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Case Report

Renal Failure due to Direct Infiltration of Chronic Lymphocytic Leukemia: Case report and Review of Treatment

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Abstract

Background: Chronic lymphocytic leukemia (CLL) is a cancer due to the uncontrolled growth and accumulation of mature B lymphocytes in the bone marrow and blood. Asymptomatic kidney involvement of CLL is fairly common but renal failure secondary to CLL is very rare.

Case Presentation: Less than twenty cases of acute renal failure due to the direct CLL infiltration have been reported in the literature. Given the rarity of this complication, there is no standard of care on how these patients' treatment should be approached. We present a case of renal failure in a patient with a longstanding history of CLL.

Conclusion: In order to guide future management, our discussion features a detailed review of the literature with a focus on the various treatment modalities used in this very rare complication.

Keywords: Chronic lymphocytic leukemia; Renal failure; Renal insufficiency; Kidney biopsy; Treatment

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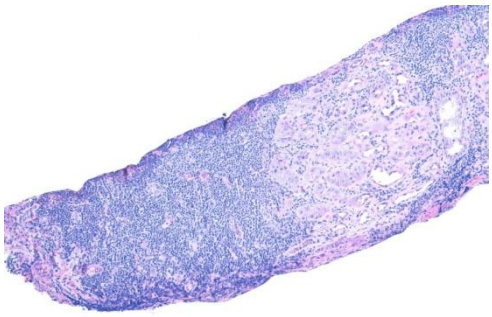
Introduction

Chronic lymphocytic leukemia (CLL) is a cancer due to the uncontrolled growth and accumulation of mature B lymphocytes in the bone marrow and blood. It is the most common form of leukemia in adults with a median age at presentation of 72 years [1]. Many patients are asymptomatic and diagnosed only after a routine blood count reveals an absolute lymphocytosis. Asymptomatic kidney involvement of CLL is fairly common with up to 90% of patients having interstitial infiltration on autopsy [2, 3]. Less than twenty cases of acute renal failure due to direct CLL infiltration without any further pathology have been reported in the literature and many different treatment options have been used with varying responses [4-16].

Case Report

Our case features an 86 year-old African American female with a past medical history of hypertension, type II diabetes mellitus, and CLL diagnosed with stage IV CLL two years prior when she presented with extensive neck, axillary, abdominal, and pelvic lymphadenopathy (LAD). Blood counts done at that time revealed a white blood cell (WBC) count of 64.6 103/μL and flow cytometry on peripheral blood confirmed the diagnosis of CLL. Pt was initially treated with bendamustine which was discontinued after two cycles due to poor compliance with follow up along with poor renal function, creatinine of 1.95 mg/dL. Given her age and other comorbidities the patient was then placed on chlorambucil however the patient was noncompliant with her treatment leading to disease progression and a decline in her performance status. Chlorambucil was discontinued 20 months after the initial diagnosis of her CLL. Presentation to our institution for altered mental status and hypoglycemia was approximately five months after discontinuation of chemotherapy, 25 months after the initial diagnosis of her CLL. Creatinine was found to be 4.2 mg/dL with a baseline around 1.9 mg/dL five months prior. Renal ultrasound was consistent with medical renal disease showing bilateral echogenic appearing kidneys with prominent renal pelvises and trace perinephric fluid. Bilateral kidney size was mildly increased on ultrasound with the right kidney 12.4 x 4.8 x 5.5 cm and left kidney 12.5 x 4.5 x 5.3 cm. Protein electrophoresis with immunofixation of urine and serum did not show any monoclonal protein. Creatinine reached a maximum value of 5.7 mg/dL. Due to the rapid rate of decline in kidney function a renal biopsy was performed which demonstrated dense infiltration of small lymphoid cells consistent with low grade B cell lymphoma as well as some focal segmental glomerulosclerosis [Figure 1-2]. Immunohistochemistry showed positive staining for CD19 [Figure 3] and mild staining for CD3 [Figure 4] whereas CD20, CD5, cyclin D1, and CD10 were negative. Due to a continued poor performance status and declining renal function no chemotherapy was restarted. Two months later creatinine was stable at 4.75 mg/dL. The patient eventually entered hospice care and as lost to follow-up.



