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Proliferative glomerulonephritis and mantle cell lymphoma: a rare association

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SUMMARY

Renal involvement in mantle cell lymphoma (MCL) is rare. We present the case of a man followed for MCL presented with acute kidney injury and positive antineutrophil cytoplasmic antibody (ANCA) type anti proteinase 3 (PR3). He was treated as for a rapidly progressing glomerulonephritis with cyclophosphamide and methylprednisolone followed by oral prednisone. Renal biopsy revealed diffuse endocapillary proliferation and segmental extracapillary proliferation in four glomeruli. Immunohistochemistry confirmed the renal invasion of lymphomatous cells. He started improving his renal function shortly after starting treatment. The coexistence of renal MCL infiltration, extracapillary proliferation and ANCA positive is exceptional.

BACKGROUND

Lymphomas are a group of cancer developing from lymphocytes. Mantle cell lymphomas (MCLs) are an aggressive subtype of B-type non-Hodgkin's lymphomas (NHLs). Kidney injury secondary to lymphomas varies widely.

The aim of our work is to present a case of MCL that developed kidney injury secondary to proliferative glomerulonephritis and to discuss the diagnostic and therapeutic challenges in the clinical course.

CASE PRESENTATION

The patient was a previously healthy 56-year-old man without known diseases. He presented bilateral cervical node enlargement. A surgical biopsy was performed. Immunohistopathology examination concluded to an MCL CD20+, CD5+ and cyclin D1+. The patient was subsequently referred to haematology department for further treatment. He was proposed for R-CHOP21 chemotherapy. During initial assessment, serum creatinine (SCr) values started to increase from 110 µmol/L to 535 µmol/L in a 3 months period, a normal serum phosphorus at 0.87 µmol/L, a normal lactate dehydrogenase (LDH) at 133 IU/L and a normal uric acid at 320 µmol/L. The patient was then referred and admitted in the nephrology department before receiving chemotherapy.

On admission, the patient was in good general condition. Physical examination revealed a weight of 60 kg (body mass index (BMI)=20 kg/m²). Blood pressure was 11/6 mm Hg. Cardiopulmonary

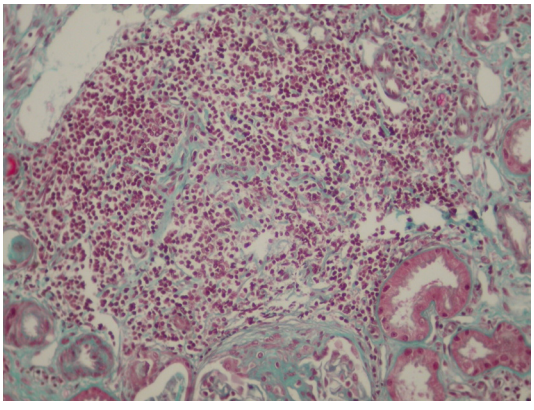

Figure 1 Renal biopsy (×200); focal interstitial lymphocytic infiltrate; tubular atrophy; and vascular wall thickening.

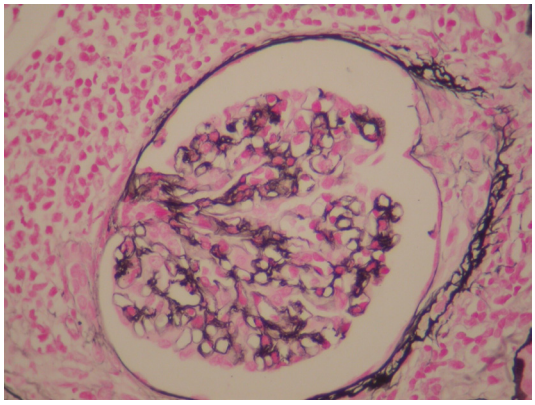

Figure 2 Renal biopsy (×400); endocapillary cellular proliferation; glomerular basement membrane is thin; interstitial infiltrate surrounding the glomerulus.

