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Case Report

Non-Hodgkin lymphoma and glomerulonephritis. What kind of relation?

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Introduction

Glomerular injury in the setting of neoplasia is generally regarded as one example of paraneoplastic disorder [1]. The prevalence of overt paraneoplastic renal disease is unknown but probably quite small [2].

In lymphoid malignancies, glomerular injury is rare, and has been mainly observed in patients with Hodgkin disease, although a small number of patients with non-Hodgkin lymphoma (NHL) has been described. The association of glomerulonephritis (GN) and NHL is so rare, that some authors have questioned whether this association is genuine [3,4].

We report on a patient with NHL—diffuse well differentiated B-cell lymphoma—in association with crescentic GN, in which the glomerular involvement seems related to M-component secretion.

Case report

A 50-year-old white woman was admitted to our hospital in April 1992 with asthenia, fever, and weight loss. She was pale and presented with supraclavicular adenopathy. Blood pressure was 130/80 mmHg. The histological examination of the adenopathy revealed a well-differentiated diffuse lymphocytic lymphoma with plasmocytic differentiation. Immunohistochemical examination showed expression of μ/k chains. A thoracoabdominal computer tomographic scan (CT) revealed enlarged retroperitoneal lymph nodes. Bone marrow biopsy showed extensive involvement with lymphoma. The serum creatinine was 1.5 mg/dl (132.6 µmol/l), 24-h urine protein excretion was 1 g. Urinalysis showed numerous red blood cells (r.b.c.), without casts. Serum calcium and uric acid were within normal limits. Serum immunoglobulins levels were IgM 8.92 g/l, IgG 24.3 g/l, and IgA 0.43 g/l. Serum immunoelectrophoresis with monospecific antisera showed a marked elevation of IgM and a polyclonal elevation of IgG. Serum complement levels were normal. Rheumatoid factor and antinuclear antibodies were negative. Cryoglobulins were not found. Renal biopsy (scanty material) on light-microscopy showed crescentic glomerular lesions, endocapillary proliferation and focal interstitial infiltrate with mononuclear cells (Figure 1A).

Therapy with cyclophosphamide, vincristine, and prednisolone (CVP) was begun. One month later serum creatinine returned to normal (0.8 mg/dl; 70.72 µmol/l), without significant proteinuria. After 9 months of treatment a revaluation revealed interstitial infiltration of bone marrow with lymphocytes, the CT scan showed no enlarged retroperitoneal lymph nodes or other abnormalities. Serum creatinine was 0.84 mg/dl (74.25 µmol/l). Serum immunoglobulins levels were IgM 1.02 g/l, IgG 2.62 g/l, and IgA 0.22 g/l. Three months after cessation of therapy the patient had episodic gross haematuria. Renal function began to deteriorate (serum creatinine 2.4 mg/dl; 212.16 µmol/l) and urinary protein excretion was 10 g/day. Urinary sediment was active (> 50 r.b.c./h.p.f. and r.b.c. casts), serum albumin was 28 g/l. Renal ultrasound was normal. Serum calcium and uric acid were normal. A new revaluation of bone marrow disclosed the same pattern and CT scan showed no lymph nodes. Serum immunoglobulins were IgM 5.15 g/l, IgG 4.17 g/l, IgA 0.33 g/l. Complement levels were normal and no cryoglobulins were detected. A second renal biopsy was performed, showing 15 glomeruli, with crescentic lesions (mostly cellular) and endocapillary proliferation in over 75% of them (Figure 1B). Some glomeruli showed total hyalinization. Immunofluorescence study showed staining for IgM and IgG deposits in glomeruli.

Therapy with cyclophosphamide and prednisolone was reinstituted. Renal function stabilized for 2 months without regression of the nephrotic syndrome. Serum immunoglobulins returned to values within the normal limits. Afterwards, renal function deteriorated pro-