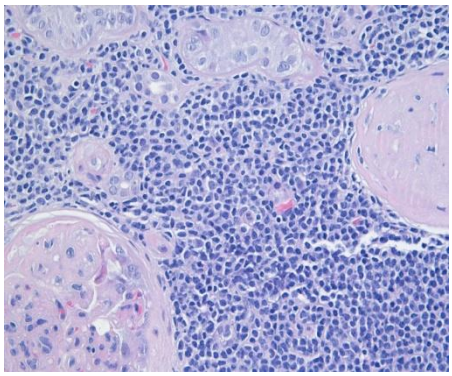
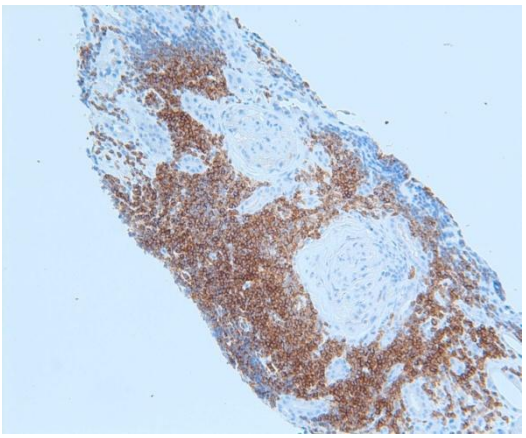


Fig1(left) Low magnification of kidney biopsy demonstrates dense infiltration of small lymphoid cells consistent with low grade B cell lymphoma.

Fig2(right) Higher magnification of kidney biopsy demonstrates dense infiltration of small lymphoid cells consistent with low grade B cell lymphoma as well as some focal segmental glomerulosclerosis.



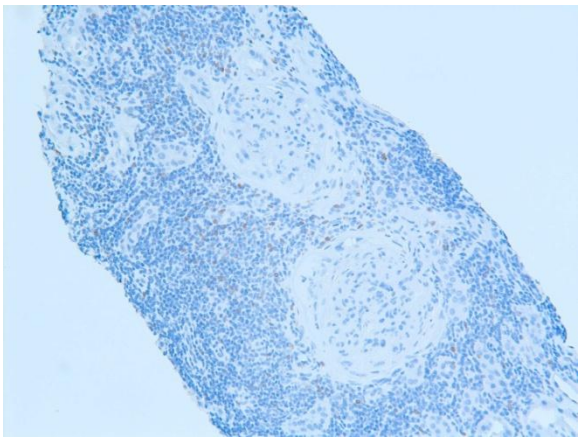


Fig3(left) CD19 staining of kidney biopsy demonstrates dense infiltration of small lymphoid cells consistent with low grade B cell lymphoma. Cells at the edge are artifactually negative.

Fig4(right) CD3 staining of kidney biopsy demonstrates dense infiltration of small lymphoid cells consistent with low grade B cell lymphoma.

Discussion

Renal insufficiency is not uncommon in CLL patients as it can be seen in 7.5% of patients at the time of initial diagnosis and another 16.2% at some time during the disease course [17]. CLL can affect renal function via direct infiltration of B lymphocytes, deposits of immunoglobulin fractions, genitourinary obstruction from abdominal lymphadenopathy, cryoglobulinemia, paraneoplastic processes, and from tumor lysis syndrome with uric acid nephropathy [17-19].