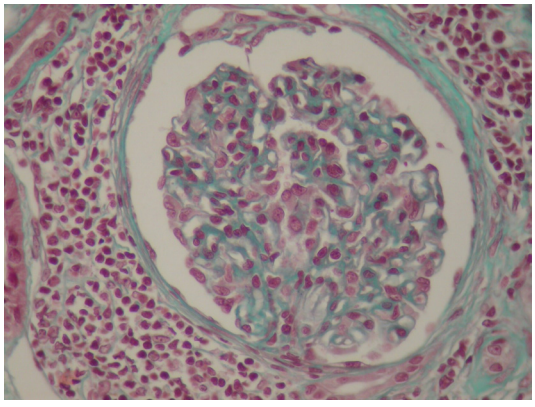

Figure 3 Renal biopsy (×400); high-power view of a glomerulus; mesangial expansion and endocapillary proliferation; podocyte hypertrophy; thickening of Bowman's capsule; and lymphomatous cell infiltrate surrounding the glomerulus.

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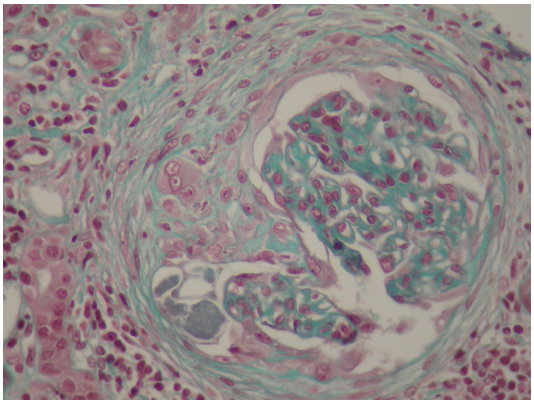

Figure 4 Renal biopsy (×400); fibrocellular crescent in a glomerulus; endocapillary cellular proliferation; and tubular atrophy.

auscultation was normal. Cervical examination was significant for several bilateral palpable nodes. There was no lower limb oedema. Urine output was 1 L of haematic urine per day. Ultrasonography of the kidney revealed two normal size kidneys.

Initial laboratory investigations showed an elevated SCr of 535 µmol/L. His blood leucocyte count was 4.810^3, haemoglobin was 6.4 g/dL and platelet count was 155. 10^3; 24-hour urine proteinuria was 1.1 g. Hepatitis B, C and HIV serology were all negative. Anti-glomerular basement membrane antibodies were negative. ANCA type proteinase 3 (PR3) was positive at 26 IU/mL. Antinuclear antibodies were also positive at 1/200 and could not be typed. The C3, C4 and CH50 fractions of the complement were within normal limits.

Our patient was treated as for a rapidly progressing glomerulonephritis with cyclophosphamide and methylprednisolone followed by oral prednisone.

Renal biopsy was performed subsequently. It showed diffuse endocapillary proliferation with mild diffuse mesangial expansion. There were many circulating leukocytes in the capillary lumen. Four glomeruli showed segmental extracapillary proliferation and one glomerulus had a circumferential fibrocellular crescent. There was interstitial fibrosis estimated at 20% of the cortical area. There was a diffuse interstitial infiltration of mononucleated cells. Immunohistochemistry staining revealed that those cells were CD20 and cyclin D1 positive, confirming the renal invasion of lymphomatous cells. CD5 staining was performed but showed negative, most probably because of a technical problem. Immunofluorescence was positive for IgG, IgM, C3, C1q and light chains. IgA and fibrinogen were negative (figures 1–6). Electron microscopy was not performed because it is not a routine investigation in our country.

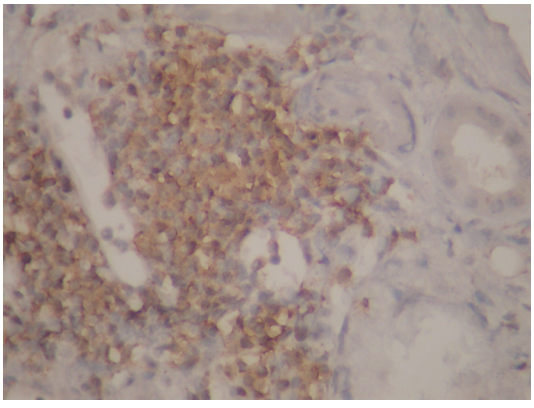

Figure 5 Renal biopsy (×400); interstitial infiltrate positive staining for CD20.

