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CASE REPORT

Renal Failure with Granulomatous Interstitial Nephritis and Diffuse Leukemic Renal Infiltration in Chronic Lymphocytic Leukemia

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Renal dysfunction is uncommon in patients with leukemic infiltration of the kidney due to Chronic Lymphocytic Leukanemia (CLL). Granulomatous interstitial nephritis (GIN) is also rare, but a characteristic hallmark of certain diseases such as sarcoidosis and tuberculosis. GIN has been associated with medications, infections, inflammation, Wegener's granulomatosis, and jejuno-ileal bypass. GIN combined with leukemic infiltration by CLL is very uncommon.

We present a 72-year-old male with Binet stage A CLL who developed progressive renal failure over a period of four years requiring maintenance dialysis. During the course of his illness, he underwent renal biopsies at different time intervals, revealing varying degrees of involvement by GIN together with leukemic infiltration.

Keywords renal impairment, GIN, CLL

CASE

A 72-year-old male with Binet stage A CLL underwent renal biopsy in view of renal impairment with a gradual increase in serum creatinine from normal to 240 μmol/L. His other medical problems included hypertension, hypercholesterolemia, non-insulin-dependent diabetes mellitus, and peripheral vascular disease. He was on nifedipine, doxazosin, atorvastatin, aspirin, and frusemide.

The first renal biopsy showed that the glomeruli were negative for immunoglobulin and complement components. There was no evidence of an active glomerulonephritis and no active crescents. The collecting tubules contained hyaline casts with some lymphocytic tubulitis. The interstitium showed confluent and diffuse moderate infiltration by lymphocytes, plasma cells, and some eosinophil polymorphs. There were numerous non-necrotizing epithelioid cell granulomata that included epithelioid macrophages and many Langhan's type giant cells (see Figure 1). Special stains for acid alcohol fast bacilli and fungi were negative. Congo red staining for amyloid was also negative. The appearances were consistent with renal infiltration with CLL and concurrent GIN. However, there was no obvious cause for the GIN. His chest CT scan revealed bilateral pleural plaques consistent with previous exposure to asbestos. In addition, there was an extremely smooth and well-defined pleural lesion in the left lower lobe measuring 2.1 cm, a biopsy of which showed inflammatory cells only. The serum ACE was normal. It was felt that the findings were most probably related to renal sarcoidosis; however, there was no conclusive evidence. He was treated with prednisolone and also received six courses of chlorambucil. This treatment was complicated by recurrent

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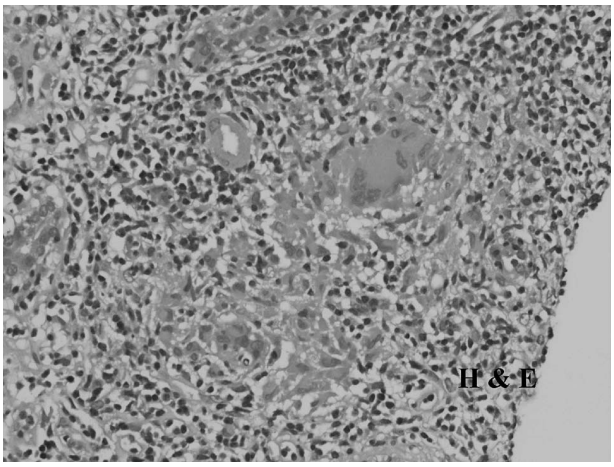

Figure 1. Renal H&E. Renal granulomatous interstitial nephritis.

chest infections needing frequent antibiotics. He was started on replacement therapy with monthly intravenous immunoglobulin in view of hypogammaglobulinemia.

Subsequently, after 2½ years, he had another renal biopsy in view of his creatinine rising from 240 to 540 μmol/L. This renal biopsy again showed confluent areas of florid and destructive lymphocytic tubulitis. The interstitium, in addition to a diffuse, moderate to intense infiltrate of lymphocytes, also showed non-necrotizing epithelioid granulomata with similar features to the previous biopsy. The dense infiltrates of mature lymphocytes stained strongly with CD5, CD20, CD23, CD79a, and BCL-2. The interstitial mononuclear cells, especially those associated with the tubulitis, stained strongly positively with CD3. Moderate numbers of interstitial mononuclear cells together with epithelioid cells within granulomata stained strongly positively for CD68 (PGM1). The features were again suggestive of diffuse and severely active GIN in addition to infiltration of the renal parenchyma by CLL. The predominant cause of parenchymal destruction in this biopsy was GIN. Special stains for acid-alcohol fast bacilli and fungi were again negative. His hematological parameters had remained stable with Hb 14g/L WC 13×10^9/L, lymphocytes 7.7×10^9/L, and platelets 143×10^9/L . He was again treated with steroids.