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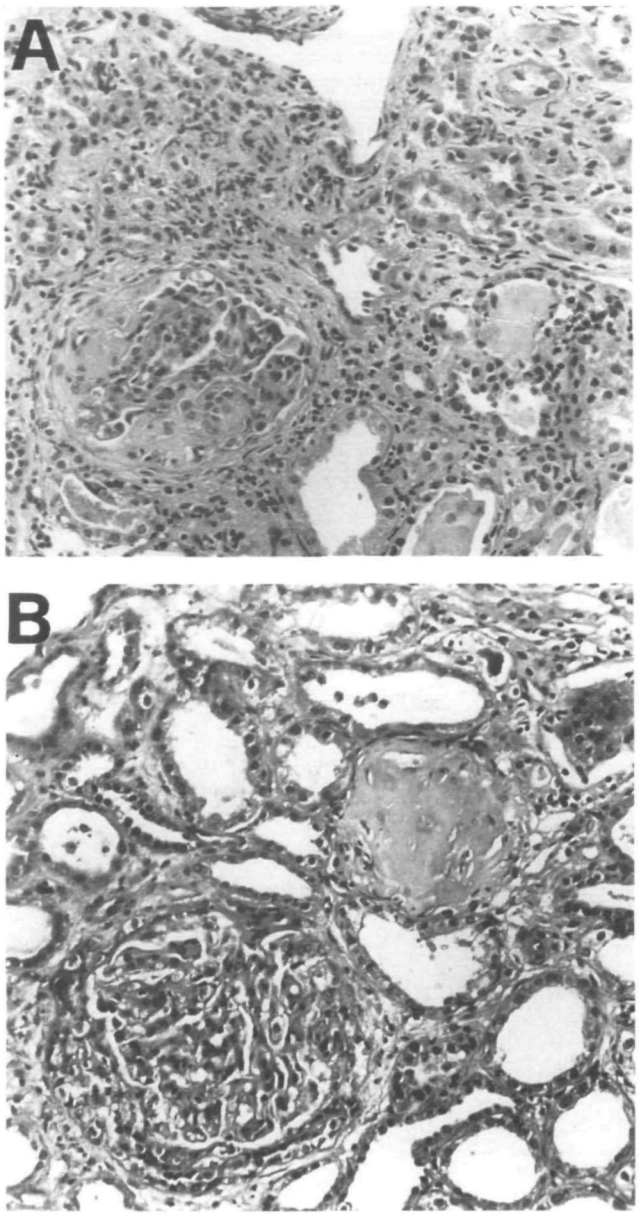

Fig. 1. A. Glomeruli with fibrous crescents and interstitial mononuclear infiltration (LM; H&E). B. Glomeruli with cellular crescents and total sclerosis (LM; H&E).

gressively, leading to the need of regular dialysis 1 year later, despite adequate control of blood pressure and low-protein diet.

Discussion

Renal failure in the setting of lymphoma is usually attributable to direct infiltration of the kidney by malignant cells, obstruction of both ureters by tumour mass, sudden increase in serum calcium or uric acid, and amyloidosis with dehydration [5].

A limited number of cases of GN have been described in patients with non-Hodgkin lymphoma, diffuse, well-differentiated lymphocytic lymphoma being one of the most common subtype of lymphoma associated with GN [1,3].

The diagnosis of GN usually has a close temporal relation with that of lymphoma. Impaired renal function is the most common presentation of renal involvement in non-Hodgkin lymphoma, severe morphological types of GN (including 8 cases of crescentic GN) being the most common [3,6–8].

A pathophysiological relation between lymphoma and GN has been clearly shown [9]. GN can be caused by cryoglobulinaemia in which the cryoglobulins can either be considered as immune-complexes (type II) or remain of undetermined nature (type I). The secreted M-component can injure glomeruli through a non-cryoglobulin-mediated mechanism. There is a high percentage of M-component in blood and/or in renal biopsy from patients with GN and well-differentiated B-cell lymphoma, in sharp contrast to the low incidence usually reported in series without renal involvement [9,10]. In our patient, the first kidney biopsy, although with scanty glomeruli, showed crescentic lesions and endocapillary proliferation. After initiation of therapy directed to lymphoma, renal function returned to normal; this could be ascribed to a response of the glomerular lesion. With therapy the M-component became undetectable. After cessation of CVP therapy, the renal function deteriorated, with reappearance of the M-component and the re-emergence of the crescentic GN. Renal function was then stabilized with cyclophosphamide plus prednisolone therapy, with posterior deterioration to end-stage renal failure related to the more advanced GN.

Petzel *et al.* [6] has described a case of circulating M-component, with crescentic, immune complex GN. Whether the glomerular injury was initiated by the M-component is not established, although it seems to play an important role.

The reappearance of crescentic GN a short time after cessation of therapy suggests that the continuation of therapy may have postponed the emergence of renal failure. Thus, alteration in renal function in the setting of lymphomatous disorders, after exclusion of the usual causes of renal failure, should lead to prompt evaluation of renal histology (specially in the subgroup of patients with an M-component). Renal function can be improved and probably normalized by chemotherapy [8,9].

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