given aspirin, and buccal nitrate prior to the procedure. A 6 French sheath was inserted, 12 000 u of heparin given and 11 of dextran-40 infused. A Palmaz-Schatz stent was inserted using a Europass (Cordis) balloon after which there was an excellent angiographic result. A heparin infusion of 1-500 U.h⁻¹ was instigated and thereafter given to maintain the activate clotting time (ACT) between 200-250 s.

The 6 F sheath was removed immediately and the radial artery puncture site healed without incident. However, 4 days later the patient complained of painful upper legs and difficulty in walking. On examination there was minor lower abdominal tenderness, extension of both hips was associated with some discomfort; and there was an area of paresthesia on the outer right thigh in the distribution of the lateral cutaneous nerve. The pre-procedural haemoglobin had fallen from 13 to 10, the INR was 1-5 and ACT 236 s. A lower abdominal CT scan demonstrated bilateral areas of increased density in the iliacus muscle (Fig. 1), consistent with haematoma. The patient remained stable and the heparin was therefore continued with a target ACT range of 150-200 s until the INR was greater than 2. The patient was discharged on aspirin and warfarin 10 days after the initial procedure with no residual complications.

Intracoronary stents are increasingly used during angioplasty to treat abrupt vessel closure and reduce restenosis. Rigorous anticoagulation regimens are currently used to reduce thrombotic occlusion of stents. The resulting potential for bleeding complications at the femoral artery puncture site is high with an incidence of major bleeding complications of between 6% and 7%[1]. The trans-radial approach to percutaneous balloon angioplasty and stenting[2] should reduce the risk of haematoma formation and allow the patient to mobilise more quickly. However, this patient developed a significant iliacus haematoma despite regular bedside ACT measurements and good anticoagulation control. Further research into locally delivered anticoagulant release systems which may allow less stringent anticoagulation regimens in the future continues to be an important clinical need despite this new approach to coronary stenting.

References


Coronary bypass grafts in a young girl with sitosterolemia

Few cases of sitosterolemia have been published since 1973 when Bhattacharyya first reported[3] a new inherited sterol storage disease.

We report a case of sitosterolemia with premature coronary artery disease which required surgical intervention. A 16-year-old Caucasian girl was referred to us for further investigation after hospitalization elsewhere for chest pain and changes in electrocardiographic precordial leads.

Her family history showed that one uncle had died aged less than 60 from a stroke. At clinical examination no tendon or tuberous xanthomas were found. The electrocardiogram showed an anterior myocardial infarction. A chest X-ray revealed a heart of normal size. Dobutamine echocardiography showed viable tissue in the anteroseptal wall and an ischaemic response in the inferior wall. Thallium 201 showed a scar in the anterior wall. Laboratory examination results were normal including amino acid profile (homocysteine, methionine), vitamin E, A, carotene, lipids, lipoproteins and apolipoproteins. The blood sitosterol was measured by flow cytometry and was found to be 19 mg. dl⁻¹.

Coronary arteriography showed occlusion of the left anterior descending and >70% stenosis of the middle right coronary artery, with a 100% occlusion of the posterior descending artery (Fig. 1). At selective angiography both carotid arteries and the abdominal aorta were normal. She had double aortocoronary bypass surgery performed and was discharged with cholestyramine 8 g daily.

In this very rare disease only homozygous subjects manifest an increase of total plasma sterol concentrations, particularly sitosterol, and tendon xanthomas, despite the normal plasma cholesterol concentration. The mechanism for the development of xanthomas and atherosclerosis in these patients is not clearly understood. In normal persons, plant sterols are poorly absorbed and preferentially excreted by the liver. Bhattacharyya et al.[3] suggested that the metabolic defect in sitosterolemia is a combination of enhanced intestinal absorption and a sluggish turnover of sitosterol in the body compared with normal humans. Sitosterol absorption is increased 7- to 16-fold. These altered processes result in a 13 to 17-fold increase of the total sterol and a 22 to 38-fold increase in the sitosterol levels. The slow turnover of sitosterol in these

Figure 1 CT scan of a transverse section through the pelvis. Large arrows point to the iliacus muscles and surrounding haematoma, small arrows point to the psoas muscles.

Figure 1 Left coronary artery (upper panel) and right coronary artery (lower panel).
patients is the result of decreased excretion of sitosterol into the duodenal bile. Salen et al.\(^1^3\) postulated that decreased hepatic sitosterol excretion into bile helps conserve sterols in the body, while diminished cholesterol synthesis is observed, 26 to 28% lower than that of normals. Nguyen et al.\(^4\) suggested that the reduced cholesterol synthesis is due to a deficiency of 3-hydroxy-3-methyl glutaryl coenzyme A (HMG-CoA) reductase. They investigated the activity of HMG-CoA reductase in mononuclear leucocytes taken from sitosterolemic patients and controls and found that mononuclear leucocytes from control subjects contained almost twice the total HMG-CoA reductase activity and nearly two to four times the amount of enzyme protein compared to those of sitosterolemic patients.

