Hypothyroidism presenting as hypercholesterolaemia and simvastatin-induced myositis

YT Hung, VTF Yeung

We report on a 50-year-old woman who presented with hypertension. She was given simvastatin for hypercholesterolaemia. The creatine kinase level was 3180 U/L at the 3-month follow-up visit, which was thought to be due to simvastatin treatment. Although treatment was discontinued, the creatine kinase level 4 months later remained higher than 3000 U/L. Echocardiography revealed mild pericardial effusion and normal left ventricular function; the electromyogram was also normal. The patient subsequently showed signs and symptoms suggestive of hypothyroidism, which was confirmed by measurements of the concentration of thyroid-stimulating hormone (>100 mU/L) and free thyroxine (<2 pmol/L). Thyroxine replacement therapy normalised the creatine kinase and cholesterol levels. This case illustrates the importance of excluding underlying causes of hypercholesterolaemia before contemplating lipid-lowering therapy.

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Key words: Hypercholesterolemia; Hypertension/complications; Hypothyroidism; Lipids/blood; Myositis/chemically induced

Introduction

Dyslipidaemia, occurring alone or in association with other metabolic disorders such as diabetes mellitus, is becoming increasingly common in Hong Kong as the trend of adopting a westernised diet and sedentary lifestyle continues. Hypercholesterolaemia is well recognised as a major risk factor of cardiovascular disease.[1,2] However, simply treating the hypercholesterolaemia without looking for the underlying cause of disease could lead to a delay in appropriate management. We report a case of hypercholesterolaemia secondary to hypothyroidism to illustrate this point.

Case report

A 52-year-old woman presented to the medical unit at Our Lady of Maryknoll Hospital with hypertension without an identifiable cause in May 1997. Her blood pressure was well controlled with atenolol. Baseline investigations included renal and liver function tests and a complete blood picture—all gave normal results. Screening for hyperlipidaemia revealed that the total cholesterol level was 8.79 mmol/L (normal level for individuals aged ≥50 years, <6.85 mmol/L) and the high-density lipoprotein–cholesterol level was 0.60 mmol/L (normal range for females, 0.80-2.35 mmol/L). The level of triglycerides was 1.79 mmol/L (normal range, 0.40-1.83 mmol/L) and the low- density lipoprotein (LDL)–cholesterol level was calculated to be 7.38 mmol/L (normal range, 1.30-4.90 mmol/L). The patient was given simvastatin 5 mg/d at night.

The creatine kinase (CK) level was checked 3 months later and was found to be 3180 U/L (normal range, 0-130 U/L). Simvastatin-induced myositis was suspected, and drug treatment was discontinued. The CK level decreased to 1785 U/L 2 weeks after stopping treatment, but it rebounded to 3502 U/L 2 weeks later. During the next few weeks, the CK level remained elevated at >2000 U/L. The chest X-ray revealed gross cardiomegaly, and a subsequent echocardiogram (ECG) showed fair left ventricular function but moderate pericardial effusion. Because the ECG also showed T-wave inversion over the left chest leads and because the patient complained of vague chest discomfort, a cardiac catheterisation procedure was performed. The examination confirmed fair left ventricular function with no evidence of coronary artery disease.

In July 1998, the patient reattended the medical unit for myositis. She had a yellowish discoloration of

Department of Medicine and Geriatrics, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wongtaisin, Hong Kong
YT Hung, MB ChB, FHKAM (Medicine)
VTF Yeung, MD, FRCP

Correspondence to: Dr YT Hung

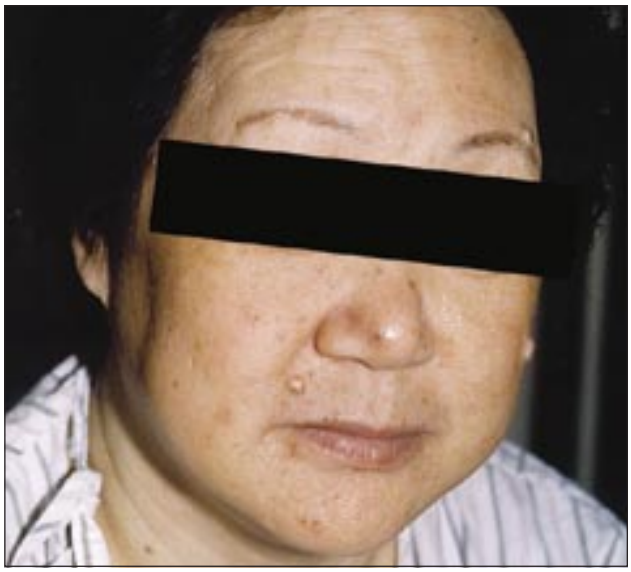

Fig. Patient with hypothyroidism showing loss of the lateral third of the eyebrow and carotenaemia

the skin (suggestive of carotenaemia) and had lost the lateral third of her right eyebrow (Fig). She also showed classic delayed relaxation of the ankle jerk. A clinical diagnosis of hypothyroidism was suspected and confirmed by the fact that the thyroid-stimulating hormone level was high, at >100 mU/L (normal range, 2-11 mU/L) and the free thyroxine level was low, at <2 pmol/L (normal range, 10-36 pmol/L). The patient was subsequently given thyroxine replacement therapy. Her latest ECG revealed completely resolved pericardial effusion, and the CK level normalised to 97 U/L. The total cholesterol level decreased to 5.66 mmol/L and the LDL-cholesterol level decreased to 3.84 mmol/L.

Discussion

The proven survival benefit and efficacy of 3-hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors in primary and secondary prevention trials has resulted in their frequent prescription as first-line therapy for hypercholesterolaemia in clinical practice.[3,4] Potential side effects of statins include myositis, rhabdomyolysis, and hepatitis, particularly when given with fibrates and other medications that may interfere with the cytochrome P450 system.[5]

Hypothyroidism, diabetes mellitus, and drug treatment are the first few differential diagnoses quoted as causes of secondary hyperlipidaemia in a standard medical textbook.[6] As Hong Kong residents adopt a more westernised diet and sedentary lifestyle, an increasing number of patients with hypercholesterolaemia is predicted. There is a tendency to attribute hypercholesterolaemia to obesity and diet without consideration of the other possible causes. The patient in this case was mistakenly prescribed simvastatin for hypercholesterolaemia, which was secondary to undiagnosed hypothyroidism. As a result, her elevated CK level was wrongly attributed to the use of simvastatin, which was expected to recover after the cessation of drug treatment.

This case report illustrates the importance of looking for underlying causes of hyperlipidaemia. Rather than simply prescribing drug treatment, physicians should take a detailed history and perform a physical examination to rule out metabolic disorders, alcoholism, and the concomitant use of drugs (eg diuretics or β-blockers). The prevalence of hypothyroidism in patients referred for hyperlipidaemia has been reported to be 4.2% in a Dutch study, which recommended screening all patients with hyperlipidaemia for hypothyroidism.[7] Performing baseline biochemical screening tests can provide further clues to the underlying disorder. These tests should include measurement of the CK level and liver function tests, and they should be performed before contemplating lipid-lowering agents.[8] In addition, this approach prevents the prescription of lipid-regulating drugs for patients with contraindications and avoids wrongly incriminating these drugs as a cause of the possible subsequent altered biochemistry.

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