Partial lipodystrophy in coeliac disease

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Abstract

The association of coeliac disease and partial lipodystrophy is described. The patient also had deficiencies of serum IgA and C3 complement (the latter associated with partial lipodystrophy). In addition, there was subclinical dermatitis herpetiformis confirmed by skin biopsy. The facial wasting of fully developed partial lipodystrophy may be misinterpreted as a sign of malabsorption but the facial, upper limb, and truncal lipodystrophy contrasts with normal pelvic and lower limb appearances.

Partial lipodystrophy (PL) is a disorder of indefinite aetiology. The diagnosis depends on the presence of noticeable global reduction of adipose tissue above the waist contrasting with normal appearances of the buttocks and lower limbs, coupled with C3 hypocomplementaemia. PL is associated with a number of other abnormalities including glomerulonephritis (usually mesangiocapillary),¹⁻³ diabetes mellitus, hyperlipidaemia, hepatomegaly, mental retardation,⁴ and Sjogren's syndrome.⁵ Various other immunological abnormalities have been reported in isolated cases of PL. Its association with coeliac disease (CD) and dermatitis herpetiformis (DH) has not been documented before. We describe a patient with PL, CD, DH, and bronchial asthma. In addition her serum C3 complement and serum IgA values were subnormal. Thus, a wasted facies in a patient with well controlled CD should raise the possibility of PL.

Case report

Our patient, an 18 year old white woman, had been diagnosed as having CD at the age of 7. The diagnosis had been made after examination of a small intestinal biopsy specimen. She was started on a gluten free diet and remained on this until she was 10, at which time she stopped the diet. Nine months later she presented to the paediatrics department of this hospital with reactivated steatorrhoea. A repeat jejunal biopsy specimen showed subtotal villous atrophy and she restarted the gluten free diet. The villous atrophy resolved and her steatorrhoea stopped. At that time she also had symptomatic bronchial asthma that required treatment with a bronchodilator.

Despite the apparently satisfactory treatment of her CD, persistent severe wasting of the face, upper limbs, and trunk – contrasting with normal appearances of the pelvis and lower limbs – was noted at outpatient follow up over a one year interval after reversal of the subtotal villous atrophy. She was questioned about her diet but this seemed adequate. Her serum thyroxine value was normal. PL was suspected clinically.

Low serum C3 complement values (which are a feature in 70% of patients with PL)⁶ were detected, initially at 180 ng/l (normal range 500–1200 ng/l) and ranging from 103–246 ng/l over the following four years. The PL has progressed during the eight years since it was first diagnosed and is now quite striking (Figs 1 and 2).

Serum immunoglobulin electrophoresis profiles have persistently shown mildly depressed IgA values ranging between 0.22 and 0.31 g/l (normal range 0.55–4.0 g/l) with normal IgG and IgM values. A skin biopsy specimen with immunofluorescence staining showed speckled deposits of IgA in the papillary dermis in keeping with DH but no overt skin disease has been detected clinically on follow up. The patient's HLA profile is A1, B8, BW6, and DR3, consistent with CD and DH.^{7,8} Her glucose tolerance and fasting plasma insulin profiles have remained normal over the past four years.

Discussion

This is the first documented patient with CD and PL. Although PL is an uncommon disorder, it may go undiagnosed when it occurs in patients with wasting diseases, for example steatorrhoea. The facial and upper limb wasting is striking, however, in comparison with a relatively normal

Figure 1: Partial lipodystrophy. The facial, upper limb, and truncal wasting contrasts with the normal appearance of the legs.

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Figure 2: The characteristically cadaverous facies of partial lipodystrophy.

lower limb appearance and the facial wasting in particular should arouse suspicion (Fig 2), particularly when a small intestinal biopsy specimen shows controlled CD.

PL is associated with a serum complex, the so-called C3 nephritic factor,⁹ which seems to stabilise the C3 convertase enzyme in plasma resulting in accelerated C3 complement factor degradation. Thus the persistent plasma C3 hypocomplementaemia emphasises the importance of the wasting. Approximately half of all patients with PL and C3 hypocomplementaemia progress to develop noticeable mesangiocapillary glomerulonephritis over a five to 20 year period from the onset of PL.⁶ Eight years after the onset of PL in this patient there is no overt evidence of glomerular damage but constant vigilance is necessary. Clinically inapparent mesangiocapillary glomerulonephritis in patients with PL and C3 nephritic factor is well described¹⁰ but without clinical or biochemical evidence of renal impairment in this patient a renal biopsy is not justified at the present.

Insulin resistance with impaired glucose tolerance or frank diabetes mellitus is a feature in some 20% of patients with PL¹¹ but a series of glucose tolerance tests with matched plasma insulin concentrations shows no evidence of hyperglycaemia or hyperinsulinaemia in our patient.

The cause of the low serum IgA values is not clear. There is an increased incidence of selective IgA deficiency in patients with CD compared with the general population (2% v 0.14%).¹² The IgA deficiency, however, although selective (with normal IgG and IgM values), is not sufficiently low to satisfy the definition of selective IgA deficiency (ie less than 50 mg/l). Low serum IgA values are not a recognised feature of PL.

The HLA profile including haplotypes B8 and DR3 is typical of CD. There is no known HLA association with PL.

PL has been reported in combination with a number of immunological disorders other than mesangiocapillary glomerulonephritis and Sjogren's syndrome.⁵ Scleroderma has been described in a patient with generalised lipodystrophy who also developed Hodgkin's disease.¹³ Thyrotoxicosis, myasthenia gravis, and idiopathic thrombocytopenic purpura have been reported in a single patient with PL.¹⁴ Diabetes mellitus¹⁵ and Sjogren's syndrome¹⁶ are also associated with CD, thus a broad but poorly understood immunological link may exist between PL and CD. This is, however, the first patient in whom the coexistence of these disorders has been noted. PL should not be misdiagnosed as uncontrolled malabsorption since the full blown physical features are very distinctive, particularly the contrast in subcutaneous fat deposition between the upper and lower halves of the body (Figs 1 and 2).

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