CASE REPORTS

The interrelationship between hypocomplementaemia, partial lipodystrophy and mesangiocapillary glomerulonephritis

MARION A. WAKEFIELD
M.B., B.S., M.R.C.P., D.C.H.

Paediatric Department, Stoke Mandeville Hospital, Aylesbury, Buckinghamshire

Summary

A further case of mesangiocapillary glomerulonephritis, partial lipodystrophy and hypocomplementaemia with reduced serum C_3 levels is reported. The father of the patient was also found to have C_3 deficiency. This lends support to the hypothesis that C_3 deficiency may be the primary disorder relating these conditions and there is evidence in this case that the deficiency may be genetically determined.

It is suggested that the complement state of close relatives, particularly younger siblings, of patients with these disorders should be investigated and, if abnormalities are found, they should be followed-up in order to elucidate the role of hypocomplementaemia in these uncommon disorders.

Introduction

In 1958 it was first suggested that renal disease was associated with lipodystrophy (Gellis, Green and Walker, 1958) and in 1964 an association between nephritis and lipodystrophy was noted (Senior and Gellis, 1964). In 1972 an association between mesangiocapillary glomerulonephritis, partial lipodystrophy and hypocomplementaemia was reported (Williams, Scopes and Peters, 1972) and in 1973, three similar cases were reported by Peters *et al.*, who suggested that there might be a link between complement activation and these uncommon disorders. A further example of this association is now reported from a boy whose father was also found to have hypocomplementaemia although showing no clinical evidence of either partial lipodystrophy or renal dysfunction.

Case report

A 12½-year-old boy was admitted to Stoke Mandeville Hospital following a small haematemesis which was attributed to tonsillitis. He was noted to have partial lipodystrophy and examination of the family photograph album showed that this had become apparent at the age of 7 years.

One month later, he was readmitted with generalized oedema, hypertension (blood pressure 180/130 mmHg), heavy proteinuria (6.3 g/24 hr) and haematuria. His blood urea was 35 mg/100 ml; electrolytes normal; urine protein selectivity index 0.186; serum C_3 = 40 mg/100 ml (normal = 60-120 mg/100 ml); haemoglobin 8.3 g/100 ml; ESR 200 mm; WBC 9900/mm³; anti-streptolysin titre less than 250 Todd u. The oedema responded to bendrofluzide and the hypertension responded to methyl dopa but the urea rose from 35 mg/100 ml to 88 mg/100 ml in 10 days.

Because of deteriorating renal function, he was transferred to Guy's Hospital. On admission, the urea was 74 mg/100 ml; glomerular filtration rate (GFR) (single injection ⁵¹Cr-labelled EDTA), 18 ml/min/1.73 m² surface area (SA); serum C_3 , 18 mg/100 ml. A renal biopsy confirmed a diagnosis of mesangiocapillary glomerulonephritis.

He was treated initially with azothiaprime, prednisolone, dipyridamole and heparin. After 20 days of treatment, his GFR had risen to 32 ml/min/1.73 m² SA but he then developed severe abdominal pain and vomiting and a barium meal suggested a duodenal ulcer. His treatment was stopped and the symptoms settled. Gastroscopy did not confirm the ulceration but in the 2 weeks that treatment was discontinued, the plasma creatinine rose from 1.2 mg/100 ml to 5.7 mg/100 ml. He then developed acute appendicitis and, following an emergency appendicectomy, his renal function deteriorated further and he is now dialysis-dependent.

Complement investigations

Investigation of the complement state of the patient's parents and his sister who were all clinically normal, revealed that his father had low serum C_3 levels of 45 mg/100 ml and 55 mg/100 ml when measured on two separate occasions; his sister had a C_3 level at the lower limit of normal of 60 mg/100

ml, and his mother had a C_3 level of 136 mg/100 ml (normal, 60–120 mg/100 ml).

Circulating nephritic factor was not demonstrated in the serum of either his father, sister or mother, nor initially in the patient's serum. Subsequent examination of the patient's serum has revealed nephritic factor on one occasion. The C_4 level was normal in all four members of the family.

