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# Bone Marrow and Kidney Findings at Odds: A Case Report and Review of Literature of Divergent Pathology in Chronic Myeloid Leukemia

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## Abstract

Chronic myeloid leukemia (CML) is a hematologic malignancy driven by the *BCR-ABL1* fusion gene, which results in the abnormal proliferation of myeloid cells. The disease typically has two phases: chronic (CP) and blast crisis (BC). Extramedullary blast crisis (EBC) in CML refers to the presence of blast cells in extramedullary sites, irrespective of the blast proliferation occurring in the bone marrow. Renal infiltration of blasts as the initial presentation of CML is exceedingly rare. We present a case of a 51-year-old man with renal failure. Renal biopsy showed myeloperoxidase staining blasts, with bone marrow in CP. Based on the presence of EBC, the patient was diagnosed with CML in BC, despite the CP in the bone marrow, a rare occurrence that challenges conventional diagnostic pathways.

**Keywords**

- acute kidney injury
- blast phase
- chronic myeloid leukemia
- chronic phase
- extramedullary blast crisis
- tyrosine kinase inhibitors

## Introduction

Chronic myeloid leukemia (CML) is a hematologic malignancy driven by the *BCR-ABL1* fusion gene, which results in the abnormal proliferation of myeloid cells. The disease typically has two phases: chronic (CP) and blast crisis (BC), with most patients initially presenting in the CP, characterized by a relatively stable clinical course. However, progression to BC can occur, characterized by ≥20% blasts in peripheral blood or bone marrow.[1]

Extramedullary blast crisis (EBC) in CML refers to the presence of blast cells in extramedullary sites, irrespective of the blast proliferation occurring in the bone marrow. Extramedullary involvement, particularly in the kidneys, is a rare and under-recognized phenomenon.[2,3] This case report highlights a unique presentation of CML in BC, with renal involvement, despite the bone marrow remaining in the CP. Such a clinical scenario is uncommon and challenges our understanding of the systemic effects of CML. This case emphasizes the importance of considering renal dysfunction in patients with CML due to leukemic infiltration, even in the CP or during BC, and the complexities involved in managing such atypical presentations.

## Case Report

- A 51-year-old man, with no prior comorbid conditions, presented with a 1-month history of decreased urine output, abdominal discomfort, and bilateral lower limb

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swelling up to the knee. His medical and family history were unremarkable. On examination, he exhibited pallor, pedal edema, and splenomegaly.

A complete hemogram revealed significant abnormalities: hemoglobin of 8.2 g/dL, total leukocyte count of 243,000/µL with a left shift, and a platelet count of 800,000/µL. Severe renal impairment was noted, with urea of 175 mg/dL and serum creatinine of 11.5 mg/dL. Lactate dehydrogenase was elevated at 350 U/L, but other parameters (uric acid, potassium, phosphate, and calcium) were normal. Due to fluid overload, the patient required hemodialysis after a nephrology consultation. Bone marrow aspiration and biopsy showed overwhelming leukocytosis with a myeloid left shift and 4% blasts, consistent with CML in CP (►**Fig. 1**). Reverse transcription polymerase chain reaction for *BCR-ABL1* confirmed the presence of the p210 transcript, and no tyrosine kinase domain mutations were detected. An ultrasound of the abdomen revealed enlarged kidneys with grade 2 renal parenchymal changes. Given the rarity of renal failure in CP CML, a renal biopsy has been performed under the nephrology team to exclude other coexisting etiologies contributing to the renal dysfunction. The kidney biopsy showed interstitial infiltration composed of myeloid precursors, eosinophils, and large atypical cells, staining positive for myeloperoxidase and Cluster of Differentiation 34 on immunohistochemistry. This was suggestive of direct infiltration of renal parenchyma by the blast cells. Patient is diagnosed with myeloid BC (►**Figs. 2**–**4**).

