Urology Case Reports 2 (2014) 183–185

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

Renal Bleeding Due to Extramedullary Hematopoiesis in a Patient With Chronic Myelogenous Leukemia☆

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ARTICLE INFO

Article history:
Received 5 August 2014
Accepted 7 August 2014
Available online 6 September 2014

Keywords:
Chronic myelogenous leukemia
Extra-medullary hematopoiesis
Hematuria
Renal infiltration

ABSTRACT

Chronic myelogenous leukemia (CML) is a myeloproliferative disorder that normally presents in middle-aged adults. Renal infiltration and extramedullary hematopoiesis in renal tissue has been rarely reported. This case report presents a patient with CML and renal insufficiency who developed gross hematuria. Efforts at controlling the hematuria led to a cascade of events propelled by the underlying disorder that ultimately led to a radical nephrectomy, multiorgan failure, and prolonged hospitalization. We suggest that management of gross hematuria in clinically stable patients with CML, suspected of having extramedullary hematopoiesis, should prioritize treatment of the myeloproliferative disorder over efforts to control bleeding.

Introduction

Chronic myelogenous leukemia (CML) is a myeloproliferative triphasic disorder characterized by the hyperplasia of fairly differentiated granulocytic cells that normally presents in middle-aged adults. Clinical manifestations of CML common to all phases of the disorder include abnormal routine blood tests, constitutional symptoms of fatigue and weight loss, abdominal pain, and abnormal bleeding episodes. CML has variable clinical presentations and prognosis depending on disease phase and time of diagnosis.[1] Renal involvement and extramedullary hematopoiesis associated with CML are rare but have been reported.[2-4]

Case presentation

A 53-year-old African-American man with a history of peptic ulcer disease, anxiety, renal insufficiency (baseline creatinine level, 1.7 mg/dL) was admitted for gross hematuria and left flank pain. He works as a mechanic, is married, and was a former smoker. His family history is significant for prostate cancer and high blood pressure. He was recently diagnosed with CML during an admission for weight loss, easy bruising, and fatigue. A bone marrow biopsy showed hyperplastic granulocytes with a maturation pattern consistent with CML. Further genetic analysis showed cells with a translocation between chromosomes 9 and 22, the genetic hallmark of CML. The cells were also positive for the genetic product of the translocation, a defective or deregulated tyrosine kinase, also known as the BCR-ABL protein, which is essential to the pathogenesis of the disorder. During that admission, he developed hematuria and bloody stools. A computed tomography scan of his abdomen and pelvis showed mild left hydronephrosis without obvious mass or stone, and his hematuria resolved. His gastrointestinal bleeding work-up included an esophagogastroduodenoscopy and colonoscopy. Several polypectomies resulted in prolonged bleeding, which ultimately resolved.

Before definitive treatment for his CML could be started, he again developed hematuria with mild left flank pain. Upper tract imaging was negative for an overt renal mass, and a cystoscopy found gross blood from the left ureteral orifice (Fig. 1). Ureteroscopy was performed, but no obvious cause of bleeding was found. Cytology showed left renal pelvis urine abundant in acute and chronic inflammatory cells with no evidence of malignancy.

Because of persistent bleeding without a treatable source, the patient was sent to interventional radiology for an angiography examination. A pseudoaneurysm was noted in the left renal artery at a small branch in the lower pole, and it was subsequently embolized (Fig. 2). The patient's bleeding stopped and his hematocrit remained stable until 2 days later when he became hypotensive because of sudden blood volume loss. He required vasopressors and intensive care admission. A repeat arteriogram revealed a site of bleeding into the retroperitoneum remote from the initial embolization (Fig. 3A). The patient continued to have hemodynamic instability and continued blood loss (Fig. 3B). Ultimately, he was taken for an emergent left nephrectomy (Fig. 4).

