history should be obtained from patients who have undergone nephro-ureterectomy for transitional cell carcinoma of the ureter or kidney, since arresting the damage to the remaining kidney is of paramount importance.

The incidence of carcinoma of the urothelium in this country is increasing and it is possible that phenacetin may be partly responsible. Since the mechanism of tumour production by phenacetin is likely to be the same as the other aromatic amides, one can expect the latent period before a tumour appears to be similar to that from aromatic amides. It is therefore possible that there will be a further increase of transitional cell carcinoma of the uro-

thelium, even if other aetiological factors are not considered.

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Postgraduate Medical Journal (April 1978) **54**, 286–291.

Partial lipodystrophy with nephrotic syndrome

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Summary

A patient with nephrotic syndrome in association with partial lipodystrophy is reported. The features of partial lipodystrophy are well recognized and the renal lesion is a mesangiocapillary glomerulo-nephritis of a dense deposit type with an associated depression of C3. This type of kidney involvement is becoming increasingly recognized as common in the syndrome of partial lipodystrophy.

Introduction

Partial lipodystrophy is a rare syndrome which has been defined as 'symmetrical loss of fat from the face with or without disappearance of fat from the arms, chest, abdomen and hips but with normal distribution on the lower extremities' (Nelson, Vaughan and MacKay, 1969). The aetiology is unknown but an infective illness is present often at the onset (Poley and Stickler, 1963). The syndrome

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is commoner in females (four females : one male) and usually presents at between 5 and 15 years of age. The most extensive review of the literature is that of Senior and Gellis (1964) in which 77 cases were reported. A renal disorder occurred in 20% of these patients and a wide variety of types were noted (pyelonephritis, acute and chronic glomerulo-nephritis, calyceal dilatation, hydronephrosis, haematuria, asymptomatic proteinuria and the nephrotic syndrome). Other associated abnormalities were – central nervous system disturbance; hepatomegaly; hyperlipaemia; abnormal glucose tolerance tests and one case of diabetes mellitus, as well as single reports of abnormal pigmentation, hirsutism and episodic diarrhoea.

Recent interest has been in the associated renal lesions. The purpose of this communication is to describe a patient with the nephrotic syndrome in association with partial lipodystrophy, in whom renal biopsy studies were performed with immunofluorescent and electron microscopical findings.

History

The patient was a 17-year-old schoolgirl with known partial lipodystrophy. She presented with a one-month history of ankle oedema with slight swelling of the face and hands. There was no preceding illness before the onset of these symptoms and in particular there was no preceding sore throat or upper respiratory tract illness. In other respects she had been well.

In infancy and childhood she had enjoyed good health but at the age of six years she had been referred to hospital for 'cervical lymphadenopathy'. This was not considered to be significant but she was noted to have marked loss of subcutaneous fat affecting the face, arms and trunk and a diagnosis of partial lipodystrophy was made (Fig. 1). She was kept under review until the age of 14 years and was then discharged as her development was satisfactory and she was well. There were no other illnesses before the onset of ankle oedema.

There was no family history of partial lipodystrophy, diabetes mellitus or renal disease, but it was noted that her sister had severe congenital skeletal abnormalities and that two of three brothers had undescended testes.

On physical examination, at the age of 17 years, she was an intelligent and well developed girl (Fig. 2). There was some slight loss of subcutaneous fat from the face but otherwise fat distribution was normal. She was pale but there was no hirsutism or abnormal pigmentation. Pitting oedema was present in both lower limbs extending to the knees. There was no other evidence of fluid retention. Her pulse was 84/min and regular, blood pressure 140/75 mmHg and examination of the praecordium was normal. The chest, abdomen and central nervous system were normal.

Considerable proteinuria was found on routine testing in the out-patient clinic and she was admitted for more detailed study of her renal function.

