The patient with glomerulonephritis and lipodystrophy

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In 1979, heavy proteinuria and microscopic haematuria were discovered in a 25-year-old man following an upper respiratory tract infection. He was hospitalized in a nephrology unit. Physical examination disclosed lower-limb oedema and blood pressure of 175/110 mmHg. A striking clinical feature (Figure 1) was complete, symmetrical loss of fat from the face, the arms and the upper part of the trunk. The association of urinary signs of glomerulopathy and of lipodystrophy immediately suggested that the renal lesions would consist of type 2 membranoproliferative glomerulonephritis with dense deposits in the glomerular and tubular basement membranes. This ‘Augenblick-diagnose’ (first-glance diagnosis) was confirmed by renal biopsy and by laboratory results.

Figure 2 illustrates the typical appearance of dense deposit disease as found on renal biopsy. Capillary walls were thickened by ribbon-like deposits in the basement membranes, which strongly took up various stains, including light green and PAS. On Masson’s trichrome they stained dark green. Some segments of Bowman’s capsule were similarly thickened. The same dense deposits were visible in the tubular basement membranes, as shown on Figure 3.

Immunofluorescence with antiserum to C3 gave a positive reaction in glomeruli (Figure 4) and tubules (not shown).

Laboratory work-up disclosed nephrotic syndrome and incipient renal insufficiency with a serum creatinine level of 160 μmol/l. The patient was more anaemic than would have been expected from mildly impaired renal function. This was explained by finding haemolytic anaemia, with a positive Coombs’ test using an anticomplement reactant. Other immunological features consisted of decreased levels of C3, normal levels of C4, and presence of C3 NeF (nephritic factor), which indicated complement activation through the alternate pathway.

The course was relentless to renal failure and maintenance haemodialysis. The patient received a renal transplant, which was rejected. A second renal transplantation was carried out 5 years ago, with lasting success. Subsequent corticosteroid treatment has resulted in a weight gain of 25 kg. This excess weight was due to an increase in fat localized in the lower half of the body. Hence lipodystrophy is presently still more striking than at the time of discovery of the disease.

Suggested reading

The interested reader will find relevant bibliography, electron microscopy pictures and discussion of the relationships among lipodystrophy, type II MPGN and the complement activation system, in the following references:

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Fig. 1. Appearance of the face and neck. There is a complete loss of subcutaneous fat. The cheeks are emaciated, giving a false impression of unusually high cheekbones.

Fig. 2. Glomerulus and Bowman’s capsule. All capillary loops are thickened and appear dark green on Masson’s trichrome. Similar dense deposits are present within Bowman’s capsule. Mesangial cell proliferation is not equally distributed through the glomerular tuft.

Fig. 3. Dense deposits within the tubular basement membranes.

Fig. 4. Immunofluorescence with anti-C3 antiserum. The dense deposits are granular, but their density is such that they underline some capillary loops in a linear fashion.