Extrarenal malignancy and the nephrotic syndrome

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SYNOPSIS The clinical and histological findings are described of a patient who presented with the nephrotic syndrome and was found at necropsy to have a bronchial carcinoma. Amyloidosis, renal vein thrombosis, and neoplastic infiltration of the kidneys were excluded. The kidneys showed a diffuse glomerulonephritis of mesangiocapillary type. The possible aetiological association between these two conditions is discussed.

The association of the nephrotic syndrome with extrarenal malignancy is not an uncommon one (Lee *et al*, 1966; Lewis *et al*, 1971; da Costa *et al*, 1974). The vast majority of renal disease in relation to malignancy is that of membranous nephropathy.

Lee *et al* (1966) included one case of lobular glomerulonephritis in their series while Lewis *et al* (1971) reported one case of mesangiocapillary glomerulonephritis (MCGN) associated with carcinoma of the breast. MCGN has been reported on two occasions in lymphoma (Muggia and Ultmann, 1971; Hyman *et al*, 1973).

This appears to be the first report of MCGN associated with a bronchial neoplasm.

Case Report

A 50-year-old man was admitted to hospital in January 1974 with a history of chronic bronchitis. A diagnosis of nephrotic syndrome of uncertain aetiology was made together with mild right-sided heart failure secondary to extensive pulmonary fibrosis. Three months later he was readmitted with a blood urea of 200 mg/100 ml and was dialysed. In view of his past history of pulmonary tuberculosis antituberculosis therapy was begun. His condition improved and he remained static for four months, when he developed superior vena caval obstruction. A chest x-ray at this time showed a mass in the right upper mediastinum. He died shortly afterwards.

NECROPSY

There was a necrotic tumour (3 × 3 × 2 cm) at the hilum of the right lung with abscess formation in the middle and lower lobes. The liver and regional nodes showed metastatic tumour deposits. The

kidneys were grossly unremarkable. The renal veins were patent.

Histology

Sections from the lung showed a moderately well-differentiated squamous-cell carcinoma. The lung abscess was a pyogenic lesion; stains for acid-fast bacilli and fungi were negative.

The kidneys showed a diffuse glomerulonephritis of mesangiocapillary type with a lobular pattern of the glomerular tufts (fig 1). Electron microscopy of the renal tissue showed electron dense deposits in the mesangium and along the capillary basement membrane in a subendothelial position (fig 2). Mesangial interposition was also demonstrated. Immunofluorescent studies were not done.

Discussion

Loughridge and Lewis (1971) reported immune complex glomerulonephritis in a patient with the nephrotic syndrome and squamous carcinoma of the bronchus. At necropsy immunoglobulins eluted from the glomeruli reacted specifically with the patient's tumour cells. This study provided direct evidence that the mechanism of renal disease in patients with cancer might be mediated by immune complexes composed of antitumour antibody and tumour antigen.

However, the incidence of the nephrotic syndrome does not appear to be higher in patients with known tumour-associated antigens, for example, malignant melanoma. Costanza *et al* (1974) have recently demonstrated carcinoembryonic antigen-antibody complexes in glomeruli of a patient with colonic carcinoma and the nephrotic syndrome.

Following animal studies Germuth and Rodriguez (1973) postulated that the anatomical localization of

Fig 1 *Mesangiocapillary glomerulonephritis with a 'double contour' (arrow) appearance of the glomerular capillary walls due to mesangial interposition. PASM $\times 300$*

Fig 2 *Electron micrograph showing glomerular capillary loop with subendothelial electron dense deposits (arrows). $\times 12,000$*

immune complexes in nephritis depends solely on the size of the complexes. Small complexes formed in antigen excess appear to localize on the epithelial side of the glomerular basement membrane, whereas larger complexes formed in antibody excess appear in a subendothelial mesangial position.

In human membranous nephropathy, immune complexes are found in the subepithelial space, whereas in MCGN the complexes appear in the mesangium and subendothelial space.

It may be that the type of renal lesion produced by tumour antigen-antibody complexes is related to the size of these complexes, which in turn depends to some extent on the pattern of antibody response of the patient to his tumour.

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