CASE REPORT

Membranoproliferative Glomerulonephritis Secondary to a Low-Grade Lymphoproliferative Disorder: A Rare Cause of Renal Dysfunction

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Abstract Chronic lymphocytic leukemia is a B-cell neoplasm with an indolent clinical course. Most patients are asymptomatic and are diagnosed incidentally on a routine blood count. The malignant cells of this low-grade neoplasm infiltrate various organs and tissues. However, the resultant end organ damage is a rare phenomenon. Here we describe a case of chronic lymphocytic leukemia that presented with an unusual cause of acute renal dysfunction. The patient had deranged renal parameters with a nephrotic range proteinuria. The uncommon cause for his renal problem was membranoproliferative glomerulonephritis diagnosed by performing a kidney biopsy. Moreover, the acute renal dysfunction in this patient mandated an appropriate treatment and as of now there are no well-established treatment protocols for chronic lymphocytic leukemia with nephrotic syndrome. The patient was successfully treated with rituximab and bendamustine based on the expertise and judgement of the clinician.

Keywords Chronic lymphocytic leukemia · Renal dysfunction · Membranoproliferative glomerulonephritis · Treatment

Introduction

Chronic lymphocytic leukemia (CLL) is a low grade lymphoproliferative neoplasm characterized by the proliferation of monoclonal B lymphocytes in the blood, bone marrow, lymph nodes, and spleen. It is the most common neoplasm in the western world [1]. The leukemic cells infiltrate the lymphoid as well as the extralymphoid tissues and organs, however, despite infiltration of leukemic cells the target organ damage is uncommon. Renal involvement has been described in 63–90 % of all CLL patients who underwent postmortem autopsy [2]. The cause of deranged renal function in CLL could be due to direct invasion by leukemic cells, bulky lymphadenopathy causing pressure symptoms or treatment related tumor lysis syndrome. Rare causes include light chain nephropathy, renal amyloidosis, granulomatous interstitial nephritis, minimal change disease and membranoproliferative glomerulonephritis (MPGN) [3]. We also narrate one such rare cause of acute renal dysfunction in a patient with CLL. The kidney biopsy helped us identify the unusual cause of renal dysfunction to be MPGN which was secondary to the deposition of monoclonal antibodies and light chains by the malignant cells. The patient's condition improved after treatment with rituximab and bendamustine.

Case Report

A 70-year-old man presented with puffiness of face and progressively increasing swelling of both lower limbs for 1 year. His physical examination was remarkable for

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elevated blood pressure of 170/90 mmHg and hepatosplenomegaly. Complete hemogram revealed hemoglobin of 9.4 g/dL, total leucocyte count (TLC) of $127 \times 10^9/L$ and platelet count of $3.9 \times 10^9/L$. The absolute lymphocyte count was $119 \times 10^9/L$. Peripheral blood film (PBF) showed 94 % lymphocytes with 23 % smudge cells (Fig. 1a). Biochemical investigations showed deranged renal function tests (RFT) with a blood urea of 63 mg/dL (range 20–40 mg/dL) and serum creatinine of 2.8 mg/dL (range 0.6–1.2 mg/dL). 24 h urine protein was markedly increased to 11.8 gm/litre. Liver function tests were within normal limits. Ultrasound abdomen confirmed a mild hepatosplenomegaly and renomegaly (right kidney 12.0 cm, left kidney 11.7 cm). A clinical suspicion of a chronic lymphoproliferative disorder presenting with renal failure and nephrotic range proteinuria was kept in mind. Bone marrow examination revealed 51 % lymphocytes with a diffuse pattern of distribution (Fig. 1b). Immunophenotyping by flow cytometry confirmed the diagnosis of CLL with a matutes score of 4/5. Since, no apparent cause for his renal dysfunction could be found a kidney biopsy was performed. It showed MPGN with extensive infiltration by a B cell lymphoproliferative disorder confirmed to be CLL by immunohistochemistry (IHC) (Fig. 2). The patient was categorized into Binet stage C, with renal involvement in form of MPGN. He was started on chemotherapy with rituximab and bendamustine and after 6 cycles, the patient was in complete hematological remission along with normalisation of blood urea and serum creatinine levels and marked improvement in the proteinuria with a well controlled blood pressure.