A recent study by Strati et al. found that in CLL patients, the most common reasons for renal biopsy was renal insufficiency in 69% and nephrotic syndrome in 31%. The study showed that the most common findings in those renal biopsies were membranoproliferative glomerulonephrosis (MPGN), CLL infiltration as the primary etiology, and minimal change disease (MCD), respectively. This study had a total of six patients, the largest amount of patients with direct CLL infiltration as the

primary cause of renal failure. Half of the patients (n=3) had a diffuse pattern on renal biopsy affecting >50% of the cortex and the other half (n=3) a focal pattern affecting 20-30% of the cortex. The mechanism of renal failure in these patients was thought to be due to CLL infiltration compressing the renal tubules and microvasculature leading to obstruction and ischemia [6]. Of those six patients, two-thirds had relapsed or refractory CLL. Another study by Da'as et al. evaluated 700 patients with CLL and of those, five had proven renal infiltration but none with renal failure related directly to the leukemic infiltration, further proving the rarity of this disease processes [20].

In total, less than six cases in the literature include renal failure as the initial presentation of CLL [4,9,10,16]. In a report by Rifkin SI [5] it is stated that kidney size on ultrasound is roughly split in half between normal and increased. The most common pattern seen on kidney biopsies was dense interstitial infiltration predominantly in the cortex with many cases having some degree of glomerular fibrosis/sclerosis. One study did however have a more focal infiltration of the kidneys [14]. Most important is the absence of immune complexes in the biopsies making these cases due to direct infiltration of CLL.

As mentioned previously, there is no agreed upon standard of care for the treatment of renal failure secondary to CLL. The combination of the alkylating agent chlorambucil, one of the earliest forms of treatment for CLL, and prednisone was used in three cases [7,10,12]. There was improvement in both the overall disease as well as the renal function but later recurrence of renal failure in one of the cases [10]. Another case showed improved renal function with single agent chlorambucil [13]. The combination regimen of cyclophosphamide, vincristine and prednisone (CVP) has also been used and demonstrated a rapid improvement in renal function and subsequent disease remission [16]. The addition of rituximab to the CVP regimen in two patients with renal failure secondary to CLL produced a long term remission in one patient but the other patient, while there was an initial response to treatment, ultimately relapsed with renal insufficiency again one year later [6]. Cyclophosphamide was used in combination with methylprednisolone with a good response [9] and with fludarabine at which time renal impairment continued [15].

The anti-CD20 monoclonal antibody rituximab was used in multiple different combinations: with methylprednisolone leading to improvement in renal function but recurrence of renal insufficiency at a later time [6], with the purine analog fludarabine and cyclophosphamide with partial remission but no improvement in renal function and continued dialysis [4], with fluderabine and prednisone yielding a partial response [5], and with the purine analog pentostatin and cyclophosphamide without renal improvement but avoidance of dialysis [6]. Another monoclonal antibody against CD20, afatumumab, was used in combination with methylprednisolone yielding significant improvement in renal function but recurrence at a later time [6].

Phillips JK et al [7] showed that the combination of external beam radiation to the renal bed followed by oral chlorambucil and prednisone resulted in substantial improvement in renal function. This is the only known case where external beam radiation therapy was used for renal CLL infiltration.

With the constant flow of new advancements in CLL therapy, it will be interesting to see how the prognosis of this rare complication will change. Given the rarity of this condition it is unlikely there will be a prospective double-blind study to evaluate what the optimal treatment is for patient with renal failure secondary to CLL. Treatment should be individualized with attention on the array of side effects and contraindications of many of these chemotherapeutic medications along with the patient's comorbidities. Recognition of this rare phenomenon is crucial as prompt recognition and intervention may reverse renal damage and recover function. Until now, regardless of the treatment modality, there seems to be a high recurrence rate.