Investigations

Haemoglobin 11.7 g/dl; WBC 11.2×10^9 /l, consisting of 6.7×10^9 /l neutrophils, 3.92×10^9 /l lymphocytes, 0.336×10^9 /l eosinophils and 0.224×10^9 /l monocytes, and ESR was 50 mm in the first hour. Culture of a throat swab produced commensal organisms only and an anti-streptolysin titre was less than 200 Todd u./ml. Antinuclear factor was negative. A 50 g oral glucose tolerance test was normal. Fasting total lipids were elevated at 9.1 g/l consisting of 8.8 mmol/l cholesterol and 1.39 mmol/l triglycerides. Lipid electrophoretic pattern was normal. Chest X-ray and intravenous pyelogram were normal.

The urine contained persistent protein ranging between 2.8 to 7.0 g/24 hr but no glycosuria was

present. Urine microscopy revealed pus cells, epithelial cells and red cells but repeated urine cultures were sterile. Blood urea was 3.3 mmol/l, and electrolyte analysis showed a sodium of 140 mmol/l, potassium 4.5 mmol/l, chloride 110 mmol/l, standard bicarbonate 23 mmol/l. Fasting serum calcium was 2.13 mmol/l. Serum creatinine was 53.1 μ mol/l and creatinine clearance was 120 ml/min. C3 level was less than 8% of expected value. Total plasma proteins were 45 g/l with albumin of 17.5 g/l, globulin 27.5 g/l with a slightly raised α_2 -globulin on electrophoresis.

In view of the persisting proteinuria, renal biopsy was performed. This showed a mesangiocapillary glomerulonephritis with epithelial crescents present in some 20% of glomeruli, and moderate numbers of polymorphs in most tufts (Fig. 3). Immunofluorescence microscopy revealed granular deposition of IgM, IgC, fibrin/fibrinogen and C3 on thickened capillary walls indicating an immune complex disease. The chief feature on electron microscopy was the uniform dense black deposit in the basement membrane of glomerular capillaries (Fig. 4).

Treatment and progress

She was commenced initially on a high protein (120 g protein) low salt diet. Despite this she had persistent ankle oedema and was therefore given bendrofluazide 10 mg daily. As there was no response to this she was given amiloride in addition. However, over the following nine months she developed progressively more severe ankle oedema with a deterioration in renal function. A trial of high dose furosemide therapy was made with no relief of her symptoms and on three separate occasions she required infusions of salt-poor albumin to reduce her oedema. She had continued to have heavy proteinuria and 9 months after presentation her blood urea had risen to 15.5 mmol/l with a serum creatinine of 392 μ mol/l and a creatinine clearance of between 12.4 and 13.6 ml/min. Her blood pressure was 120/65 mmHg.

In view of her deterioration a repeat renal biopsy was performed. This showed, as before, mesangiocapillary glomerulonephritis of dense deposit type but now large crescents were present in over 70% of glomeruli indicating deterioration since the previous biopsy (Fig. 5).

Within 10 weeks of this repeat biopsy she was readmitted with features of cardiac failure severe enough to make her orthopnoeic. Her pulse was 120/min; blood pressure 140/100 mmHg and jugular venous pressure was elevated by 4 cm; a pre-systolic triple rhythm was audible over the praecordium with numerous fine crepitations throughout both lung fields. The liver was tender and palpable 7 cm below the costal margin and there was marked sacral and ankle oedema.

FIG. 1. The patient aged 9 months to 13 years. (a) 9 months, (b) 2½ years, (c) 4 years, (d) 6 years, (e) 11 years, (f) 13 years.

FIG. 2. The patient aged 17 years.

Blood urea was now 39.9 mmol/l, sodium 135 mmol/l, standard bicarbonate 20 mmol/l, serum creatinine 1107 μ mol/l with inorganic phosphorus 4.42 mmol/l. Haemoglobin was 6.1 g/dl, white cell count 10×10^9 /l, platelets 37×10^9 /l and no red blood cell fragmentation was seen on blood film. Blood and urine cultures were sterile and only commensal organisms were grown from a throat swab. Urine output had fallen to 500 ml per day.

The patient was digitalized, given high flow oxygen and 500 mg furosemide and 250 mg aminophylline were given by intravenous injection. Urine output did not increase and a further injection of 1.0 g furosemide had no effect. She was therefore treated with

FIG. 3. The glomerulus shows a lobular pattern with increased numbers of mesangial cells and thickened capillary walls around the periphery of the lobules. MSB, $\times 225$.

peritoneal dialysis along routine lines. In 36 hr dialysis 5.0 kg of fluid was removed and blood urea had fallen 24.3 mmol/l. Following peritoneal dialysis a repeat chest X-ray showed clearing of pulmonary oedema.

