

## SHORT CASES IN CARDIOLOGY

## A cautionary tale of undetected hyperlipidaemia: implications for coronary artery bypass grafting

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A 54 year old man was referred to the lipid clinic at Hammersmith Hospital. In 1984 he had been investigated in a hospital in London because of exertional chest pain of increasing frequency. Within a month he was admitted to a second hospital with acute and extensive myocardial infarction. Angiography, performed in a third hospital, showed triple vessel disease and he underwent coronary artery bypass grafting (CABG) with four saphenous vein grafts. He remained reasonably well until 1991 when he was admitted to a fourth hospital with a second myocardial infarction. A subsequent angiogram at a fifth hospital showed impaired left ventricular function and occlusion of three of his four vein grafts. A few months later positron emission tomography was performed in a sixth hospital which showed an anteroapical myocardial infarct and reversible inferolateral ischaemia.

Though this patient had been investigated in six major hospitals during the past 9 years there is no record of his serum cholesterol ever having been measured until 1993 when he asked this of his general practitioner. The result was 10.6 mmol/l and he was then referred to our lipid clinic.

DNA analysis showed that the patient had familial defective apolipoprotein B<sub>100</sub> (FDB), an inherited condition characterised by impaired binding of low density lipoprotein (LDL) caused by an amino acid substitution in the receptor binding domain of apolipoprotein B; in affected individuals this results in hypercholesterolaemia with a raised LDL cholesterol and premature atherosclerosis.<sup>1</sup> In people with FDB the clinical presentation and response to treatment are often indistinguishable from familial hypercholesterolaemia.

This unfortunate example of repeated failure to detect hyperlipidaemia both before and after CABG raises two important issues.

### Evidence that hyperlipidaemia adversely affects graft survival and that treatment is beneficial

A postmortem study of 99 vein grafts from normal and hyperlipidaemic patients dying within 5 years after CABG showed that vein graft atheroma was five times more common in those who were hyperlipidaemic.<sup>2</sup> And a long-term angiographic follow up of 132 grafts known to be patent 6-12 months after CABG showed that 38% were unchanged at 10-12 years, 32% had changes suggestive of

atherosclerosis, and 30% had occluded.<sup>3</sup> Patients with lesions or occlusion of their grafts had significantly higher concentrations of total cholesterol, triglyceride, and LDL apolipoprotein B, and significantly lower concentrations of high density lipoprotein (HDL) cholesterol than those without lesions.

In the Cholesterol Lowering Atherosclerosis Study (CLAS) the effect on the progression of disease in native vessels and vein grafts of diet plus 30 g colestipol and 4 g nicotinic acid daily was compared with diet plus placebo.<sup>4,5</sup> Angiograms were obtained after two years in 162 of 188 non-smoking men who entered the study (CLAS I) and again in 103 subjects after four years (CLAS II). In patients treated for 2 or 4 years the combination of diet, colestipol, and nicotinic acid resulted in a 34-36% greater reduction in LDL cholesterol and 35% greater increase in HDL cholesterol than in those treated with diet and placebo. Angiographic findings showed that the rate of appearance of new lesions was significantly reduced in the treated patients both in native vessels (14% drug treated *v* 40% placebo) and bypass grafts (16% drug treated *v* 38% placebo).

The beneficial effect of lipid lowering drugs in preventing lesions was evident both in patients with cholesterol concentrations of 4.8-6.2 mmol/l and in those with concentrations above 6.2 mmol/l. These findings suggest that even slight increases in serum cholesterol promote the occurrence of late occlusion of vein grafts and that intensive lipid lowering treatment helps to counteract this tendency.

### Guidelines for intervention and target concentrations for LDL cholesterol after CABG

In 1993 The British Hyperlipidaemia Association published its guidelines for the treatment of hyperlipidaemia.<sup>6</sup> The highest priority was accorded to patients with existing CHD and those who had had CABG. In this category lipid lowering drugs are recommended if, despite diet, the total cholesterol concentration remains above 5.2 mmol/l or LDL cholesterol is above 3.4 mmol/l or both. The recommended target concentration for LDL cholesterol in such patients is <3.4 mmol/l. In the United States the recommended target concentration for LDL cholesterol ( $\leq 2.6$  mmol/l) is even lower.<sup>7</sup>

Despite these guidelines the management

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of hyperlipidaemia after CABG seems inadequate according to a recent report of a retrospective audit carried out in 100 consecutive Welsh patients.<sup>8</sup> There was no record that serum lipids had been measured in 17 and in a further five lipids had been measured but the results were not in the case notes; lipid values were included in less than half of all the discharge summaries. Of the 41 patients with a serum cholesterol above the median (6.7 mmol/l) only 12 (27%) were referred to a dietitian and eight (19%) were prescribed lipid lowering drugs. These workers concluded that few CABG patients were managed appropriately.

We therefore propose that all patients admitted for CABG should have their lipid profile checked preoperatively; all patients with total cholesterol >5.2 mmol/l or LDL cholesterol >3.4 mmol/l should be given dietetic advice and have their lipid concentrations checked again at 3 months after operation; those who remain above these values should be treated with an appropriate lipid lowering drug. We hope that this will slow the rising rate of re-do procedures, which in 1989 and 1991 accounted for 2.4% and 3.8% of all CABGs done in Britain (UK Cardiac Surgical Register, Society of Cardiothoracic Surgeons of Great Britain and Ireland). Currently in our unit the re-do rate is 11% compared with just under 14% in the Cleveland Clinic in 1985, despite the fact that one third of their original grafts came from the internal mammary artery.<sup>9</sup>

It seems appropriate for us to conclude by quoting from a recent editorial by Roberts: "Thus, because secondary prevention is in the hands of cardiologists and because cholesterol lowering has proven benefit after atherosclerotic events, cardiologists must increase their

knowledge of and use of low-fat, low-cholesterol diets and lipid-lowering agents".<sup>10</sup>

Additional support for this view can be gleaned from the recent data reported by Law *et al* which suggest that a 20% reduction in serum cholesterol by lipid lowering drugs would halve the mortality from coronary heart disease of middle aged people.<sup>11</sup>

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