His renal function continued to deteriorate with creatinine rising further to 860 μmol/L, and he was started on maintenance dialysis. The renal biopsy on this occasion showed that the glomeruli were not enlarged, and several showed mild to moderate ischemic shrinkage and periglomerular fibrosis. Throughout the cortex, there was compression and replacement of tubular elements by a diffuse and moderate-to-intense infiltrate of mononuclear cells. There was no real evidence of tubulitis. There were areas of moderate to considerable tubular atrophy along with moderate arteriolar hyalinosis. Congo red staining for amyloid remained negative. There was no evidence of an active glomerulonephritis or crescents. The glomeruli remained negative for immunoglobulin and complement components. There was diffuse and intense infiltration of mononuclear cells in the renal cortex and peri-capsular adipose tissue by CLL (CD5, CD20, CD23 positive; see Figures 2 and 3). There was no evidence of an active GIN. There was a background of chronic tubulo-interstitial fibrosis, the extent of which was difficult to assess due to the intensity of the leukemic infiltrate. The overall impression was diffuse leukemic infiltration on background of chronic tubulo-interstitial disease.

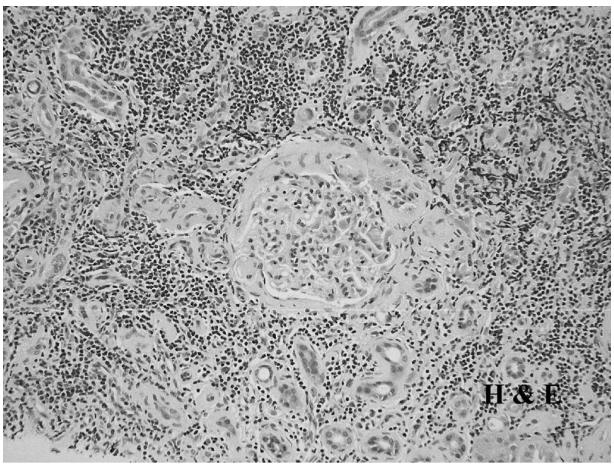

Figure 2. Renal H&E. Diffuse infiltration of the renal cortex by CLL with background of chronic tubulo-interstitial fibrosis.

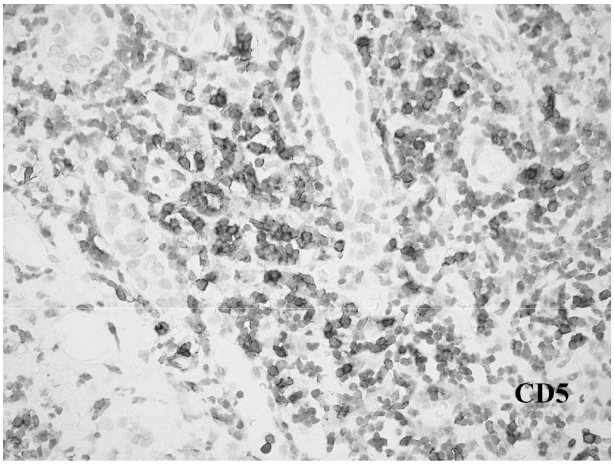

Figure 3. Renal CD5. Diffuse interstitial mononuclear cell infiltrate staining strongly positive with CD5 antibody.

His CT study showed small volume nodes in the cervical region with extensive para-aortic lymphadenopathy, the largest measuring 4.2×2.4 cm, as well as a 4.0×2.4 cm node in the right external iliac region. The liver and spleen were normal in size. Both the kidneys were atrophic. His bone marrow trephine biopsy showed moderate disease bulk CLL with good hemopoiesis. He was started on cyclophosphamide, vincristine, and prednisolone (CVP) chemotherapy and continued on thrice weekly maintenance hemodialysis. However, he died due to sepsis following cellulitis.