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http://dx.doi.org/10.1016/j.eucr.2014.08.001

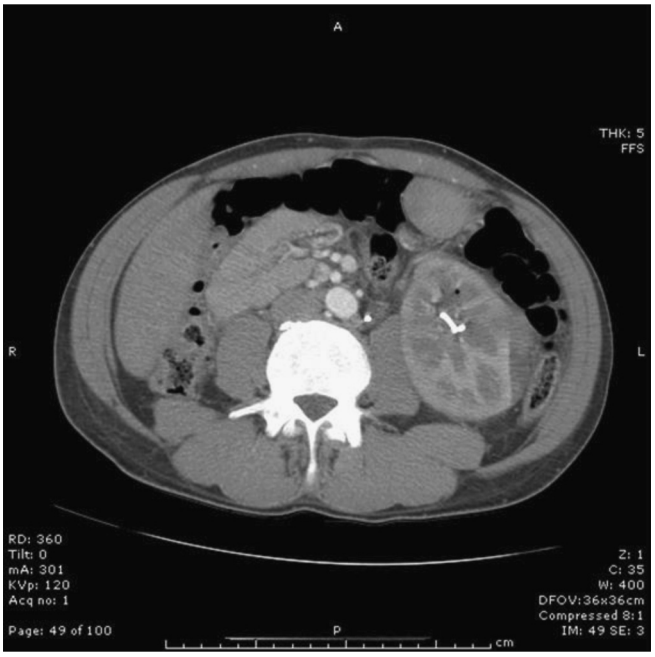

Figure 1. Computed tomography scan (October 11, 2013) showing fluid in the left collecting system with no obvious mass or stone.

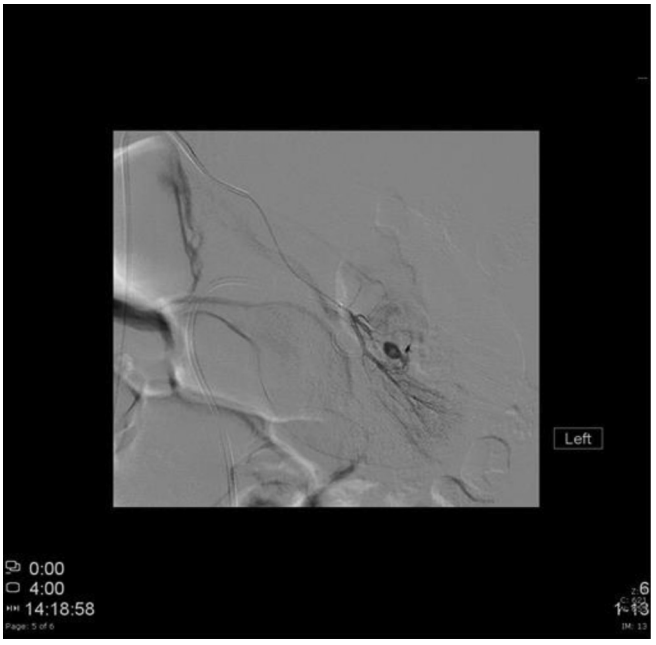

Figure 2. Angiogram (October 11, 2013) showing a pseudoaneurysm in the left renal artery at a small branch in the lower pole. It was subsequently embolized through interventional radiology.

Final pathology of the removed kidney, several days later, showed CML infiltration with diffuse extramedullary hematopoiesis.

Postoperatively, the patient required prolonged respiratory support and hemodialysis. Hydroxyurea and colchicine were initiated to control the patient's leukocytosis and tumor lysis syndrome. He experienced 2 episodes of cardiac arrest and required prolonged vasopressor support. He was started on imatinib, a tyrosine kinase inhibitor, which has been shown to be an effective targeted therapy for CML. Fortunately, his condition improved and he was discharged on hospital day 71 on hemodialysis.

Discussion

Our patient presented with documented CML and gross hematuria of unknown source. The initial differential included infiltration of CML, urinary malignancy, infection, and nephritis. A review of the literature allowed us to have the foresight to put CML infiltration high on our differential for the source of the spontaneous bleed. Although rare, a CML infiltrated kidney has been reported by Hyams et al[2] to present exactly like our patient. In their 2009 case report, their patient diagnosed with a myelomonocytic variant of CML, presented with spontaneous gross hematuria that cleared and then reappeared with no major findings on cystoureteroscopy, much like our patient. Their patient also carried the necessity of nephrectomy owing to continued bleed. Pathology showed CML infiltrate and extramedullary hematopoiesis of the removed kidney, also much like our patient.

