



Statin-induced muscular symptoms : A report of 3 cases

A.J. Shyam KUMAR, Shaun K. WONG, Glynne ANDREW

North West Wales NHS Trust, Ysbyty Gwynedd, Bangor, United Kingdom

Although the prescription of statin medication has increased worldwide and especially in Europe, its musculoskeletal side effects and their management strategy has not been highlighted in orthopaedic literature.

We present three cases of statin-induced musculoskeletal symptoms which presented to an orthopaedic department. There were two patients with statin induced muscle pain (one in the thigh and one around the hip), and one with both myositis (with raised creatine kinase) and lupus-like symptoms. All of the symptoms resolved with stopping the statin. Muscle pain (often with normal creatine kinase) is the commonest side effect of statins. It is usually bilateral, but two of our cases presented with unilateral symptoms which made it more difficult to exclude a primary orthopaedic pathology.

The widespread use of statins is likely to lead to an increase in the number of patients presenting to orthopaedic surgeons with muscle pain. It is important to consider muscle pain induced by statins in the differential diagnosis of acute or chronic pain in the limbs.

Keywords : statins ; side effects ; muscle pain.

including polyarthralgia. We present three cases of statin-related musculoskeletal side effects which were diagnosed and treated in our department in the last one year. Two were admitted with severe acute pain which on assessment was muscle pain due to statins. One was seen as an elective patient and was noted to have a raised creatine kinase, muscle pain and arthralgia.

Statin are now widely used as lipid lowering agents. The use of statins across Europe has increased considerably in recent years. In the UK alone, the amount of statin consumption has increased more than 120% (17). Some researchers have even considered it to be the new aspirin (6). Low dose statins can now be purchased over the counter by people at moderate risk of heart disease according to eligibility criteria developed by the Royal Pharmaceutical Society of Great Britain (18). In view of the current widespread use of this medication, orthopaedic surgeons need to be aware

INTRODUCTION

Statin may cause a variety of musculoskeletal side effects, but this has not been previously highlighted in the orthopaedic literature. The main musculoskeletal side effects are muscle symptoms ranging from mild muscle pain to acute rhabdomyolysis (5). Others include a lupus-like syndrome

■ Andalat J.S. Kumar, FRCS, Specialist registrar, All Wales trauma & orthopaedics higher specialist training scheme.

■ Shaun K. Wong, MB chB, Senior house officer.

■ Glynne Andrew, MD, FRCS, Consultant.

Department of Trauma & Orthopaedics, Ysbyty Gwynedd, Bangor, United Kingdom.

Correspondence : A.J. Shyam Kumar, Flat-23, Rhos Gwyn, 493 Abergele road, Colwyn bay, LL29 9AE, United Kingdom.

E-mail : ajshyamkumar@hotmail.co.uk

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of the common modes of presentation of both statin-induced myopathy and statin-induced lupus and their management strategy.

CASE REPORT

1. A 63-year-old lady presented to the casualty department with pain in the right thigh and knee. She attributed the pain to walking 3 miles on holiday a week prior to presentation. The pain had increased in the past two days.

A knee aspiration did not reveal any organisms on Gram's staining. The CRP was < 10 mg per litre and ESR was 32 mm/h. The patient was treated with analgesics. On follow-up she was seen to have quadriceps wasting on the same side. An MRI of the knee was arranged which was normal. A month after the initial presentation, the patient presented again with severe pain in the right thigh. Clinical examination revealed a full range of knee movement but the patient was tender over the mid quadriceps muscle. She was taking atorvastatin 20 mg per day. Creatine kinase was normal and the CRP was again < 10 mg per litre. The statin medication was stopped and the patient's pain was marginally better after 24 hours. Within days she reported complete pain relief and two months after discharge from the hospital she had complete pain relief and did not need further analgesia.

2. A 53-year-old man presented to the accident and emergency with a 3 days history of right hip pain. He was afebrile and there was no history of trauma. Local examination of the right hip revealed tenderness over the posterior aspect of the greater trochanter region and the inguinal region. The patient was limping and had an antalgic gait. Active movements of the right hip were painful. Passive range of movements of the right hip was flexion 90°, abduction 30°, adduction 10° and 20° of internal and external rotation. The CRP was 13 mg per litre and the white cell count was 9.8 per cubic mm. The patient was taking atorvastatin 20 mg daily since 18 months prior to the admission. The statin was stopped and pain disappeared completely after two days.