DISCUSSION

This patient had varying degrees of involvement with granulomatous interstitial nephritis along with leukemic infiltration at different time intervals. There is only one other case report with both these features, in which bisphosphonate alendronate was implicated.[1]

Interstitial nephritis is common, representing 1–15% of renal biopsies in large reported series; however, GIN is relatively rare, noted in only 0.9–5.9% of biopsies of acute interstitial nephritis.[2–4] Adverse drug reactions are the most frequent cause. The drugs implicated include antibiotics, NSAIDS, diuretics, allopurinol, ACE inhibitors, all-trans retinoic acid, omeprazole and anticonvulsants.[4] Infectious causes such as tuberculosis and inflammatory conditions such as sarcoidosis, Crohn's disease, and Wegener's granulomatosis have been reported.[2]

Leukemic infiltration of kidneys can be seen in 60–90% of patients with CLL as demonstrated on autopsy.[5,6] However, renal dysfunction is uncommon. There have been occasional reports in the literature describing renal dysfunction following leukemic infiltration with CLL.[7–12] The pathogenetic mechanisms contributing to renal dysfunction include uric acid nephropathy, light chain nephropathy, amyloidosis, hypocalcemia, urinary obstruction, glomerulonephritis and cryoglobulinemia.[11] The treatment modalities used in this setting include chemotherapy (with agents such as chlorambucil, cyclophosphamide, steroids) and renal bed irradiation.[8] Patients with CLL are offered chemotherapy if there is evidence of cytopenias, disease-related symptoms, high-grade transformation, or autoimmune complications.

It is uncertain whether our patient's altered immunity along with hypogammaglobulinemia could have predisposed to granuloma formation. The etiology of the GIN in our patient is unclear. Although diuretics are implicated, they were started in our patient only after the onset of renal impairment. Renal sarcoidosis was thought to be the most likely cause though there was no conclusive evidence. There was varying involvement by GIN (predominant earlier in the course of illness) and leukemic infiltration due to CLL (predominant later). This dual pathology resulted in an unrelenting course terminating in end stage renal failure.

REFERENCES

1. Pena de la Vega L, Lager D, Habermann T, Leung N. Acute granulomatous interstitial nephritis secondary to bisphosphonate alendronate sodium. *Renal Failure.* 2005;27:485–489.
2. Mignon F, Mery JP, Mougenot B, Ronco P, Roland J, Morel-Maroger L. Granulomatous interstitial nephritis. *Adv. Nephrol. Necker Hosp.* 1984;13:219–245.
3. Viero RM, Cavallo T. Granulomatous interstitial nephritis. *Human Pathol.* 1995;26(12):1347–1353.
4. Vanhille P, Kleinknecht D, Morel-Maroger L, Kanfer A, Lemaitre V, Mery JP, Callrd P, Dracon M, Laederich J. Drug-induced granulomatous interstitial nephritis. *Proc. Eur. Dial. Transplant Assoc.* 1983;20:646–649.
5. Barcos M, Lane W, Gomez G, et al. An autopsy study of 1206 acute and chronic leukemias (1958 to 1982). *Cancer.* 1987;60:827–837.
6. Schwarrtz J, Shamsuddin A. The effects of leukemic infiltrates in various organs in chronic lymphocytic leukemia. *Hum Pathol.* 1981;12:432–440.
7. Comerma-Coma MI, Sans-Boix A, Tuset-Andujar E, Andreu-Navarro J, Perez-Ruiz A, Naval-Marcos I. Reversible renal failure due to specific infiltration of the kidney in chronic lymphocytic leukemia. *Nephrol Dial Transplant* 1998;13:1550–1552.
8. Phillips JK, Bass PS, Majumdar G, Davies DR, Jones NF, Pearson TC. Renal failure caused by leukemic infiltration in chronic lymphocytic leukemia. *J Clin Pathol.* 1993;46:1131–1133.
9. Tucker B, Brown A, d'Ardenne A, Cattell WR. Reversible renal failure due to renal infiltration and associated tubulointerstitial disease in chronic lymphocytic leukemia. *Nephrol Dial Transplant.* 1990;5:616–618.
10. Pagniez D, Fenaux P, Delvallez L, Dequiedt P, Gosselin B, Tacquet A. Reversible renal failure due to specific infiltration in chronic lymphocytic leukemia. *Am J Med.* 1988;85:579–580.
11. Boudville N, Latham B, Cordingly F, Warr K. Renal failure in a patient with leukemic infiltration of the kidney and polyomavirus infection. *Nephrol Dial Transplant.* 2001;16:1059–1061.
12. Erten N, Saka B, Caliskan YK, Belsisik S, Karan MA, Tascioglu C. Acute renal failure due to leukemic infiltration in chronic lymphocytic leukemia: case report. *International Journal of Clinical Practice.* 2005;59:53–55.