Case Report

Renal Vein Thrombosis as Presentation of Non-M3 Acute Myeloid Leukemia in an Adult Patient

Abstract

A 46-year-old male presented with left flank pain and was found to have left nephromegaly with renal vein and inferior vena cava (IVC) thrombus. On hematological evaluation, he had leukocytosis and thrombocytopenia. Further evaluation revealed acute myeloid leukemia (AML). Following initial cytoreductive therapy and supportive care for hyperleukocytosis, he underwent left simple nephrectomy with IVC thrombectomy. Postoperatively, he developed massive thrombosis of infrahepatic IVC with renal failure. Renal venous thrombosis as a rare presentation of AML in adults with leukemic hyperleukocytosis has not been reported. In the absence of clear guidelines, early diagnosis and management are desirable.

Keywords: *Acute myeloid leukemia, renal vein thrombus, thrombectomy*

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Introduction

Leukemic hyperleukocytosis is defined as total leukocyte count (TLC) >100 × 10^9/L. In acute myeloid leukemia (AML), leukocytosis is entirely composed of blasts in most cases. Although the TLC is usually higher in acute lymphoblastic leukemia (ALL), patients with AML are more likely to have serious complications and organ dysfunction related to high white blood cell (WBC) count.[1]

The majority of catastrophic blast cell aggregations and thrombus formation involve the central nervous system and the pulmonary circulation. Renal vein thrombosis (RVT) with leukemic hyperleukocytosis in AML has been reported in 17-month-old child by Murray *et al*.,[2] but RVT as a presentation of AML in an adult has not been reported previously.

Case Report

A 46-year-old male without any known comorbidity presented with left flank pain and vomiting for 15 days. He also had intermittent fever for the past 1 week, but there was no hematuria, history of passage of stones, or lower urinary tract symptoms. On examination, the patient had fever (104°F) and tachycardia (110/min). The left flank was tender, and an ill-defined lump was palpable in the left flank. Ultrasonography done elsewhere revealed left nephromegaly, and the patient was referred to us with a provisional diagnosis of acute left pyelonephritis. Blood reports showed anemia (Hb 6.7 g/dL), leukocytosis (TLC 181 × 10^9/L), and thrombocytopenia (9 × 10^9/L). Serum creatinine was 0.6 mg/dl (normal: <1.4 mg/dL). He was further evaluated with contrast-enhanced computed tomography of the abdomen which was suggestive of non enhancing left kidney with filling defect in the renal vein [Figure 1]. Prothrombin time, activated partial thromboplastin time, thrombin time (TT), and plasma fibrinogen levels were normal. Peripheral smear examination showed blast cells. A subsequent bone marrow examination confirmed the diagnosis of an AML French–American–British (FAB) M1 [Figure 2]. Myeloblasts were 90%, with fine chromatin, 1–2 prominent nucleoli, and Auer rods. Flow cytometry showed AML with expression of CD13–25%, CD14, CD33–99%, CD117–41%, cytoplasmic myeloperoxidase–78%, negative for CD34 and human leukocyte antigen-antigen DR. In view of severe thrombocytopenia and hyperleukocytosis, nephrectomy was initially deferred. A cytoreductive therapy (hydroxyurea and cytarabine) was given for hyperleukocytosis along with adequate hydration, platelets, and appropriate antibiotics prophylaxis. Further evaluation with magnetic

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resonance imaging (MRI) showed RVT extending into inferior vena cava (IVC) for 2 cm with partial occlusion of IVC lumen. Heparin could not be started in view of persistent low platelets count. The TLC decreased to 60 × 10^9/L after 4 days of cytoreductive therapy. Tc-99m Diethylenetriaminepentaacetic acid scan revealed a nonvisualized left kidney. After platelet transfusion (single donor apheresis), the patient underwent left simple nephrectomy with IVC thrombectomy. Intraoperatively, a hard thrombus was present completely occluding the renal vein and extending into the IVC lumen for 2 cm [Figure 3]. He had satisfactory immediate postoperative recovery with adequate urine output till the 3rd postoperative day, and serum creatinine was 0.7 mg/dL. On the 4th postoperative day, there was sudden fall in urine output with mild swelling of the bilateral lower limb. His TLC was 39 × 10^9/L, platelet count was 20 × 10^9/L, and serum creatinine was 1.8 mg/dL. Lower limb Doppler showed no evidence of deep venous thrombosis. On the next day, limb swelling increased, urine output decreased, and serum creatinine rose to 2.1 mg/dL. Abdominal MRI showed extensive thrombosis of bilateral common iliac veins and infrahepatic IVC [Figure 4]. He was started on unfractionated heparin (UFH) as desperate measure in spite of low platelets. Hemodialysis was done for acute renal failure on the 6th postoperative day. The patient developed sudden cardiac arrest on the following day and could not be revived.