3. A 78-year-old man was seen in the orthopaedic clinic with pain in the left knee. He gave a history of diffuse oedema and intermittent rash over the left lower leg for the past year. The fingers of both hands appeared puffy with moderate swelling in the hands, and marked restriction of hand grip and finger range of motion. Examination of the knee revealed features consistent with osteoarthritis of the knee. The patient was taking rosuvastatin 10 mg per day since one month prior to the clinic consultation. He was referred to the rheumatologist and a creatine kinase estimation was 247 units per litre (Normal 24-195 for males). The CRP was less than 10 mg per litre. The statin was stopped and the hand swelling and rash completely resolved over a period of a few weeks. Hand function improved. The creatine kinase also returned to normal. The likely diagnosis appeared to be a combination of statin-induced myositis and statin-induced lupus. Further investigation did not seem warranted.

DISCUSSION

Muscle pain (as opposed to bone or joint pain) is not considered a common presenting complaint to orthopaedic services. Given the very widespread use of statins, and the incidence of muscle side effects while on these drugs, it seems likely that the number of patients presenting with this symptom may increase. It is important that muscle pain is included in the differential diagnosis when assessing patients presenting with pain. In our cases, alternative differential diagnoses considered included patellofemoral pain, a meniscal tear (excluded in the first patient by an MRI scan) and hip joint sepsis.

Three types of muscle disorders associated with statins have been defined. They are myalgia – muscle pain or muscle weakness without CK elevation, myositis – pain or weakness with CK elevation and rhabdomyolysis- muscle symptoms with CK elevation greater than 10 times the upper limit of normal, usually associated with myoglobinuria (11). The most common muscle side effect reported is myalgia. The incidence of muscle complaints

among patients being treated in a practice setting ranges from 0.3%-33% (2). Statin induced myalgia is usually symmetrical, involving large proximal muscle groups and resolves with discontinuation of the medication (15). The presence of unilateral symptoms (as in two of our patients) makes diagnosis more difficult.

Several specific risk factors for statin-induced myopathy are recognised. Older age, alcohol abuse, small stature, chronic renal disease, hypothyroidism, and diabetes are well established risk factors for developing myopathy with statin therapy (3,4). Drugs affecting statin metabolism like fibrates, cyclosporine, macrolide antibiotics, warfarin, digoxin and azole antifungals can potentiate the effects of statins (14). The consumption of large amounts of grapefruit juice is also considered to be a risk factor for statin induced myopathy (10). It is thought that the prevalence of muscle pain is greater in athletes taking statins. In professional athletes suffering from familial hypercholesterolaemia it was found that only 20% tolerated statin treatment without side effects (9).

When a patient on statin therapy presents with myalgia, a thorough history and clinical examination should be undertaken to rule out any other causes of myalgia. Creatine kinase levels may be normal even in the presence of statin-induced myopathy (12). If the creatine kinase levels are high, then renal function and urine myoglobin should be checked and a medical referral may be appropriate. In most patients the CK levels are normal and the current statin may be stopped to relieve the symptoms. The general practitioner in charge of the patient should be informed of this action and these patients may need restarting of the same drug with a lower dose after the symptoms subside. Simvastatin 80 mg (but not lower doses) appears to cause the highest frequency of rhabdomyolysis. Fluvastatin and pravastatin which are weak inhibitors of HMG-CoA reductase appear to cause the lowest frequency of rhabdomyolysis (2,7). Some authors recommend trying an alternate statin or another class of lipid lowering medication (16). Attempts have been made to decrease the muscle symptoms with coenzyme Q10 prophylaxis in patients, but the results are equivocal (15).

Muscle pain may also occur after major orthopaedic surgery, where surgical access may incise or retract muscles for protracted periods. Statins are known to impair muscle's ability to appropriately respond and recover from physical exertion, potentially resulting in skeletal muscle damage (16). The National Lipid Association Statin Safety Assessment Task Force in the United States has recommended counselling of patients on statins regarding the increased risk of muscle complaints if a surgical operation is to be undertaken (8). Other authors have recommended discontinuing statins before major surgery (1,13). At the least, the effects of statins should be assessed in patients complaining of an unexpected degree of muscle pain after surgery.

In conclusion, the widespread use of statins is likely to lead to an increase in the number of patients presenting to orthopaedic surgeons with muscle pain. It is important to include myalgia in the differential diagnosis of limb pain, to assess biochemical evidence of muscle damage, and in such patients to assess the effect of stopping the statin on the muscle pain.

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