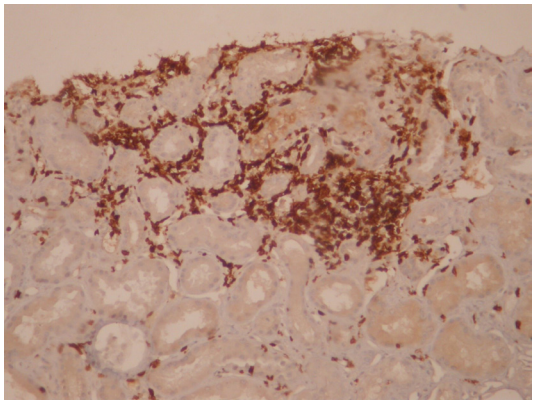

Figure 6 Renal biopsy (×200); interstitial infiltrate positive staining for cyclin D1.

OUTCOME AND FOLLOW-UP

Our patient started improving his renal function shortly after starting treatment. After 1 month, SCr was 144 µmol/L and proteinuria was negative. After 4 months, SCr was 90 µmol/L.

DISCUSSION

Glomerular injury secondary to lymphomas is well documented in this case report[1] although its exact incidence is not precisely known. MCL is indeed a rare subtype of NHL. Several case reports have been published on glomerular involvement of MCL. Some of the histopathological findings are minimal change disease, focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis (MPGN), proliferative glomerulonephritis, lupus nephritis, crescentic C3 glomerulonephritis and ANCA-associated pauci-immune crescentic glomerulonephritis.

The originality in our case lies in the fact that we did not expect to find a proliferative glomerulonephritis as the cause of the renal failure. Seeing the positivity of the ANCA, we expected a pauci-immune crescentic glomerulonephritis. One could argue that the interstitial inflammation was the cause of the renal failure. However, our patient had proteinuria, haematuria, endocapillary and extracapillary proliferation, all features suggestive of a glomerulonephritis. Also, in the context of haematopoietic malignancy, it is possible to have a tumour lysis syndrome but our patient did not receive chemotherapy before the setting of the kidney injury and he had normal phosphorus, LDH and uric acid. The rapidity of the recovery of the renal function might suggest a paraneoplastic disorder. ANCA positivity is possible in various diagnosis such as HIV infection, subacute endocarditis, rheumatoid arthritis, neoplasia and haematological malignancies.[2–5] Although ANCA positivities in Hodgkin's lymphomas were observed, positivities in NHL are yet to be proved.[6] We hope to see ongoing research to prove a role of ANCA in NHL. There has been a case report of a 77-year-old man presenting with acute kidney injury (AKI). Renal biopsy showed patchy B-cell lymphocytic aggregates positive for cyclin D1 associated with diffuse pauci-immune crescentic glomerulonephritis and positive serum PR3-ANCA. His renal function partially improved under cyclophosphamide, vincristine and prednisone.[7]

A case of MCL first presenting as immune complex glomerulonephritis found very similar histological features to our patient.[8] Although the initial presentation of our patient was renal

function degradation in the setting of MCL, the following course was very similar. He was treated with a rituximab, cyclophosphamide, doxorubicin, vincristine and prednisolone (R-CHOP) regimen. Their patient had a normal SCr at a 1-year follow-up.

Another case was reported of a 65-year-old man with a newly diagnosed MCL, presenting with AKI shortly after receiving his first-cycle chemotherapy. Renal biopsy showed crescents with isolated mesangial granular C3 deposition. Genetic testing identified homozygous deletion spanning the CFHR1 and CFHR3 genes. Renal function partially improved under corticosteroid therapy and chemotherapy.[9]

The case of a 77-year-old Japanese man, diagnosed 15 years ago with MCL, presenting with AKI, was also reported. Renal biopsy showed diffuse class IV lupus nephritis associated with interstitial infiltration of MCL cells and serologic tests for lupus were positive (anti-doublestranded DNA antibodies).[10]

An MPGN pattern of injury associated with MCL has also been reported in many cases.[11 12]

Learning points

- Mantle cell lymphoma (MCL) is a rare subtype of non-Hodgkin's lymphoma.
- Glomerulonephritis associated to MCL is rare and its pathophysiological mechanisms are poorly understood.
- The treatment with cyclophosphamide was efficient.

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