Fulminating hyperlipidaemia

M. C. BATESON
M.B., M.R.C.P.

Ninewells Hospital, Dundee, Scotland

Summary

A case is described of severe recurrent ischaemic heart disease associated with rapidly increasing and ultimately massive hyperlipidaemia.

The case is discussed, with suggestions for management of similar problems.

Introduction

Massive hypertriglyceridaemia has been recorded in association with acute alcohol abuse (Zieve, 1958), with oestrogen therapy (Molitch, Oill and Odell, 1974), with impaired fatty acid incorporation into adipose tissue and severe chylomicronaemia (Carlson, Eriksson and Walldius, 1974) and in glycogen storage disease and diabetic ketoacidosis (Carlson, Fröberg and Orö, 1972). There may be associated jaundice, haemolysis and abdominal pain with or without pancreatitis. Disorders of circulation, including increased platelet adhesiveness, red cell aggregation and plasma viscosity with reduced fibrinolysis are probably a constant feature.

Although the condition usually responds well to treatment by management of any precipitating cause, and appropriate diet and drug therapy, the case reported was resistant to these manoeuvres and manifested progressive and ultimately fatal hyperlipidaemia.

Case report

The patient was a female born in 1906. She had an apparently completely successful mastectomy for carcinoma in 1955. Otherwise, she enjoyed good health until 1970 when she was seen in the medical outpatient department with angina pectoris. There was no family history of premature ischaemic heart disease. She was teetotal, but smoked 40 cigarettes/day. Her blood pressure was 170/90 mmHg, and her weight was 65 kg (ideal for height 56 kg), but there were no other physical signs. She was persuaded to stop smoking and prescribed glyceryl trinitrate with apparent benefit. Her serum chol-

esterol was noted to be 9.6 mmol/l. Her serum triglycerides were not measured although the serum was not noted to be turbid.

In October 1974 she was admitted as an emergency with severe chest pain, and serial ECGs demonstrated an acute inferior myocardial infarction, which was complicated by the development of left ventricular failure. Her weight was now 67 kg. Fasting serum lipids on the day following admission showed a cholesterol of 10.2 mmol/l and triglycerides of 8.8 mmol/l. Cellulose acetate electrophoresis showed a very marked increase in the pre- β -lipoprotein, a moderate increase in β -lipoprotein and a trace only of chylomicrons. Preparative ultracentrifugation followed by lipoprotein electrophoresis excluded broad- β disease, and the patient was considered to have endogenous hypertriglyceridaemia (Fredrickson Type IV). She was commenced on a 4.2 MJ low carbohydrate reducing diet. Transient glycosuria was noted during this admission.

In February 1975 she was readmitted with further severe chest pain and ECG changes of an inferolateral myocardial infarction, complicated by pulmonary embolism 10 days later. She was treated with heparin, and then warfarin subsequently. Her serum lipids remained abnormal with a cholesterol of 10.7 mmol/l and triglycerides of 7.2 mmol/l. Transient glycosuria again occurred. Since her weight had not fallen despite claimed adherence to diet, her energy intake was further restricted to 3.4 MJ daily.

A glucose tolerance test was performed in March 1975 which indicated diabetes mellitus, with a blood glucose of 14 mmol/l and glycosuria at 2 hr.

In May 1975 she was admitted with myocardial ischaemia, without further ECG changes diagnostic of infarction, and her serum lipids showed a cholesterol of 15.4 mmol/l and triglycerides 30 mmol/l. In July 1975 she was readmitted with further myocardial ischaemia and her serum lipids were again disturbed, with a cholesterol of 27 mmol/l and triglycerides >20 mmol/l, although her weight had

fallen to 64 kg. Because of congestive cardiac failure she was started on digoxin and frusemide.

She was admitted for evaluation in September 1975. She had gross lipaemia (cholesterol 20 mmol/l and triglycerides 58 mmol/l) and thus most of her serum biochemistry was vitiated. Thus, when the serum lipoproteins were removed by ultracentrifugation or dialysis, estimations on the supernatant yielded uniformly spuriously elevated and inconsistent results. In addition, the patient had a succession of severe illnesses which precluded exact investigation in a baseline state. An intravenous fat tolerance test could not be performed for the same reason, and also the risk of a dangerous rise in viscosity. Her serum thyroxine was apparently normal at 91 nmol/l and protein electrophoresis showed only an elevated α_2 -globulin. There were no antithyroid antibodies, latex fixation was negative and there was no antinuclear factor. The Mantoux reaction (1 : 1000) was 1 cm induration and 2 cm erythema at 2 days. Her haemoglobin was 13.9 g/dl and white cell count $7.0 \times 10^9/l$. The platelet count was normal $240 \times 10^9/l$, but platelet function studies were invalidated by the turbidity of the blood.

A liver scan showed only hepatomegaly and a liver biopsy showed extensive fatty change in the hepatocytes.

She was commenced on clofibrate 2 g daily in addition to her diet and after one month her serum cholesterol was 19 mmol/l and triglycerides 30 mmol/l.

She was readmitted in November 1975 with shortness of breath and a different sort of chest pain. She was found to have a pericardial friction rub and a fever in addition to a new pansystolic murmur. Pericarditis and mitral incompetence were diagnosed. Warfarin was discontinued. She rapidly became pain-free on a short course of prednisolone in high dosage. It was felt the origin of her pericarditis and mitral incompetence was possibly a further painless myocardial infarct. The serum lipids remained elevated with a cholesterol of 16 mmol/l and triglycerides of 24 mmol/l.

It was considered that no further response to clofibrate was likely and nicotinic acid therapy was substituted with gradual increase in dose to 3.0 g daily, which had to be reduced to 2.0 g daily because of flushing. There was only partial response, with a fall of cholesterol to 9.9 mmol/l and of triglyceride to 20 mmol/l.

