Nephrotic syndrome and mesenteric infarction secondary to metastatic mesothelioma

C K T Farmer, D J A Goldsmith

Abstract
Malignant mesothelioma can present insidiously with progressive breathlessness and chest pain. Paraneoplastic, or non–chest related, presentations are very rare. The case of an elderly man with occupational exposure to asbestos who presented with nephrotic syndrome due to minimal change nephropathy in the context of advanced pleural mesothelial malignancy is reported.

(Postgrad Med J 2001;77:333–334)

Keywords: malignant mesothelioma; minimal change nephropathy; nephrotic syndrome

Case report
In late 1997 a 66 year old retired man was admitted with a short but rapidly progressive history of peripheral oedema, exertional breathlessness, and extreme fatigue. He was hypotensive (90/60 mm Hg), breathless at rest, and pale, with decreased left chest wall movements, bilateral basal inspiratory crepitations, and anasarca. Investigations showed proteinuria of 30.0 g/l, plasma albumin of 15 g/l, haemoglobin 112 g/l, erythrocyte sedimentation rate 110 mm/hour, and plasma creatinine 115 µmol/l.

He had been a telephone engineer until 1994, and undoubtedly exposed to asbestos. He had a strong family history of raised cholesterol, myocardial infarction, and thyroid disease. He had been perfectly well until 1994 when he was admitted with a myocardial infarction for which he was given streptokinase. He had developed haemoptysis, left lung pneumonia, and a right tension pneumothorax. Eventually he left hospital, but remained unwell with intermittent left heart failure and angina. An angiotensin converting enzyme inhibitor, antianginals, and diuretics were started. He remained hypotensive and required inotropic support for 18 days during which time he developed haemoptysis, left lung pneumonia, and a right tension pneumothorax. Eventually he left hospital, but remained unwell with intermittent left heart failure and angina. An angiotensin converting enzyme inhibitor, antianginals, and diuretics were started. A small left sided pleural reaction/effusion remained visible on the chest radiograph.

In early 1997 he was referred for a respiratory opinion with a recent history of two upper respiratory tract infections and progressive breathlessness. The chest radiograph showed extensive left pleural and parenchymal shadowing. Sputum cytology was normal. Pulmonary function testing showed a mild obstructive pattern. Fibreoptic bronchoscopy was normal. High resolution computed tomography of the chest was thought to show pleural pathology and basal interstitial pulmonary fibrosis (fig 1). Rheumatoid factor was noted to be positive (1/320 titre). A trial of prednisolone 40 mg was started but with no benefit. He became unwell with nephrotic syndrome and was referred for a renal opinion.

He was given intravenous diuretic and 20% albumin. A chest radiograph showed extensive pleural reaction/effusion on the left, and a smaller effusion on the right. Renal ultrasound showed two normal sized non-obstructed kidneys with preserved corticomedullary differentiation. Echocardiography showed a dilated left ventricle with globally poorly function and with apical thrombus. Investigations for autoimmune and plasma cell disease were negative. Blood clotting studies were normal. Fibrinogen concentrations were raised (8.6 g/l; normal range 2.0–4.0 g/l). Renal biopsy showed 10 glomeruli that were normal on light microscopy. Sirius red staining for amyloid was negative. Immunofluorescence was negative. Electron microscopy showed extensive foot process fusion and no evidence of immune deposits. A diagnosis of nephrotic syndrome secondary to minimal change nephropathy (MCN) was made and he was started on oral 40 mg prednisolone daily, 150 mg ranitidine twice a day, and intravenous heparin then oral warfarin (48 hours after the renal biopsy) because of the echocardiographic findings of apical thrombus and the significant thrombotic tendency seen in severe nephrotic syndrome.

Shortly afterwards he had a small haematemesis with mild epigastric tenderness. Endoscopy showed mild distal oesophagitis and old gastritis but no bleeding point and no duodenal pathology. Anticoagulation was immediately reversed. However, he developed acute small bowel obstruction as shown by increasing abdominal pain, left iliac fossa tenderness, abdominal distension, faeculent vomiting, obstructive bowel sounds, and dilated small bowel loops on abdominal radiography. Serum amylase was normal. The haemoglobin concentration was stable at this stage. He rapidly became more breathless and hypotensive, required elective controlled intubation and mechanical ventilation with inotropic circulatory support, and died on the intensive care unit six hours later.

At postmortem examination the left pleural space was obliterated by old adhesions and by...
The best known association between malignancy and MCN is that seen in Hodgkin’s lymphoma. Possible mechanisms to explain the association include the elaboration of vascular permeability factor, cytokines, and chemokines by tumour cells.

Renal lesions in the context of pleural mesothelioma are extremely unusual—only five cases of nephrotic syndrome with mesothelioma exist in the literature, of which only one showed MCN and mesothelioma. In that case, treatment of nephrotic syndrome with prednisolone and cyclophosphamide was ineffective, while subsequent treatment of the pleural tumour with doxorubicin and dacarbazine was ineffective against the tumour but improved the patient’s nephrotic syndrome.

Metastatic mesothelioma is exceptionally unusual, but has been reported. The prior lung problems in this patient (pulmonary oedema, pneumonia, and contralateral pneumothorax) hindered the diagnosis until late in the course of the illness.

The cause of the infarction of the duodenum and jejunum was not clear. The options include embolisation from the heart (antemortem echocardiography had shown extensive left ventricular apical thrombus but none was seen postmortem), arterial thrombosis (rare but well documented in nephrotic syndrome), atheroembolism from an ulcerated aortic plaque, or hypotensive/watershed infarction on the background of aortic/mesenteric atheroma. The prothrombotic tendency in severe nephrotic syndrome is well described and anticoagulation recommended.

In summary we present a case of MCN in association with metastatic pleurally based sarcomatous mesothelioma.

The authors would like to thank Dr Kirkham, Consultant Histopathologist, Royal Sussex County Hospital, Brighton, Sussex.

The prior association with metastatic pleurally based sarcomatous mesothelioma has been reported.

Discussion
Renal lesions in the context of malignancy (both carcinoma and lymphoma) have been recognised for more than three decades. These are typically of membranous nephropathy, and are more rarely, renal amyloidosis, mesangiocapillary glomerulonephritis, renal vasculitis (antineutrophil cytoplasmic antibody positive and negative), and MCN. The development of membranous nephropathy, an immune complex mediated form of glomerular injury, in patients with malignant tumours has been proposed to be the result of deposition of tumour antigens and antitumour antibodies in the glomerulus, or to changes wrought by the malignancy on the immune system engendering greater susceptibility to such immune complex mediated damage from exogenous or endogenous antigens. While initial reports suggested as much as 10% of membranous nephropathy was secondary to underlying malignancy, this figure is now thought to be a significant overestimate of the true frequency.
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Postgrad Med J 2001 77: 333-334
doi: 10.1136/pmj.77.907.333

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