case report.
5. **Availability of data and material:** The data supporting this study's findings are available from the corresponding author, upon reasonable request.

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