ADVERSE DRUG REACTION

Simvastatin-induced bilateral leg compartment syndrome and myonecrosis associated with hypothyroidism

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A 54-year-old hypothyroid male taking thyroxine and simvastatin presented with bilateral leg compartment syndrome and myonecrosis. Urgent fasciotomies were performed and the patient made an uneventful recovery with the withdrawal of simvastatin. It is likely that this complication will be seen more often with the increased worldwide use of this drug and its approval for all arteriopathic patients.

Compartment syndrome occurs when there is compression of nerves, blood vessels and muscle within a defined fascial envelope as can occur within the compartments of the leg. Aetiologies include limb trauma, ischaemia, fractures and drugs causing myonecrosis and subsequent swelling. The perfusion pressure falls below the tissue pressure resulting in a compromise to the circulation. It is essential to reduce the compartmental pressures at an early stage in order to minimise tissue oedema and myonecrosis and allow reperfusion of the compartmental tissues. This is done by compartment fasciotomy which can be a limb salvaging procedure.

We report a case of bilateral leg compartment syndrome and myonecrosis in a 54-year-old hypothyroid male on thyroxine and simvastatin. This patient initially presented to his general practitioner with weight loss and sweating. His thyroid function tests revealed a reduced thyroid stimulating hormone level of 0.03 and an elevated free T4 level of 63.2. A thyroid scan revealed an enlarged thyroid gland with increased homogenous uptake supporting a diagnosis of Graves' disease. The patient was treated with radioiodine isotopes and thereafter on follow-up commenced on thyroxine 25 µg daily for subsequent hypothyroidism.

In routine follow-up his blood cholesterol levels were elevated at 6.5 mmol/l and he was started on simvastatin 20 mg nocte by his general practitioner. The patient acutely developed generalised muscle pains and was unable to walk with intense bilateral calf pain after 1 month. At the time of presentation, both legs were tense, swollen and tender with creatinine kinase levels in the range of 6000 IU/l. Blood results were: urea 6.4, creatinine 149 and cholesterol 5.9 mmol/l.

Urgent fasciotomies were performed and the patient made an uneventful recovery with the withdrawal of simvastatin. The fasciotomy wounds healed very well and did not require any skin grafting for closure. A yellow card report was sent to the Medicines and Healthcare products Regulatory Agency (MHRA) for the adverse drug reaction.

DISCUSSION

Myopathy and myoglobulinuria are rare with the use of simvastatin, and compartment syndrome needing fasciotomies is extremely rare. There are two reported cases of this phenomenon, one occurring in a patient with schizophrenia on risperidone and simvastatin¹ and the second in a patient on simvastatin alone.² It was postulated in the first case that there was an effect on the cytochrome P450 enzymes leading to elevated drug levels. There is

also an association with the use of simvastatin for hypercholesterolaemia in hypothyroidism causing myositis.^{3,4} There has also been a report of myopathy and rhabdomyolysis in a patient with hypothyroidism, diabetes mellitus and hypertension.⁵

With the increased worldwide use of this drug and its approval for all arteriopathic patients it is likely that this complication will be seen more often. We present this case for our fellow physicians to be more vigilant with monitoring for myonecrosis and particularly compartment syndrome when prescribing this drug.

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Figure 1 Fasciotomies for simvastatin induced compartment syndrome showing myonecrosis. Informed consent was obtained for publication of this figure.

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IMAGES IN MEDICINE.....

A second corneal arcus?

A 57-year-old woman presented with a three week history of grittiness and redness in both eyes. She had noticed polyuria, nocturia and extreme lethargy over the preceding four to six months. She was taking bendroflumethazide 5 mg daily and atenolol 50 mg daily for essential hypertension. Ocular examination revealed bilateral arcus senilis, which was cream coloured and most prominent at the superior limbus. In addition, there were pure white deposits in a linear pattern on the cornea, concentrated at the medial and lateral aspects of the limbus, associated with pearly white nodules on the conjunctiva and marked conjunctival injection (fig 1). The corneal appearances were those of a second arcus. She also had bilateral pedal oedema. Investigations revealed a serum calcium of 3.8 mmol/l, serum urea of 16.3 mmol/l, serum creatinine of 616 μ mol/l in the presence of a metabolic alkalosis (arterial pH 7.58, bicarbonate 37 mEq/l). The circulating intact parathyroid hormone concentration was 4 pmol/l (normal range 10–65 pmol/l). She admitted to dyspepsia for which she had been

self-medicating with calcium and magnesium carbonate tablets (“Rennie”). The diagnosis of acute milk alkali syndrome exacerbated by thiazide use was made. She remains well on a proton pump inhibitor, with normocalcaemia and normal renal function more than four years after her initial presentation.

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Figure 1 A cream coloured arcus senilis is visible, most prominent at the superior limbus. In addition, chalky white deposits can be seen in a linear pattern on the cornea, concentrated at the medial and lateral aspects of the limbus, associated with pearly white nodules on the conjunctiva and marked conjunctival injection.