Myxoedema revealed by simvastatin induced myopathy

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Secondary causes of hypercholesterolaemia should be considered before starting hypolipidaemic treatment

With the increasing use of hypolipidaemic agents, more cases of toxic myopathy and rhabdomyolysis related to these drugs are becoming apparent.¹ This effect is not specific to one class of compounds: almost all hypolipidaemic agents have been implicated, including statins, fibrates, and nicotinic acid.²⁻⁴ Renal impairment, hypoalbuminaemia, and the use of drug combinations, such as statins with fibrates or cyclosporin, predispose to and potentiate muscle toxicity.¹

Hypercholesterolaemia is a common feature of myxoedema and may be the sole presentation of the disease. Indeed, as a result of the widespread use of cholesterol screening, increasing numbers of hypothyroid patients may present with hypercholesterolaemia rather than the classic features of hypothyroidism.⁵ Likewise myopathy, which may be clinical or subclinical and is associated with raised plasma activities of the skeletal muscle enzymes creatine kinase and aspartate aminotransferase, can occur in hypothyroid patients.⁶ We report on a patient with myxoedema who presented with hypercholesterolaemia and developed apparent muscle toxicity after taking simvastatin.

Case report

A 42 year old man had a blood test for lipid analysis organised by his general practitioner; the results showed a cholesterol concentration of 10.9 mmol/l (desirable <5.2 mmol/l) and a triglyceride concentration of 1.97 mmol/l (normal 0.7-2.1 mmol/l). Having no apparent signs or symptoms, he was diagnosed as having primary hypercholesterolaemia and was prescribed simvastatin 10 mg daily. A second blood test six months later showed values in the normal range for cholesterol (5.7 mmol/l), triglycerides (1.1 mmol/l), total protein (74 g/l), albumin (49 g/l), bilirubin (4 µmol/l), and alkaline phosphatase (70 IU/l), but aspartate aminotransferase activity was raised (214 IU/l (12-40 IU/l)). To determine whether the raised aspartate aminotransferase activity was of liver or muscle origin, γ-glutamyltransferase and creatine kinase activities were measured in the same sample. Though γ-glutamyltransferase activity was normal (32 IU/l), creatine kinase activity was raised (>5000 IU/l (38-220 IU/l)). A diagnosis of simvastatin induced myopathy was postulated, and the general practitioner was advised to stop the drug and monitor plasma enzyme activities every two weeks.

Although simvastatin was discontinued, the raised plasma creatine kinase and aspartate aminotransferase activities failed to return to normal and eight weeks later were 2372 IU/l and 157 IU/l respectively. It seemed at this stage that, although simvastatin may have contributed to the increased plasma enzyme

activities, it could not have been the sole cause. An alternative explanation was that the patient's hypercholesterolaemia and raised skeletal muscle enzyme activities were primarily due to myxoedema, with simvastatin acting as an exacerbating factor for the development of muscle toxicity. Thyroid function tests were therefore performed; the results showed primary hypothyroidism (total thyroxine concentration <20 nmol/l (70-140 nmol/l) and thyroid stimulating hormone concentration 106 mU/l (0.3-3.8 mU/l)). All the ancillary tests leading to the final diagnosis in this case were initiated by the chemical pathology department. The patient had no signs or symptoms to suggest hypothyroidism, and he did not complain of any muscle symptoms during this episode. His general practitioner began treatment with thyroxine—100 µg/day, which was increased to 150 and 200 µg/day, with biochemical checks every four to six weeks after each dose increment (table).

Discussion

Hypercholesterolaemia is a common clinical problem. The wide availability of new, potent, and relatively safe hypolipidaemic agents makes it tempting for doctors to prescribe treatment without looking carefully for secondary causes that might not be obvious clinically. As this case illustrates, myxoedema should be considered in people with hypercholesterolaemia before starting hypolipidaemic treatment because thyroxine will usually resolve the problem, as in our case. Hypothyroidism might potentiate the toxic myopathy induced by fibrates.⁷ In our case, however, the muscle toxicity was not reversed completely by stopping simvastatin; only after starting thyroxine did the raised plasma enzyme activities fall towards normal values. Simvastatin might have exacerbated myxoedema myopathy in our case and there was a risk of the development of acute renal failure if rhabdomyolysis had been induced. There was a delay in monitoring the plasma enzyme activities after starting simvastatin treatment. A check after one month and again three months later would have been desirable.

Other causes of hypercholesterolaemia that should be borne in mind before prescribing hypolipidaemic agents are chronic renal failure and the nephrotic syndrome; affected patients are especially vulnerable to toxic myopathy induced by these drugs.^{4,8}

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Biochemical variables (with normal ranges) during thyroxine treatment

Time (weeks)	Thyroxine dose (µg/day)	Total thyroxine (70-140 nmol/l)	Thyroid stimulating hormone (0.3-3.8 mU/l)	Aspartate aminotransferase (20-40 IU/l)	Creatine kinase (38-220 IU/l)	Cholesterol (<5.2 mmol/l)
0	0	<20	106	157	2372	8.5
4	100	94	39	51	835	
8	150	111	13	36	425	4.9
20	200	155	0.6	21	84	5.3

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