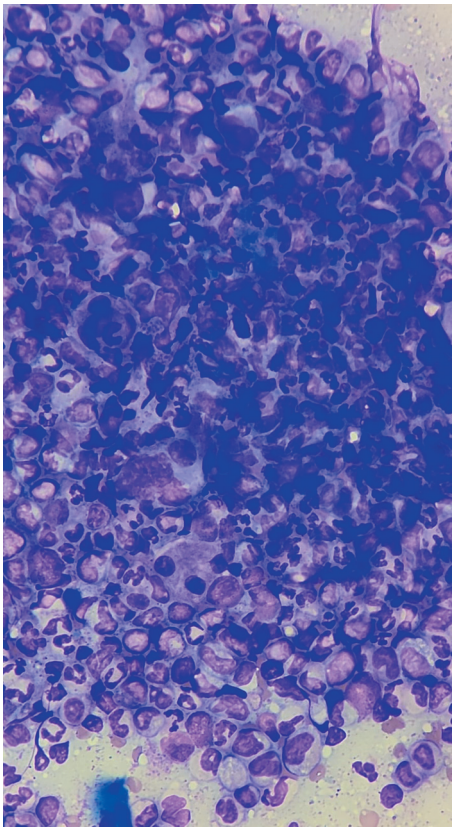

**Fig. 1** Bone marrow aspirate showing overwhelming leucocytosis with myeloid left shift.

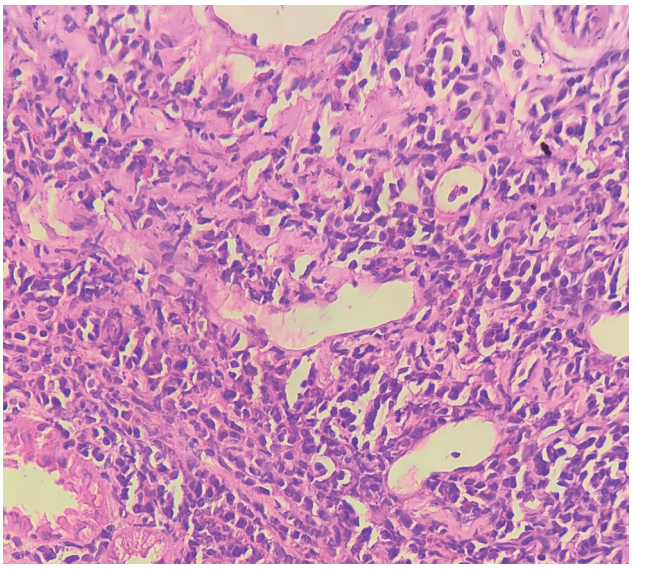

**Fig. 2** Renal interstitium showing dense infiltrate composed of myeloid precursors, eosinophils, and large atypical cells.

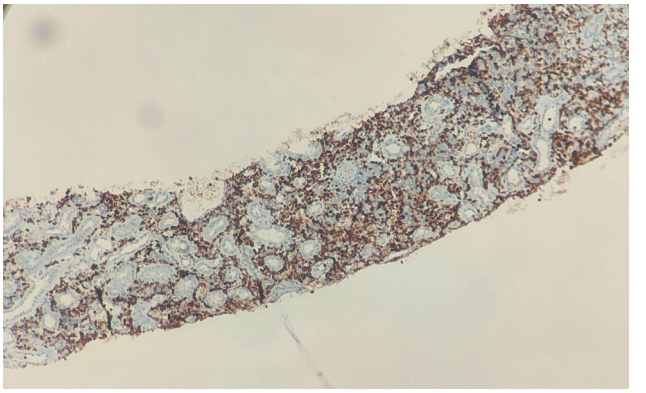

**Fig. 3** Immunohistochemistry with MPO highlights myeloid precursors. MPO, myeloperoxidase.

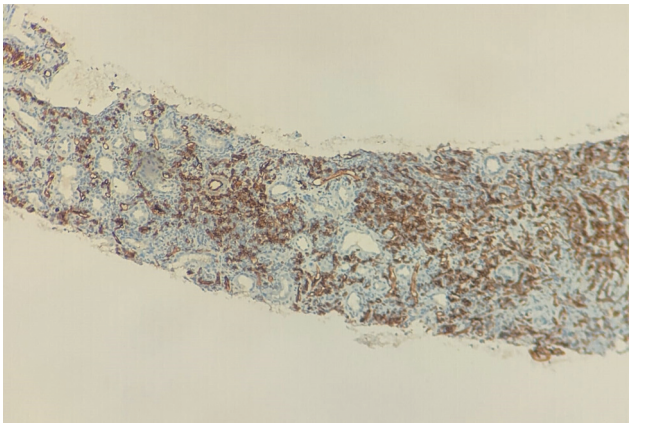

**Fig. 4** CD34 staining highlights the large atypical cells. CD34, Cluster of Differentiation 34.

 

The patient was started on tablet dasatinib 140 mg daily, with no chemotherapy. Within 3 weeks, the white blood cell count significantly declined, and renal function improved, allowing discontinuation of dialysis. Serum creatinine reduced to 0.3 mg/dL, and the renal parenchyma showed a normal echotexture on the repeat ultrasonogram, suggesting renal recovery. At 3 weeks, the patient achieved complete hematological remission. At 3 months, the *BCR-ABL1* transcript percentage (International Scale) was 15.8%, and he continues on dasatinib therapy with regular monitoring.

## Discussion

BC in CML can either be medullary or extramedullary. The lineage of the blasts can be myeloid, lymphoid, or mixed.[2] Isolated EBC with the bone marrow in CP is uncommon. Extramedullary disease can occur either as a part of a frank BC or as a predecessor of an impending BC. EBC is, after a few months, almost always followed by hematological BC, so it is considered to be an early sign of BC in the bone marrow.[3]

EBC in CML most frequently involves the lymph nodes, bones, skin, and central nervous system (CNS).[4] Two large series on EBC were reported by Inverardi et al and Specchia et al. Inverardi et al identified the bone (57%) as the most commonly involved site, followed by lymph nodes (29%), whereas Specchia et al found lymph node involvement in 86% of cases, making it the predominant site in their cohort.[3,5] These sites often present with palpable masses, neurological symptoms, or localized pain, which make diagnosis relatively straightforward. Literature on the involvement of sites other than these is lacking. Renal EBC is exceedingly rare and presents atypically, often mimicking primary renal disease rather than an extramedullary leukemic manifestation.[6] Consequently, diagnosis may only occur after significant organ damage, as in our patient who presented with severe renal dysfunction requiring dialysis. Renal biopsy was critical for diagnosis and should be considered in similar cases where unexplained renal failure occurs in CML patients.[6]

