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Review

Cryoglobulinemia in a patient with chronic lymphocytic leukemia — A case report and review of literature of renal involvement in CLL

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ABSTRACT

The incidence of glomerulonephritis, as a manifestation of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), has always been considered low. Though renal infiltration is usually detected at post-mortem, it does not often interfere with kidney function [1]. Though immunoglobulin (Ig) levels in most CLL patients are subnormal, small monoclonal Ig peaks are occasionally detected in serum. They were present in a number of reported CLL nephropathy patients, and not all were cryoglobulins; serum and glomerular staining were concordant for Ig type [2,3,4].

Myeloma, which secretes monoclonal light chains, causes nephropathy in 25% of patients. But the little presumably secreted by small plasma cell clones, without myeloma, may also be nephrotoxic. The same is true of the low secretory CLL cells, which may occasionally be associated with cryoglobulins and other nephrotoxic Igs [5].

We report a patient with early stage CLL (Rai stage 0) with cryoglobulins, which led to membranoproliferative glomerulonephritis (MPGN), and death. We located reports of 51 patients with CLL-associated nephrotic syndrome or nephropathy, mostly from MPGN related to local Ig deposits. In those patients screened for cryoglobulins, about half tested positive. Many were early stage cases, where MPGN developed long after CLL presentation, and responded to its treatment. As early diagnosis and treatment CLL-related nephropathy may be curative, we propose a prospective study to determine the incidence of hyperalbuminuria development after presentation.

Contents

1. Case report

A 60 year old, non-diabetic, Afro-Caribbean woman, with a one year history of bilateral lower leg and foot "stasis" lesions (Fig. 1A), presented to our institution with the acute onset of severe abdominal pain and hypotension without trauma. She was a thin, alert woman without

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adenopathy or organomegaly. There was 1 + leg edema, and symmetrical purple leg and foot lesions not suggestive of stasis. WBC was 44 K/μL with 54% normal appearing lymphocytes, Hb 4.4 g/dL, platelets 192 K/μL, MCV 87 fL, Cr 2.2 mg/dL, total protein 3.6 g/dL and albumin 1.6 g/dL. Scanning revealed a large right retroperitoneal hematoma from a ruptured right gonadal artery, which was successfully embolized using contrast-enhanced imaging with Visipaque®. Flow cytometry of the peripheral blood revealed an immunophenotypic pattern consistent with CLL: CD19 +, CD20 +, CD5 ±, CD23 ± , FMC7 +, CD38 + and sIg kappa +. Cytogenetic abnormalities detected by FISH showed deletion of ATM/11q, del 13q and trisomy 12. The patient's CLL was staged as Rai 0. She was hospitalized for one week and at discharge, her Hb was 8.7 g/dL and Cr 1.44 mg/dL. However, she was readmitted after a month with a creatinine of 11.4 mg/dL that was detected on outpatient follow-up. Urine protein was 600 mg/dL and dialysis was initiated. The patient's marked deterioration in renal function on readmission was unlikely from contrast employed for her original angiogram, as this agent is isotonic and its volume minimal.

A new deep necrotic ulcer was found on her right arm (Fig. 1B). Serum protein electrophoresis was negative for monoclonal bands, but an IgG kappa (κ) monoclonal band was found in the urine. Hepatitis A, B, C, CMV and HIV serologies were negative, as were ANA, ANCA and lupus anti-coagulant studies. Renal biopsy revealed MPGN and extensive segmental deposition of intraluminal hyaline material suggestive of cryoglobulin and partially organized thrombi in the large intra-renal arteries (Fig. 2A & B). Hyaline glomerular deposits were strongly positive for IgG and kappa chain, with weak IgM and lambda chain. Fibrin was seen in the mesangium (Fig. 3A–D). C1q was positive and C3 and C4 negative. Some tubules were dilated and occupied by non-fractured hyaline casts. Serum IgGκ cryoglobulin was detected. She remained dialysis-dependent and developed cerebral infarcts of the left occipital and right frontal regions. Plasmapheresis was initiated concurrently with chemotherapy almost a month after admission. The chemotherapy regimen comprised of rituximab, cyclophosphamide, vincristine and prednisone (R-CVP); of which she received a total of three cycles. Aside from reducing her lymphocyte count there was no response. She succumbed to her disease approximately a month after her last chemotherapy and plasmapheresis treatments and almost three months after her second admission.