Important to the clinical case was the patient's hemodynamic stability despite the gross hematuria. His kidney clearly did not respond well to embolization. It is highly possible that the CML infiltration made the kidney less likely to deal with postinfarction changes within the kidney and made it more susceptible to a major

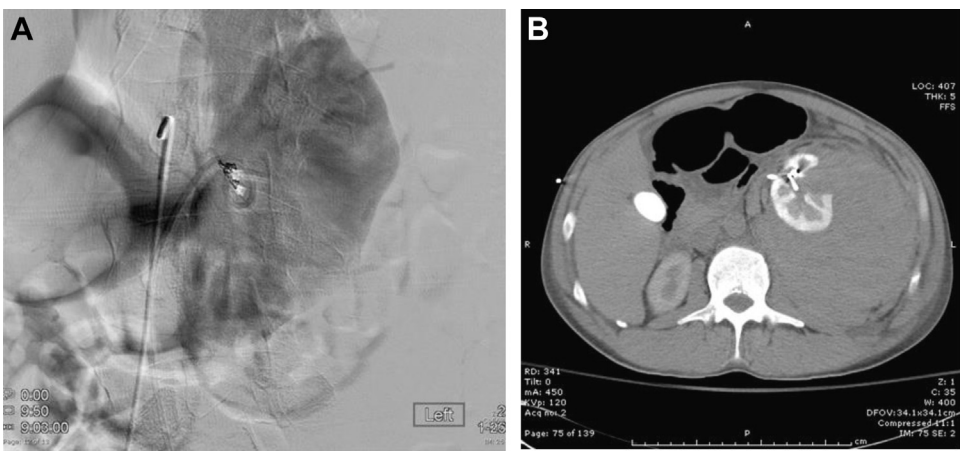

Figure 3. **(A)** Angiography (October 13, 2013) and second interventional radiology (IR) embolization. A second IR embolization was performed on the anterior segment of the left renal artery and interlobular artery using multiple 3-mm coils. The patient continued to bleed. **(B)**. Computed tomography scan (October 13, 2013) showing an increase in retroperitoneal hematoma emerging from the left kidney.

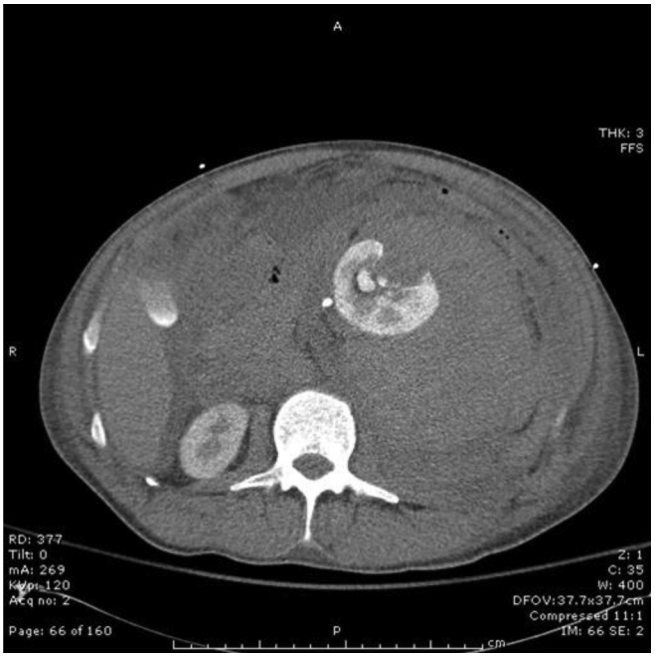

Figure 4. Computed tomography scan (October 15, 2013) showing continued blood loss. An emergent nephrectomy had to be performed.

bleed. Our experience and the literature support treatment of the underlying CML as the best course to prevent spontaneous bleeds in CML patients.[2,5] CML has been associated with both disseminated intravascular coagulation and defects in thrombopoiesis that may leave patients vulnerable to bleeding, despite a normal international normalized ratio, prothrombin time, and partial thromboplastin time.[2,5] Our patient continued to experience bleeding complications postoperatively, and it is our belief that he may have fared better if he had been able to start chemotherapy before instrumentation during cystoureteroscopy and subsequent interventional radiology procedures. These small interventions may have precipitated further bleeding events because of exacerbation of underlying coagulopathy related to intrinsic platelet dysfunction.[2]

Conclusion

In retrospect, as soon as urethrothelial malignancy was ruled out as the cause of hematuria in this patient, it is possible that definitive treatment for his underlying CML should have superseded our desire to stop his otherwise asymptomatic left renal bleeding.

Conflict of interest

Auxilium Pharmaceuticals and Eli Lilly and Company.

Acknowledgment

The authors thank Dr. Sandeep Mistry, M.D., Clinical Assistant Professor, Department of Surgery, Texas A&M College of Medicine for his contribution.

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