Reference

1. Cashen A, Van Tine BA. Hematology and Oncology Subspecialty Consult. 3rd ed. Philadelphia: ***Lippincott Williams & Wilkins***; c2012. Chapter 29, Chronic Lymphocytic Leukemia; p367-372
2. Barcos M, Lane W, Gomez GA, et al. An autopsy study of 1206 acute and chronic leukemias (1958 to 1982). ***Cancer.*** 1987, 60(4):827-837
3. Schwartz JB, Shamsuddin AM. The effects of leukemic infiltrates in various organs in chronic lymphocytic leukemia. ***Human Pathol.*** 1981, 12:432-440
4. Uprety D, Peterson A, Shah BK. Renal failure secondary to leukemic infiltration of kidneys in CLL- a case report and review of literature. ***Ann Hematol.*** 2013, 92(2):271-273
5. Rifkin SI. Acute renal failure secondary to chronic lymphocytic leukemia: a case report. ***Medscape J Med.*** 2008, 10(3):67
6. Strati P, Nasr S, Leung N, et al. Renal complications in chronic lymphocytic leukemia and monoclonal b-cell lymphocytosis: the mayo clinic experience. **Haematologica.** 2015, 100(9):1180-1188
7. Phillips JK, Bass PS, Majumdar G, et al. Renal failure caused by leukemic infiltration in chronic lymphocytic leukemia. ***J Clin Pathol.*** 1993, 42(12):1131-1133
8. Rockx MA, Rizkalla K, Clark WF. Acute renal failure and chronic lymphocytic leukaemia. *Nephrol Dial Transplant.* 2008;23:770-771.
9. Erten N, Saka B, Caliskan YK, et al. Acute renal failure due to leukaemic infiltration in chronic lymphocytic leukemia: case report. ***Int J Clin Pract.*** 2005, 59(suppl 147):53-55
10. Hewamana S, Pepper C, Jenkins C, et al. Acute renal failure as the presenting feature of leukaemic infiltration in chronic lymphocytic leukaemia. ***Clin and Exp Nephrol.*** 2009, 13(2):179-181
11. Boudville N, Latham B, Cordingly F, et al. Renal failure in a patient with leukaemic infiltration of the kidney and polyomavirus infection. ***Nephrol Dial Transplant.*** 2001, 16(5):1059-1061
12. Comerma-Coma MI, Sans-Biox A, Tuset-Andujar E, et al. Reversible renal failure due to specific infiltration of the kidney in chronic lymphocytic leukaemia. ***Nephrol Dial Transplant.*** 1998, 13:1550-1552
13. Junglee NA, Shrikanth S, Seale JR. Rapidly progressive renal failure due to chronic lymphocytic leukemia- response to chlorambucil. ***Indian J Nephrol.*** 2012, 22(3):217-220
14. Aymard B, Beghoura R, Molina TJ. Renal infiltrate by a plasmocytoid chronic B lymphocytic leukemia and renal failure: a rare occurrence in nephropathology. A case report and review of the literature. ***Nephrologie & Therapeutigue.*** 2011, 7(6):479-487
15. Ferreira AC, Brum S, Carvalho D, et al. Renal dysfunction due to leukemic infiltration of kidneys in a case of chronic lymphocytic leukemia. ***Hemodialysis International.*** 2010, 14(1):87-90
16. Haraldsdottir V, Haanen C, Jordans JGM. Chronic lymphocytic leukaemia presenting as renal failure with lymphocytic infiltration of the kidneys. ***Neth J Med.*** 1992, 41:64-67
17. Shanafelt TD, Rabe KG, Hanson CA, et al. Renal disease in patients with chronic lymphocytic leukemia (CLL). ***Blood.*** 2013, 122(21):5302
18. Jourde-Chiche N, Dussol B, Daniel L. Kidney involvement in malignant hematologic malignancies: diagnostic approach. ***Revue de Medecine Interne.*** 2010, 31(10):685-696
19. Davidson MB, Thakkar S, Hix JK, et al. Pathophysiology, clinical consequences, and treatment of tumor lysis syndrome. ***Am J Med.*** 2004, 116(8):546-554

20. Da'as N, Polliack A, Cohen Y, et al. Kidney involvement and renal manifestations in non-Hodgkin's lymphoma and lymphocytic leukemia: a retrospective study in 700 patients. ***Eur J Haematol.*** 2001, 67:158-164