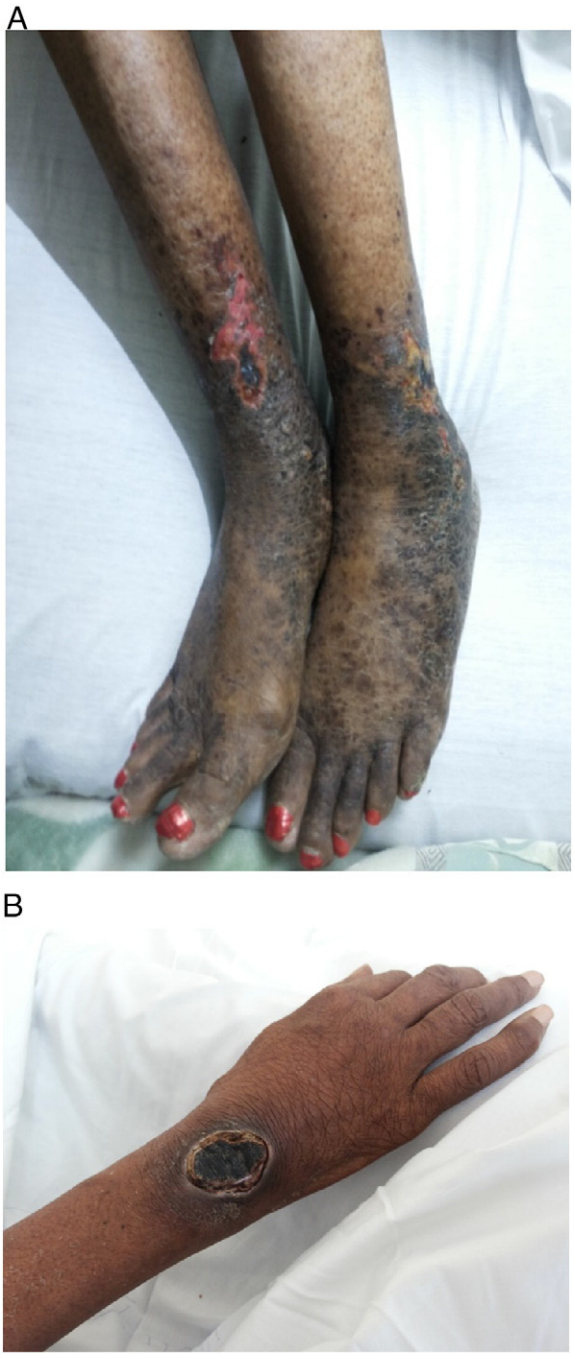

Fig. 1. (A) Bilateral lower extremity "stasis" lesions noted on patient's initial presentation. (B) Deep necrotic ulcer on patient's arm one month later.

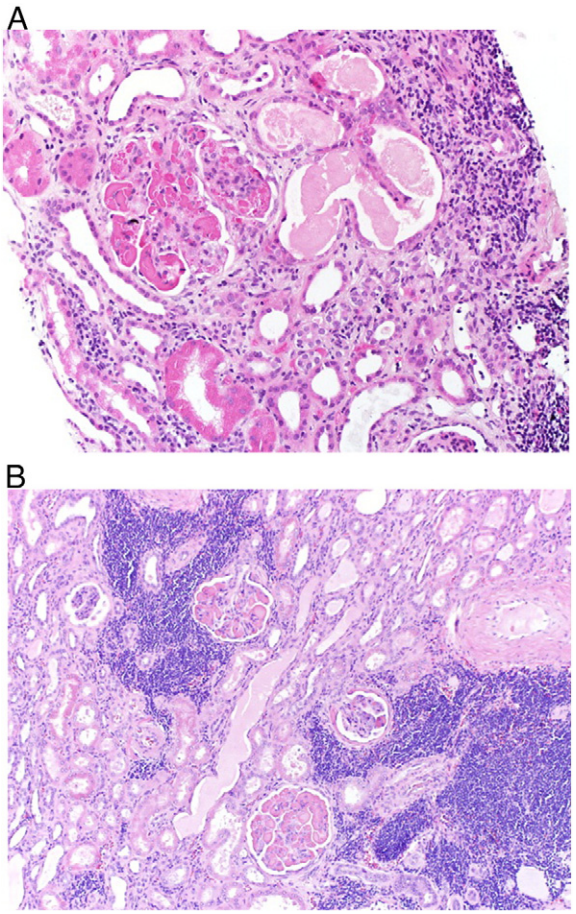

Fig. 2. Renal biopsy revealed MPGN and extensive segmental deposition of intraluminal hyaline material suggestive of cryoglobulin and partially organized thrombi in the large intra-renal arteries.