Unlike lymph nodes and CNS, which serve as common extramedullary niches for leukemic infiltration, the kidneys have limited lymphoid tissue and a unique microvascular environment, which may explain their infrequent involvement.[7] When renal EBC occurs, it can lead to acute kidney injury (AKI), requiring urgent dialysis, as seen in our case, whereas other sites typically do not cause acute organ failure.[2]

Another key distinction is treatment response. While CNS or lymph node involvement often necessitates intrathecal chemotherapy or radiation, renal EBC in our patient responded rapidly to systemic tyrosine kinase inhibitor (TKI) therapy, suggesting a potential reversibility of leukemic infiltration in the kidneys.[8–13] Given the rarity of renal EBC, clinicians should maintain a high index of suspicion in CML patients with unexplained renal dysfunction, as timely diagnosis and treatment can lead to significant renal recovery.

Few reports have described renal involvement in EBC. A case of AKI due to isolated renal BC while on treatment with imatinib has been reported by Yuzawa et al. Bone marrow examination revealed a Philadelphia chromosome, but there was no evidence of blasts.[6] In contrast, our patient presented with biopsy-confirmed renal EBC at initial diagnosis, responding rapidly to dasatinib monotherapy.

Gao et al have reported lymph nodal involvement with myeloid and T-cell lineage blasts, with marrow in CP of CML. The patient had been treated with chemotherapy and TKI therapy, and the patient had a myeloid blast-positive CNS relapse post 5 months of treatment.[14]

Treatment of BC CML typically involves a TKI combined with lineage-specific chemotherapy, aiming to induce remission and return to CP. Imatinib, dasatinib, nilotinib, and ponatinib have received approval from both the Food and Drug Administration and EMA for use in all phases of CML, including BC. Cytopenias may need TKI dose reduction or treatment interruption, along with the support of blood products and growth factors.[8]

The preferred treatment approach for myeloid BC typically involves the administration of a TKI, either alone or in combination with chemotherapy, followed by allogeneic hematopoietic stem cell transplantation. Research suggests that when managing de novo myeloid BC, initiating treatment with a TKI and subsequently evaluating the patient's response is advised. In cases where myeloid BC arises during ongoing TKI therapy, the recommended approach is to administer acute myeloid leukemia (AML)-type induction chemotherapy alongside a more potent TKI for improved outcomes.[7,8]

Patients who present with or progress to the blast phase (BP) of CML generally have poor long-term outcomes, even with current TKIs.[15] Achieving initial disease control should be followed by prompt consideration of allogeneic stem cell transplantation (allo-SCT), as this remains the most effective curative option. Evidence suggests that patients who achieve a second chronic phase (CP2) prior to transplantation experience significantly better outcomes.[16,17]

Combining a TKI with acute leukemia-directed chemotherapy—whether AML-based or acute lymphoblastic leukemia–based regimens—has been shown to enhance the likelihood of attaining CP2. The selection of a TKI should take into account prior treatment history and *BCR-ABL1* kinase domain mutation status. Once CP2 is achieved, transplantation should be pursued without delay, as progression-free survival in BP remains limited, and timely transplant plays a pivotal role in prognosis.[18] Importantly, proceeding to allo-SCT during the overt BP is generally discouraged due to inferior outcomes. Consolidation chemotherapy and TKI maintenance are recommended for patients who are not candidates for allogenic hematopoietic cell transplantation. TKI + steroids is appropriate for patients with lymphoid BC, and TKI alone is an option for those with myeloid BC, in these patients.[16,19]

To the best of our knowledge, this is the first case of EBC involving the kidneys with marrow in CP. The diagnosis was confirmed via histopathology, and the patient showed significant clinical and biochemical recovery with dasatinib alone. However, the report is limited by the lack of cytogenetics of the blast cells and a short follow-up period. Given

 

the rarity of renal EBC, this report contributes valuable insight, but larger studies are needed to determine its pathogenesis, prognostic implications, and optimal management strategies. Future studies should also explore why certain tissues serve as EBC sites and whether specific blast lineages influence tissue tropism.

## Conclusion

Our case highlights the need for vigilance in CML patients presenting with unexplained renal dysfunction. Unlike typical EBC in CML, which frequently involves lymph nodes, bones, and CNS, renal EBC is a rare but clinically significant entity that may not be accompanied by medullary BC. Given its potential to cause AKI, prompt biopsy and early TKI initiation can lead to substantial renal recovery. Clinicians should consider renal EBC in patients with CML and unexplained renal impairment, even when bone marrow findings suggest a CP.

### Patient's Consent

Informed consent has been taken by the patient.

### Funding

None.

### Conflict of Interest

None declared.

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