She was readmitted in December 1975 with an antero-septal myocardial infarction and further pulmonary embolism, and died 2 weeks later.

Post-mortem showed extensive severe atheroma, which severely involved both main coronary arteries. There was patchy fibrosis throughout the left ventricle with a recent subendocardial infarction.

There was a small haemorrhagic pericardial effusion and massive bilateral pulmonary emboli. The liver weighed 2.17 kg with centrilobular venous congestion and uniform fatty degeneration. There was no evidence of recurrent or metastatic breast carcinoma.

Discussion

It is known that any acute illness may cause temporary alterations in serum lipid levels, and this makes interpretation of values difficult, since the patient reported had 6 emergency hospital admissions in 14 months. Ideally serum lipids should be sampled 3 months or more after emergency admission, and this was clearly impractical in this patient. Except where stated the values recorded were those obtained immediately after admission, when they are least likely to be affected in this way.

In a local population screen, 4% of 99 healthy women and 14% of 282 healthy men had serum triglycerides ≥ 2.5 mmol/l. The present patient had the most severe hypertriglyceridaemia seen in 5 years at a lipid clinic, and fared badly on treatment. In 4 other cases with severe hypertriglyceridaemia (≥ 10 mmol/l) there has been a good response to dietary advice, with the addition of clofibrate 2 g/day in 3 cases. Their initial levels were 15, 10, 24 and 13 mmol/l, which fell to 1.8, 1.1, 2.9 and 2.9 mmol/l respectively after therapy. Severe hyperlipidaemia detected can sometimes be associated with alcoholism, glycogen storage disease, diabetic ketoacidosis and oestrogen therapy, but none of these was present in this severely affected patient. Thiazide diuretic therapy can be blamed for mild hyperlipidaemia (Ames and Hill, 1976), but not in this patient, who had been treated with frusemide.

The results of glucose-tolerance testing indicated that the present patient had mild maturity onset diabetes but this was at no time out of control. No other primary factors were identified nor any explanation of the severity of the progressive and ultimately massive hyperlipidaemia which apparently precipitated the patient's terminal illness. The levels of serum triglyceride detected would have had marked effects on platelet adhesion and aggregation (Nordøy, Strøm, and Gjesdahl, 1974) as well as increasing plasma viscosity, and these secondary phenomena could explain the accelerated ischaemic heart disease.

Conventional management with low-energy low-carbohydrate diet, clofibrate and nicotinic acid did not cure the hypertriglyceridaemia, though there was evidence of compliance with each of these measures. Normally the response to treatment for hyperlipidaemia should be assessed at leisurely intervals, to permit maximal benefit to be obtained from each therapy before further alteration. This

was clearly impossible with this patient, where a prompt response was particularly desirable. Other procedures which might have helped by reducing platelet adhesion and aggregation include unsaturated fat diet (Nordøy and Rodset, 1971) and drugs such as aspirin, dipyridamole, phenformin and ethyloestrenol. The course of warfarin did not prevent 2 further episodes of myocardial ischaemia, however.

The plasma viscosity might have been lowered by repeated plasmapheresis. This probably could only have been used to produce a temporary respite while other manoeuvres were employed, such as higher dose nicotinic acid therapy and possibly the recently proposed chenodeoxycholic acid (Bell *et al.*, 1973; Bateson, 1976).

The sequence of events in this patient illustrates the need for vigorous treatment of severe hyperlipidaemias, despite current scepticism about the management of lesser degrees of these disorders (Coronary Drug Project, 1975; Werkö, 1976).

References

- AMES, R.P. & HILL, P. (1976) Increase in serum lipids during treatment of hypertension with chlorthalidone. *Lancet*, **i**, 721.
- BATESON, M.C. (1976) Chenodeoxycholic acid for hypertriglyceridaemia. *Lancet*, **ii**, 962.
- BELL, G.D., LEWIS, B., PETRIE, A. & DOWLING, R.H. (1973) Serum lipids in cholelithiasis: effect of chenodeoxycholic acid therapy. *British Medical Journal*, **3**, 520.
- CARLSON, L.A., ERIKSSON, I. & WALLDIUS, G. (1974) A case of massive hypertriglyceridaemia and impaired fatty acid incorporation into adipose tissue glycerides (FIAT) both corrected by nicotinic acid. *Acta medica Scandinavica*, **194**, 363.
- CARLSON, L.A., FROBERG, S. & ORÖ, L. (1972) A case of massive hypertriglyceridaemia corrected by nicotinic acid therapy. *Atherosclerosis*, **16**, 359.
- CORONARY DRUG PROJECT (1975) Clofibrate and niacin in coronary heart disease. *Journal of the American Medical Association*, **231**, 360.
- MOLITCH, M.E., OILL, P. & ODELL, W.D. (1974) Massive hyperlipidemia during estrogen therapy. *Journal of the American Medical Association*, **227**, 522.
- NORDØY, A. & RODSET, J.H. (1971) The influence of dietary fats on platelets in man. *Acta medica Scandinavica*, **190**, 27.
- NORDØY, A., STRØM, E. & GJESDAHL, K. (1974) The effect of alimentary hyperlipaemia and primary hypertriglyceridaemia on platelets in man. *Scandinavian Journal of Haematology*, **12**, 329.
- WERKÖ, L. (1976) Risk factors and coronary heart disease – facts or fancy. *American Heart Journal*, **91**, 87.
- ZIEVE, L. (1958) Jaundice, hyperlipemia and hemolytic anemia: a heretofore unrecognized syndrome associated with alcoholic fatty liver and cirrhosis. *Annals of Internal Medicine*, **48**, 471.