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Cirrhosis in partial lipodystrophy

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Summary: A patient with partial lipodystrophy, fatty liver and cirrhosis, and autoimmune thyroid disease is described. Treatment with thyroxine led to partial improvement in the hepatic abnormality.

Introduction

Partial lipodystrophy is a rare condition characterized by absence of subcutaneous fat over the upper part of the body.[1] The aetiology is unknown, but it often follows a febrile illness in early adult life in women and is occasionally familial. Some families have partial lipodystrophy affecting the lower trunk and legs, hepatosplenomegaly and diabetes, inherited as an autosomal dominant trait.[3] The commonest complication is glomerulonephritis[2] associated with activation of the alternative pathway of complement and reduced circulating C3 levels. Hyperlipidaemia and insulin-resistant diabetes occur, but no consistent metabolic defect has been demonstrated.

We report a patient with partial lipodystrophy complicated by fatty liver and cirrhosis, and primary autoimmune hypothyroidism in whom treatment with thyroxine led to reduction in liver size and resolution of steatosis.

Case report

A 32 year old Caucasian woman was referred for investigation of cachexia and hepatomegaly. Her symptoms had started 4 years previously, when she had noticed slowly progressive abdominal distension and malaise. For two years she had noticed a 'dragging' sensation arising from the right hypochondrium and was unable to lie on her right side. She had become increasingly agitated, preoccupied with her early life, and depressed over the preceding two months, and at presentation had a psychotic episode with auditory hallucinations and delusions of persecution. In the past she had three elective Caesarian sections, with blood transfusion with the first, all children well, aged 12, 10 and 4 years. She had a tubal ligation following the third delivery. There was a history of moderately severe menorrhagia since the birth of her youngest child. Her mother had died aged 39 of a 'wasting illness' but no definite diagnosis was reached during life and no post-mortem examination was held. She had two brothers and two sisters, all in good health. She stopped smoking 4 years previously and drank one unit of alcohol per week.

On examination, there was absence of subcutaneous fat stores in the face (Figure 1), arms and trunk as far as the thighs, below which the distribution of fat was normal (Figure 2). The liver was firm, smooth and enlarged 8 cm below the costal margin. There was no ascites or splenomegaly, and no signs of chronic liver disease. A photograph of the patient at age 18 showed the same absence of facial fat, but the facial appearance was normal at 15.

Investigations included aspartate transaminase 86 IU/l (normal 5–42), but other biochemical tests of liver function were normal. Haemoglobin 9.8 g/dl, MCV 76 platelets 315 × 10^9/l, erythrocyte sedimentation rate 40 mm/h. Serum iron <5 μmol/l (11–28). Total iron binding capacity 98 μmol/l (45–75). Free thyroxine 3.6 pmol/l (8–24) TSH 41.5 mU/l (0.6–5). Fasting glucose and 50 g oral glucose tolerance test were within the diabetic range. Fasting insulin 21.3 mU/l (normal <6). Fasting cholesterol 9.1 mmol/l (3.1–6.2). Triglyceride 1.2 nmol/l (0.3–1.6). IgG 16.9 g/l (7.5–16.7), IgM 1.4 (0.4–3.7), IgA 1.7 g/l (0.9–4.5). Complement C3 2.01 g/l (0.89–2.09), C4 0.21 g/l (0.12–0.53), creatinine clearance 127 l/24 h. Twenty four-hour urine protein excretion 0.4 g (normal <0.3 g). Thyroid microsomal antibodies present 1 in 409,600 serum dilution, thyroglobulin antibodies present 1 in 80 serum dilution. Other antibodies including anti-mitochondrial anti-nuclear and smooth muscle antibodies were not detected. Hepatitis A and B serology was negative. Skeletal survey showed no bony abnormality. Computerized

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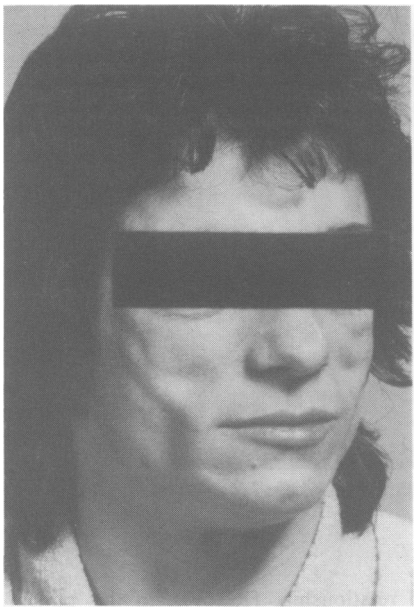

Figure 1 Characteristic facial appearance in partial lipodystrophy, with absence of subcutaneous fat.

