Necrotizing glomerulonephritis associated with Hodgkin’s disease

Sir,
The occurrence of various types of glomerulonephritis with haematological malignancies is well established [1–3]. Hodgkin’s disease has been principally described in association with minimal-change nephropathy and rarely with membranous glomerulonephritis [1,2]. We report here a patient with Hodgkin’s disease of the nodular sclerosing type, who initially presented with necrotizing glomerulonephritis, a very unusual association.

Case. A 49-year-old woman discovered a tumour in the left inguinal region almost as large as a tennis ball that grew over a few days. A computerized axial tomography (CAT) of the abdomen demonstrated splenomegaly and multiple enlarged lymph nodes para-aortal, iliac, in the left inguinal region, and around the portal fissure. At this time the serum creatinine was 1.2 mg/dl. On admission 3 days later, the serum creatinine was 3.2, BUN 36, uric acid 7.9 mg/dl. No anti-neutrophil cytoplasmic antibodies (ANCA), anti-GBM antibodies, or anti-DNA antibodies were detected (results received later). Serum complement was normal.

There was no evidence of cryoglobulinaemia, paraproteinaemia, infection with hepatitis B and C, or elevated anti-streptolysin O and anti-DNAse titre. IgG antibodies against Epstein–Barr virus (EBV) were detected. Proteinuria was present that was almost exclusively albumin (1100 mg/24 h) without detection of Bence Jones protein. The urine sediment revealed many acanthocytes and several red-cell casts. Ultrasound revealed enlarged kidneys with faded parenchyma. The clinical diagnosis of rapid progressive glomerulonephritis was established.

Therapy with intravenous methylprednisolone (500 mg/day for 3 days) was started. A renal biopsy as well as surgical removal of the inguinal lymph node was performed the next day. Figure 1 shows the periodic acid–Schiff (PAS) staining of the renal biopsy. Intra- and extracapillary proliferation with segmental necrosis and crescent was present. Immunohistological studies showed no granular or linear deposition of IgA or IgG. No dense deposits were observed on electron microscopy. A diagnosis of ongoing necrotizing glomerulonephritis without evidence of immune complexes or anti-GBM antibody deposition was made.

The excised lymph node provided the diagnosis of Hodgkin’s disease of the nodular sclerosis type. Since a bone-marrow biopsy as well as liver biopsy specimen revealed no evidence of infiltration, a stage IIA was diagnosed (Ann Arbor classification). The patient received one course of chemotherapy including cyclophosphamide, vincristine, and continuation of oral prednisone. Restaging 5 months later revealed only moderate residual lymph nodes, and the patient underwent radiation therapy for residual disease. At this time, the serum creatinine was 3.1 mg/dl. There were no signs of glomerulonephritis activity in the urinary sediment. The patient is currently being treated with ACE inhibitor.

Comment. Our case is unusual because an association of crescentic glomerulonephritis with Hodgkin’s disease has previously been described in very few cases [1,3]. The glomerular abnormalities generally observed in the early course of Hodgkin’s disease are almost exclusively membranous glomerulonephritis or minimal-change nephropathy [2]. For cases with minimal-change disease, it has been suggested that activated helper T-cells, a phenomenon known to occur in Hodgkin’s lymphoma, may produce and secrete an unknown lymphokine that influences glomerular permeability [1]. In cases with membranous glomerulopathy and Hodgkin’s disease, subendothelial, intramembranous, and subepithelial immune deposits have been described [1]. These features were clearly absent in our case. In contrast, necrotizing crescentic glomerulonephritis has been almost exclusively described in patients with non-Hodgkin lymphomas [2].

Fig. 1. Renal biopsy specimen showing intra- and extracapillary proliferation with segmental necrosis and crescent. PAS, original magnification × 360.
How Hodgkin’s disease may induce necrotizing glomerulonephritis is unclear but a few suggestions can be made. The most simple explanation would be that the glomerulonephritis is independent of the Hodgkin’s disease and the concomitant manifestation unrelated. However, this seems to be rather unlikely because of the timely association of the crescentic glomerulonephritis with the growing tumour. On the other hand, Hodgkin’s lymphoma and renal disease may be the expression of an underlying abnormality in immune regulation. Crescents in proliferative glomerulonephritis are thought to be composed of proliferating parietal epithelial cells and infiltrating monocytes/macrophages.

We have previously demonstrated that the local expression of monocyte chemoattractant protein-1 (MCP-1) plays a pivotal role in the glomerular infiltration of monocytes/macrophages [4]. It has recently been shown that the lymphoma tissue of Hodgkin’s disease, but not that of non-Hodgkin’s lymphoma, express MCP-1 and interleukin 8 (IL-8, [5]). It is tempting to speculate that patients with heavy lymphoma burden may have increased circulating levels of MCP-1 and IL-8. These small chemotatic molecules may then bind to intrinsic renal cells after glomerular filtration and could induce glomerular influx of monocytes/macrophages. However, this hypothesis does not explain why so few patients with Hodgkin’s disease develop glomerulonephritis, and certainly further abnormalities are necessary for the induction of renal disease in the presence of lymphoma.

It has recently been reported that the genome of the EBV was detected in tubules from patients with chronic interstitial nephritis, and it was implicated that this genomic integration evokes a cellular immune response resulting in tubulointerstitial influx and proliferation of immune competent cells [6]. For years, EBV has been suspected as an aetiological agent in Hodgkin’s disease on the basis of epidemiological, serological, and more recently molecular studies [7]. Although it remains currently speculative, one could suggest that EBV may also contribute to the glomerular proliferation of cells, as in the observation derived from chronic interstitial nephritis [6].

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