Thereafter a Scribner shunt was inserted and chronic intermittent haemodialysis using an RSP dialyser was started. Dialysis was carried out twice weekly in hospital and the patient remained well and was able to continue her studies until her sudden death at a party 5 months later. An official enquiry discovered that she had been drinking large quantities of vodka and orange and it was thought that death was due to a rapid and severe hyperkalaemia.

At post-mortem the main findings were pulmonary oedema, hypertensive cardiomegaly in addition to mesangiocapillary glomerulonephritis. The renal lesion showed considerable progression with more than 50% of the glomeruli totally hyalinized.

Discussion

This patient had no recognizable illness at the onset of her partial lipodystrophy. During childhood she developed typical features of lipodystrophy but, as is recognized in some patients, her features had returned substantially to normal at the time of her presentation with nephrotic syndrome. She did not have any of the other associated features of partial lipodystrophy.

Early reports of the renal lesions by Senior and Gellis (1964) and Sacerdoti and Galli (1959) did not include renal biopsy material but this is described in more recent reports (Jeune *et al.*, 1965; Lajouanine *et al.*, 1968; Hamza *et al.*, 1970; Eisinger, Shortland and Moorehead, 1972; Williams, Scopes and Peters, 1973; Peters *et al.*, 1973; Sissons *et al.*, 1976). Sissons *et al.* reviewed twenty-one patients with partial

FIG. 4. The glomerular basement membrane contains a fairly uniform dense black deposit. $\times 5620$.

FIG. 5. The glomerulus still shows the characteristic mesangiocapillary pattern and, to the left, a cellular epithelial crescent can be seen. MSB, $\times 210$.

lipodystrophy. Seven of these patients had overt nephritis and in six renal biopsy was performed. All had mesangiocapillary glomerulonephritis which now is recognized as the typical renal lesion associated with partial lipodystrophy. These patients were

shown also to have a prolonged reduction in C3 levels and positive C3 splitting factor indistinguishable from nephritic factor.

Partial lipodystrophy is a benign disorder except for those that develop the associated renal disease. However, it has become apparent that C3 and C3 nephritic factor abnormalities precede the renal disease and seem to be the determining factors producing the mesangiocapillary glomerulonephritis. All of the twenty-one patients reviewed by Sissons *et al.* (1976) had low serum C3 levels, fourteen had C3 splitting factor but ten patients had no features of renal disease. Thompson and White (1973) commented on the fact that they had three children under review all of whom had partial lipodystrophy, hypocomplementaemia and low C3 levels but with normal renal function. One of these patients had a renal biopsy with normal findings. Alper, Bloch and Rosen (1973) reported a child who presented with recurrent chest infections in association with partial lipodystrophy and this child had similar complement findings but, again, normal renal function.

The deciding factor in the progression of the renal disease is uncertain. Eisinger *et al.* (1972) suggested

that pregnancy might be a possible cause but this was not present in the patient described in this report. However, clarification of the aetiological importance of pregnancy would be valuable as most patients with partial lipodystrophy are young females and therefore are potentially at great risk.

In the nine patients reported by Eisinger *et al.* (1972), Williams *et al.* (1972), and Peters *et al.* (1973), only one patient required haemodialysis, suggesting that the initial prognosis of patients with partial lipodystrophy and associated mesangiocapillary glomerulonephritis is not bad. Deterioration in the present patient was rapid despite the fact that she came under medical care at an early stage of renal disorder. Those who advance to renal failure are no different in complement status from those who do well but the presence of crescents as part of the renal lesion seen on biopsy may be an important indicator of a progressive renal lesion. Once deterioration in renal function does occur, there is no known effective drug treatment for this form of mesangiocapillary glomerulonephritis. Corticosteroids, azathioprine and combinations of these preparations have all been given but without success (Eisinger *et al.*, 1972; Williams *et al.*, 1972; Peters *et al.*, 1973).

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