The function of low density lipoprotein (LDL) receptors is regulated by HMG-CoA reductase so that enzyme activity and LDL receptor function respond in the same way. However, in sitosterolemic homoyzogotes the opposite occurs, with a resulting enhanced LDL receptor function and low HMG-CoA reductase activity. About 76% of plasma sitosterol is carried with LDL, and there is increased uptake of sitosterol carrying LDL via LDL receptors.

The levels of sitosterol in our patient are within the range described in the literature. Normally sitosterol levels do not exceed 0.4 mg. dl\(^{-1}\).

The behaviour of drugs, such as HMG-CoA reductase inhibitors or bile acid sequestran resins has not been adequately evaluated in this disease. Nguyen et al.\(^4\) found no influence of lovastatin or a low sterol diet on cholesterol levels do not exceed 0.4 mg. dl\(^{-1}\).

Chemotherapy-induced myocardial infarction

Cardiovascular ischaemia has been recognised as a serious, but uncommon complication of treatment with several chemotherapeutic agents\(^1\). This report describes a young man who developed a myocardial infarction after completion of a chemotherapy regime.

A 30-year-old man with a mixed germ cell tumour was treated for a relapse of his condition with combination chemotherapy. He had no risk factors for ischaemic heart disease. A 10-day course of cisplatin, vincristine and methotrexate was followed by two courses of dactinomycin, cyclophosphamide and etoposide, each over a 5-day period. Three days into each of the latter two courses, he experienced several minutes of indigestion-like chest pain. Three days following completion of the final treatment he developed severe central chest pain associated with vomiting, while walking upstairs. The pain persisted for 10.5 h and had subsided on arrival in the Accident and Emergency Department. An ECG demonstrated ST elevation in the infero-lateral leads. Treatment consisted of intravenous nitrates, aspirin and full anti-coagulation with heparin; he did not receive thrombolysis. Diagnosis of myocardial infarction was confirmed with a peak CK estimation of 2489 IU. 1\(^{-1}\).

He made an uneventful recovery, and prior to discharge underwent an exercise stress test following the Modified Bruce protocol. This was classed as 'borderline positive' demonstrating up-sloping ST segment depression to a maximum of 2 mm in lead V\(_2\). He reached a maximum heart rate of 167 beats min\(^{-1}\).

To our knowledge this patient has remained asymptomatic from a cardiological viewpoint, and has received no further investigation or follow up at his own request.

The use of chemotherapy protocols containing such drugs as cisplatin, etoposide, bleomycin and the vinca-alkaloids, in various combinations, for the treatment of germ cell tumours has been associated with the ability to induce myocardial ischaemia or infarction\(^1\).\(^2\)\(^3\). This patient received cisplatin and vincristine in the initial course of treatment, but his symptoms appear more directly related to the second combination of dactinomycin, cyclophosphamide and etoposide. There is little evidence to implicate dactinomycin as a vascular toxin. However, as regards cyclophosphamide treatment, although high doses have been associated with cardiomyopathy, any ECG abnormalities or elevation of cardiac enzymes which may occur during or after cyclophosphamide infusion are thought to be secondary to myocardial necrosis rather than any localized vascular events\(^1\). This has been demonstrated at autopsy.

Several reports implicate cisplatin and vincristine in the development of myocardial infarction or ischaemia\(^1\)-\(^3\), but there is limited evidence to indicate that etoposide may be cardiovascularly toxic. In fact Scharwzer et al.\(^6\) suggested that etoposide had no such effect. The patient in their report continued treatment with etoposide for 14 months following a myocardial infarction which occurred during the treatment protocol containing bleomycin and etoposide. They proposed that the cardiovascular effects were caused by the combinations of the two agents rather than any individual effect. However, Schechter et al.\(^7\) reported a case of myocardial infarction in a 27-year-old female receiving etoposide treatment as a sole agent for persistent Hodgkin's disease. On rechallenging with this therapy following recovery from the MI, she developed severe hypotension and an ECG demonstrated new lateral T wave inversion indicative of ischaemia. They proposed that the infarction was

References


G. KOLOVOU
V. VOUARDIS
D. DROGARI
G. PALATIANOS
D. V. COKKINOS
Cardiology and Surgery Department,
Onassis Cardiac Surgery Center,
Athens, Greece

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