Kidney360

Worsening Kidney Function, Proteinuria, and Hematuria in a Patient with CLL

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Case Description

A 68-year-old woman presented to establish care for chronic lymphocytic leukemia (CLL). Two years prior, she had been diagnosed with Rai stage 0 CLL, after presenting with lymphocyte-predominant leukocytosis. At initial presentation, she complained of occasional Raynaud symptoms. Physical exam was normal. Laboratory measures showed a white-blood-cell count of 24.6 K/mm^3. Other laboratory tests including anti-nuclear antibodies, β2-microglobulin, serum protein electrophoresis, and cryoglobulin screen were all unremarkable. Observation was recommended.

Six months later, she developed hypertension (BPs up to 160s/70s). She was referred to the nephrology department, and workup revealed a serum creatinine of 0.82 mg/dl, unremarkable kidney ultrasound with Doppler, and borderline proteinuria without microscopic hematuria. During this time, her white-blood-cell count increased from 24.6 to 57 K/mm^3, and multiple antihypertensive medications were started. Over the ensuing 3 years, serum creatinine progressively worsened (1.1–1.2 to 1.8–1.9 mg/dl) and BP became more difficult to control, despite medication. Leukocytosis increased further from 101 to 123 K/mm^3, with absolute lymphocyte counts of 91–113 K/mm^3. Urine protein-creatinine ratio had increased from 0.11 to 0.30 and she developed mild, intermittent microscopic hematuria. Complement levels (C3 and C4) were normal and ANCA was negative. Given concern for progressive decline in kidney function, a native kidney biopsy was performed.

Kidney biopsy demonstrated necrotizing arteritis involving one small- to medium-sized artery, with intimal infiltration by both T cells and CLL cells, the latter of which are characterized by CD20-positive B cells with aberrant coexpression of CD5 (Figure 1). There was patchy infiltration by CLL in the interstitium and no evidence of GN or immune complex deposition. Given both the temporal association and direct involvement of CLL cells in the arteritis on the kidney biopsy specimen, ANCA-negative vasculitis was considered most likely due to CLL. The nephrology and hematology services decided to treat with 1 mg/kg per day of prednisone and obinutuzumab, a fully humanized anti-CD20 mAb. The patient completed six cycles of obinutuzumab therapy over 4 months, and prednisone was tapered over 8 months. Serum creatinine had peaked at 2.3 mg/dl, then declined to 1.7 mg/dl, and remained stable for the next 4 years. BP is better controlled on fewer medications, and she has mild proteinuria (urine protein to creatinine ratio of 0.2–0.3 mg/mg) without hematuria. The patient has complete resolution of her lymphocytosis.

CLL is a malignancy characterized by the clonal expansion of mature B lymphocytes; although it can be indolent, many patients require treatment (1). Pathologically, CLL cells are CD20-positive B cells with aberrant coexpression of the T-cell marker CD5; they are light chain restricted and express CD23 without cyclin D1. The anti-CD20 mAb, rituximab, has been widely used in CLL, where it has significantly improved outcomes when combined with chemotherapy. Second-generation anti-CD20 monoclonal antibodies with higher CD20 avidity, including obinutuzumab, have shown promising efficacy (2–4). CLL is associated with a wide spectrum of possible kidney complications, which have been previously described in the literature. The use of obinutuzumab has been reported for CLL in the context of membranoproliferative GN (5); however, to our knowledge, this is the first description of CLL-associated, ANCA-negative extraglomerular vasculitis, with successful treatment of this disease with obinutuzumab and prednisone. In addition to the demonstration of CLL cells within the arteritis, the parallel progression and subsequent improvement support a causal relationship between CLL and ANCA-negative vasculitis in this patient.

Teaching Points

- Inflammatory and noninflammatory kidney diseases are associated with CLL, and can present in an isolated fashion or concurrently.

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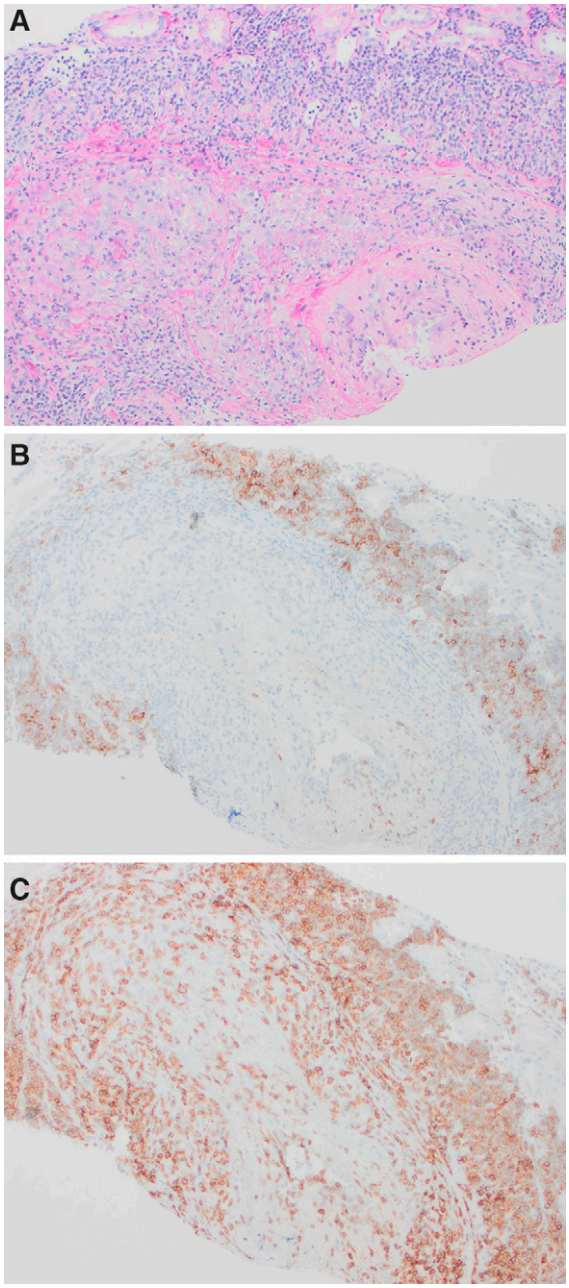

Figure 1. | Necrotizing vasculitis of a small-to medium-sized artery by CLL and T cells. (A) Infiltration of arterial intima and media by lymphocytes, with associated necrosis (Periodic acid-Shiff). (B) The arteritis is composed of an outer rim of neoplastic CD20-positive B cells. (C) The CLL cells are characterized by aberrant coexpression of CD5; also present in the central aspect of the arteritis are T cells which normally express CD5. Original magnification, ×100.

- One such kidney complication of CLL is vasculitis, which can be glomerular or extraglomerular vasculitis.
- Treating the underlying CLL, for example with anti-CD20 antibodies and steroids, can treat both the renal vasculitis and the CLL.

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Author Contribution

N.K. Andeen was responsible for data curation; N.K. Andeen and S.E. Spurgeon reviewed and edited the manuscript; and P. Chopra conceptualized the study and wrote the original draft.

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