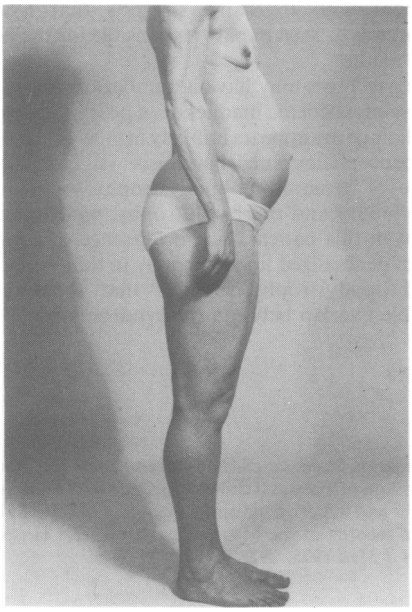

Figure 2 Absence of subcutaneous fat extends as far as the thighs, below which the fat distribution is normal.

tomography of the abdomen (Figure 3) showed diffuse fatty infiltration of the liver and confirmed gross hepatic enlargement. There was abundant intraperitoneal fat, but no subcutaneous fat. CT scan of the brain and electroencephalogram were normal. Liver biopsy showed severe fatty change and cirrhosis (Figure 4). Duodenal biopsy showed normal villi. The iron deficiency was attributed to menorrhagia and responded to oral iron replacement. The psychiatric illness responded to haloperidol. She later developed depressive features which improved on amitriptyline. Treatment with thyroxine improved her general well-being and was associated with a reduction in liver size to 2 cm below the costal margin, 6 months after treatment. Repeat CT scan (Figure 5) showed a reduction in size and liver fat content.

Discussion

Fatty liver and cirrhosis are recognized complications of generalized lipodystrophy but are not usually a feature of partial lipodystrophy. The fatty liver in generalized lipodystrophy is known to progress to cirrhosis, and is not an innocent lesion.[5] Diabetes is common in both syndromes and is of the insulin-resistant type, not associated with autoimmune disease. The aetiology of partial lipodystrophy remains unknown, and any hypothesis must attempt to explain the regional distribution of fat loss. The possibility of an autoimmune reaction is suggested by the frequent association with glomerulonephritis, the complement abnormalities, and in this patient by the association with autoimmune thyroiditis, with very high level of autoantibodies. Autoimmune thyroid disease is a common condition and has not been previously reported in association with partial lipodystrophy, and it seems unlikely that there is a true

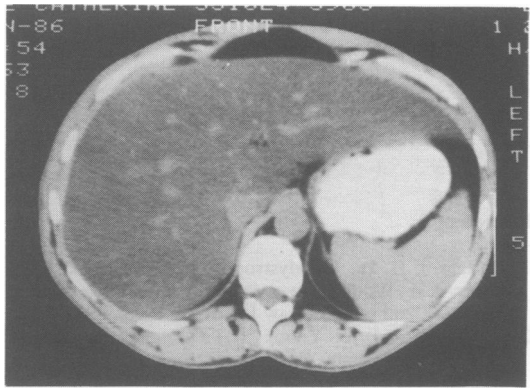

Figure 3 CT scan at presentation, showing portal vessels standing out against uniform low density of surrounding liver.

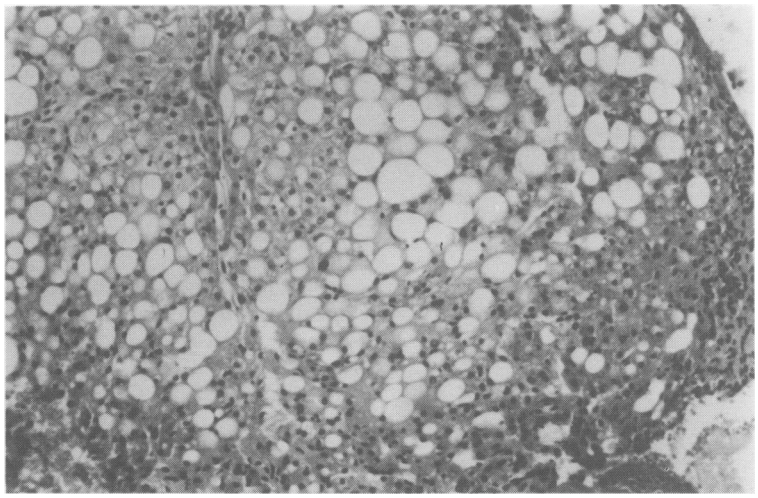

Figure 4 Liver biopsy showing fatty infiltration and cirrhosis.

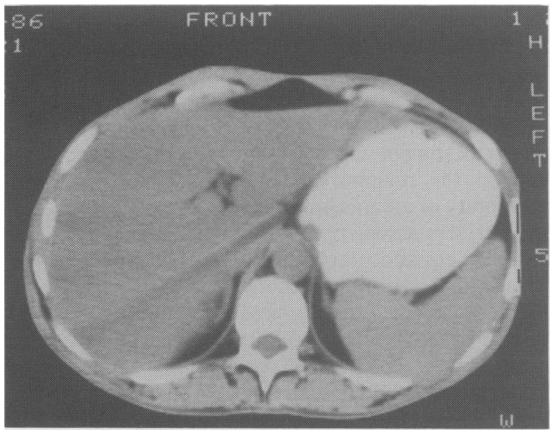

Figure 5 CT scan 6 months later, showing reduction in size and fat content of the liver.

causal relationship. However, in this patient, it is possible that hypothyroidism has exacerbated some of the metabolic features of the disease and may have contributed to the hyperlipidaemia and possibly the fatty change in the liver. Hypothyroidism is known to decrease cholesterol excretion in the bile[4] and is associated with obesity, but not fatty liver.

The reduction in liver size and fat content following treatment with thyroxine suggests that hypothyroidism was at least in part responsible for the hepatic abnormalities.

The psychosis may have a number of precipitating factors: 'myxoedema madness' is a possibility. Hepatic encephalopathy appears unlikely in view of the normal electroencephalogram. Psychosis is a recognized feature of generalized lipodystrophy, as is mental subnormality and cerebral atrophy, which were not present in this patient. The occurrence of complications of generalized lipodystrophy in this patient with partial lipodystrophy suggests that there is considerable overlap between the syndromes.

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