Discussion

The mechanism of the interrelationship between partial lipodystrophy, mesangiocapillary glomerulonephritis and hypocomplementaemia has not yet been established.

It is known that hypocomplementaemia is associated with mesangiocapillary glomerulonephritis and the hypocomplementaemia has been shown to be associated with diminished C_3 synthesis (Alper and Rosen, 1967). Hypocomplementaemia associated with this type of nephritis has also been shown to be associated with the presence of a circulating factor known as nephritic factor (C_3 NeF), which is capable of activating the complement system via the C_3b feedback cycle (Williams *et al.*, 1973). It is also known that partial lipodystrophy may be associated with hypocomplementaemia and the presence of C_3 NeF, even in the absence of renal disease (Alper, Bloch and Rosen, 1973; Thompson and White, 1973).

Among the possibilities which Peters *et al.* (1973) suggested to explain the interrelationship between these disorders were, firstly, that complement activation might be the major damaging process in these disorders and be directly responsible for both loss of subcutaneous fat and glomerular damage and, secondly, that hypocomplementaemia, caused directly or indirectly by the circulating activator, predisposes to the development of this type of nephritis, whether or not it is accompanied by clinically evident lipodystrophy.

It is of interest, that the father of this patient had a low C_3 level but no clinical evidence of lipodystrophy or nephritis, as evidenced by the absence of haematuria, proteinuria or abnormal urinary deposit. This lends support to the hypothesis that C_3 deficiency may be the primary disorder, predisposing the individual to develop either one or

both of these conditions under unfavourable circumstances, for example, after an infection, and there is evidence in this case that the C_3 deficiency may be genetically determined.

In order to elucidate the role of hypocomplementaemia in these uncommon disorders, it is suggested that the complement state of close relatives of patients with either partial lipodystrophy or mesangiocapillary glomerulonephritis, should be examined as well as that of the patients themselves. It would be particularly helpful to determine the complement state of younger siblings without evidence of either disease, and if complement abnormalities were found, to carry out follow-up studies.

Acknowledgments

I would like to thank Dr Michael Salmon for permission to publish this case and for his helpful advice; also, Dr Cyril Chantler for managing the patient when he developed renal failure and Dr D. Gwyn Williams for estimating the complement levels.

References

- ALPER, C.A., BLOCH, K.J. & ROSEN, F.S. (1973) Increased susceptibility to infection in a patient with type II essential hypercatabolism of C_3 . *New England Journal of Medicine*, **288**, 601.
- ALPER, C.A. & ROSEN, F.S. (1967) Studies of the *in vivo* behavior of human C_3 in normal subjects and patients. *Journal of Clinical Investigation*, **46**, 2021.
- GELLIS, S.S., GREEN, S. & WALKER, D. (1958) Chronic renal disease in children with lipodystrophy. *American Journal of Diseases of Children*, **96**, 605.
- PETERS, D.K., WILLIAMS, D.G., CHARLESWORTH, J.A., BOULTON-JONES, J.M., SISSONS, J.G.P., EVANS, D.J., KOURILSKY, O. & MOREL-MAROGER, L. (1973) Mesangiocapillary nephritis, partial lipodystrophy and hypocomplementaemia. *Lancet*, **ii**, 535.
- SENIOR, B. & GELLIS, S.S. (1964) The syndromes of total lipodystrophy and of partial lipodystrophy. *Pediatrics*, **33**, 593.
- THOMPSON, R.A. & WHITE, R.H.R. (1973) Partial lipodystrophy and hypocomplementaemic nephritis. *Lancet*, **ii**, 679.
- WILLIAMS, D.G., CHARLESWORTH, J.A., LACHMANN, P.J. & PETERS, D.K. (1973) The role of C_3b in the breakdown of C_3 in hypocomplementaemic mesangiocapillary glomerulonephritis. *Lancet*, **i**, 447.
- WILLIAMS, D.G., SCOPES, J.W. & PETERS, D.K. (1972) Hypocomplementaemia, membranoproliferative glomerulonephritis and nephrotic syndrome associated with partial lipodystrophy of the face and trunk. *Proceedings of the Royal Society of Medicine*, **65**, 591.