Bilateral, Simultaneous Rupture of the Quadriceps Tendon Associated with Simvastatin

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Bilateral, simultaneous quadriceps tendon rupture is a rare entity. Shah et al. [1] analyzed 66 cases published in the English-language medical literature from 1949 to 2002, and Neubauer et al. [2] performed a meta-analysis of 105 published cases in the English and German literature from 1949 to 2004. The initial diagnosis was missed in 30.5% of cases; most of the patients were male (89.3%), with a mean age of 54.5 years. The main risk factors identified were obesity, chronic renal failure, hyperparathyroidism, atherosclerosis and gout [2].

Statins (3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors) are the most effective therapeutic modalities for reducing serum cholesterol and low-density lipoprotein cholesterol levels. Musculoskeletal complications such as pain, myositis, rhabdomyolysis, myopathy and tendonitis are well known [3]. Tendon rupture associated with statin therapy is rare and it has been suggested that it may be related to the pleiotropic effect of statins on matrix metalloproteinase activity [4]. We present a case of bilateral, simultaneous quadriceps tendon rupture associated with simvastatin therapy.

Patient Description

The patient was a 58 year old man, weight 75 kg (body mass index 27), with a medical history of hypertension and hypercholesterolemia who had been treated for the previous 4 years with simvastatin (the last 2 years with 80 mg per day). He presented to the emergency department with an “electric shock” type pain while walking, without trauma, in both of his legs. Initially, it was suspected that he suffered from cerebral ischemia; this was ruled out following diagnostic workup. He was then examined by an orthopedic surgeon who noticed swelling of both knees and suprapatellar gaps. The patient was also unable to extend his knees actively. Sonographic studies revealed hematoma and complete bilateral quadriceps tendon rupture. He was admitted and underwent surgery. Intraoperatively, both tendons were completely avulsed from the cranial pole of the patella and the retinacula were ruptured [Figure]. The tendons were reattached with trans-osseous sutures and the retinacula were repaired. Postoperatively he was immobilized in a 0–15 degree flexion brace, with full weight bearing. Simvastatin treatment was discontinued.

A diagnostic evaluation was conducted to consider known risk factors of tendon rupture, including the use of anabolic steroids. Blood samples for parathyroid hormones, uric acid, renal function, anti-nuclear antibody and cholesterol were all in the normal range. Histopathology evaluation of the tendon revealed no pathological changes. Congo red staining ruled out amyloidosis.
COMMENT

Tendon rupture associated with statin therapy is rare. Until 2006, the Food and Drug Administration’s adverse-drug-effects-reporting database had collected data related to 247 cases of statin-related tendon rupture [4]. Beri and co-authors [5] published a case-control study that found no overall association between the use of statins and tendon rupture, although in subgroup analysis, statin use was found to be a significant risk factor for tendon rupture in women.

We found no reports of bilateral, simultaneous, spontaneous rupture of the quadriceps tendon associated with statin therapy, although bilateral rupture of the Achilles tendon associated with statins had been reported. The patient was evaluated for factors known to cause tendon rupture, including histopathological evaluation for special pathological changes. We were unable to determine any alternative factors, indicating that statin-related tendinous complications may be the cause. We therefore suggest that physicians consider statin-related tendinous complications.

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**Capsule**

**Exome sequencing identifies frequent mutation of the SWI/SNF complex gene PBRM1 in renal carcinoma**

The genetics of renal cancer is dominated by inactivation of the VHL tumor suppressor gene in clear-cell carcinoma (ccRCC), the commonest histological subtype. A recent large-scale screen of ~3500 genes by polymerase chain reaction-based exon re-sequencing identified several new cancer genes in ccRCC including *UTX* (also known as *KDM6A*), *JARID1C* (also known as *KDM5C*) and *SETD2*. These genes encode enzymes that demethylate (UTX, *JARID1C*) or methylate (*SETD2*) key lysine residues of histone H3. Modification of the methylation state of these lysine residues of histone H3 regulates chromatin structure and is implicated in transcriptional control. However, together these mutations are present in fewer than 15% of ccRCC, suggesting the existence of additional, currently unidentified cancer genes. Varela and co-researchers have sequenced the protein coding exome in a series of primary ccRCC and report the identification of the SWI/SNF chromatin remodelling complex gene *PBRM1* as a second major ccRCC cancer gene, with truncating mutations in 41% (92/227) of cases. These data further elucidate the somatic genetic architecture of ccRCC and emphasize the marked contribution of aberrant chromatin biology.

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**Capsule**

**Prion propagation and toxicity in vivo occur in two distinct mechanistic phases**

Mammalian prions cause fatal neurodegenerative conditions including Creutzfeldt-Jakob disease in humans and scrapie and bovine spongiform encephalopathy in animals. Prion infections are typically associated with remarkably prolonged but highly consistent incubation periods followed by a rapid clinical phase. The relationship between prion propagation, generation of neurotoxic species and clinical onset has remained obscure. Prion incubation periods in experimental animals are known to vary inversely with expression level of cellular prion protein. Sandberg et al. demonstrate that prion propagation in brain proceeds via two distinct phases: a clinically silent exponential phase not rate-limited by prion protein concentration which rapidly reaches a maximal prion titer, followed by a distinct switch to a plateau phase. The latter determines time to clinical onset in a manner inversely proportional to prion protein concentration. These findings demonstrate an uncoupling of infectivity and toxicity. We suggest that prions themselves are not neurotoxic but catalyze the formation of such species from PrPSc. Production of neurotoxic species is triggered when prion propagation saturates, leading to a switch from autocatalytic production of infectivity (phase 1) to a toxic (phase 2) pathway.

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