Discussion

CLL is a low grade B-cell neoplasm of elderly individuals. Most patients have an early-stage (Rai 0 or I) disease and are diagnosed incidentally on a routine hemogram. The symptomatic patients usually have cytopenias,

lymphadenopathy and/or splenomegaly [4]. Rarely, few patients may present with a paraneoplastic syndromes, such as nephrotic syndrome, paraneoplastic pemphigus, or angioedema. The incidence of nephrotic syndrome co-existing with CLL is a rare occurrence. The most frequent glomerular pathology accompanying CLL is MPGN. MPGN can be due to varied number of causes. Less common causes include plasma cell dyscrasias and low grade lymphoproliferative disorders resulting in the production of monoclonal immunoglobulins by a single clone of plasma cells or lymphocytes respectively [5].

Our patient was an elderly person who came to the hospital with generalized anasarca. He was found to have a deranged RFT and lymphocytosis on a routine hemogram. The bone marrow examination together with flow cytometry confirmed a diagnosis of CLL. Kidney biopsy showed infiltration by leukemic cells along with MPGN. He was started with rituximab and bendamustine. On follow up the patient showed marked improvement in hematological and nephrologic parameters. Currently, there are no well-established treatment protocols for CLL patients with accompanying nephrotic syndrome. Immunosuppressive therapy with the use of corticosteroids (alone or in combination with an alkylating agent), thalidomide, fludarabine, bortezomib, mycophenolate mofetil, cyclosporine, cyclophosphamide and rituximab all have been used in patients with variable outcomes [6–8]. At present, the treatment decisions are made purely on the basis of clinical know-how and expertise. Presence of nephrotic range proteinuria should be promptly evaluated by kidney biopsy. Either the infiltration of renal parenchyma or CLL related immunologic/paraneoplastic manifestations in the kidneys should be labeled as target organ damage. These are sufficient triggers to initiate therapy for underlying CLL even in asymptomatic patients.

To conclude, we present a case of an elderly male with CLL with successful treatment of acute renal failure due to leukemic infiltration by malignant CLL cells leading to MPGN. Despite leukemic infiltration being common in

Fig. 1 **a** PBF showing numerous lymphocytes (CLL by flow cytometry) with a few smudge cells or shadow cells of Gumprecht. X400 MGG, **b** bone marrow biopsy showing a diffuse infiltration by CLL. $\times 400$ H&E

Fig. 2 **a** Photomicrograph showing extensive infiltration of renal parenchyma by CLL cells. A preserved glomerulus can also be seen. $\times 200$ H&E, **b** high power view showing these monomorphic small sized lymphoid cells with scant cytoplasm. $\times 400$ H&E, **c**, **d** immunohistochemistry (IHC) panel for antibodies against CD20, CD23 respectively and CD5 (not shown) were positive in these lymphoid cells. $\times 200$

CLL, a detailed evaluation is recommended for patients with deranged renal parameters with no other apparent cause for deterioration. The importance of renal biopsy in appropriate diagnosis cannot be overemphasized in this regard. Also specific data on protocols highlighting treatment strategy of kidney dysfunction in chronic lymphocytic leukemia shows variable outcomes with many drugs, therefore, more studies and research work including drug trials would be extremely beneficial in future for a successful outcome.

Compliance with Ethical Standards

Conflicts of interest None of the authors of this manuscript has conflict of interest in publishing it.

Human and Animal Rights This research does not involve human or animal subject, its merely presentation of a rare entity.

Informed Consent Obtained.

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