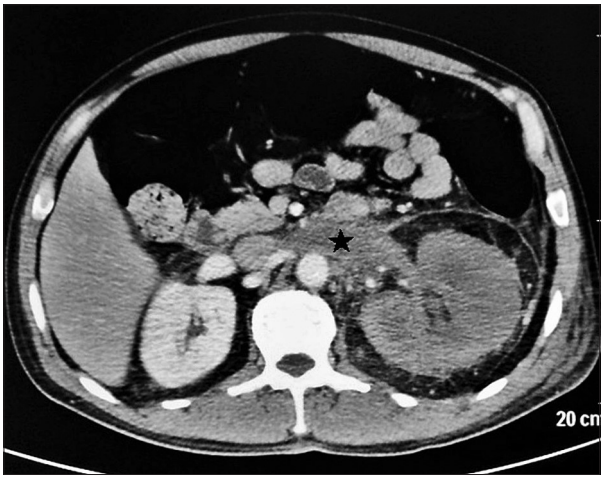

Figure 1: Contrast-enhanced computed tomographic scan showing thrombus in left renal vein (*) with enlarged nonenhanced left kidney

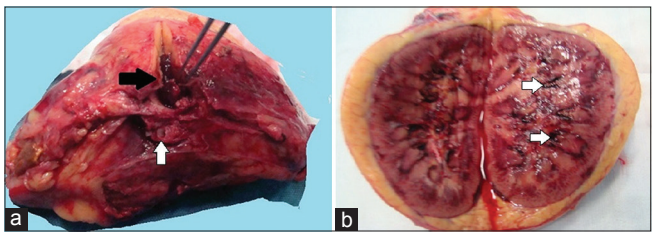

Figure 3: (a) Left nephrectomy specimen showing thrombus in renal vein (black arrow and forceps) and normal renal artery (white arrow). (b) Coronal section of the resected specimen showing thrombus in intrarenal veins (small white arrows)

Discussion

Thromboembolism is a well-known complication in the patients of acute leukemia, especially acute promyelocytic leukemia (APL). It commonly involves the venous system though the arterial system may also be affected. De Stefano *et al*. reported venous thrombosis in 80% and arterial thrombosis in 20% of patients with acute leukemia and thrombosis.[3] They also noted the distribution of cases in leukemia: 1.4% in ALL, 9.6% in APL, and 3.2% in non-M3 AML patients. The pathophysiology of thrombosis in leukemic patients is more complicated than traditional view based on the Virchow's triad of vascular stasis, impaired endothelial integrity, and hypercoagulability.[4] Observations by Kwaan and Vicuna[5] and Rickles and Falanga[6] suggested that other factors such as rapid apoptosis of

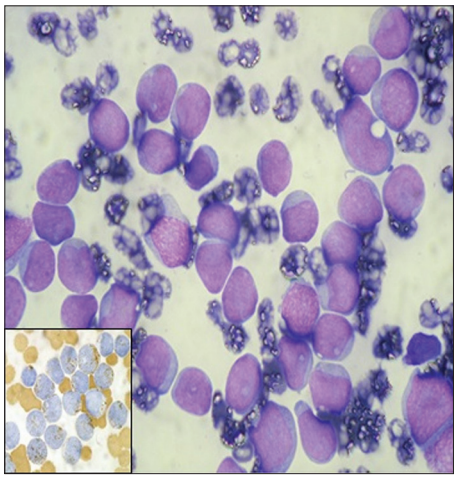

Figure 2: Leishman-stained bone marrow aspiration smears showing proliferation of large blasts with opened up chromatin and one to two prominent nucleoli and scanty cytoplasm. Inset showing granular positivity for myeloperoxidase stain in all the cells

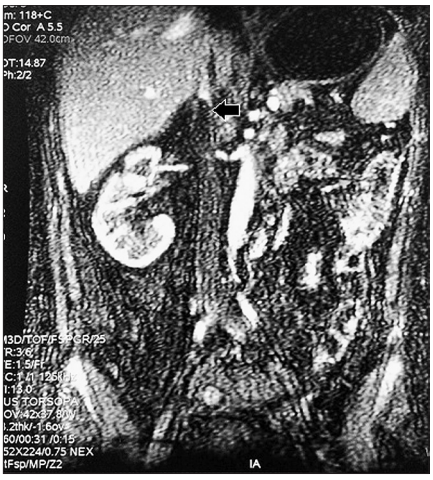

Figure 4: Postoperative contrast magnetic resonance imaging showed thrombus in infrahepatic inferior vena cava

leukemic cells and inflammatory cytokines produced by either leukemic cells or normal host cells potentiate the thromboembolism in leukemic patients. Breccia *et al*. observed a close correlation between thrombotic events in APL patients and certain biological features of leukemic cells such as CD2 and/or CD15 expression, FLT3-ITD, and bcr3 PML/RARa transcript type.[7] Although acute leukemic patients have high risk of thromboembolism, the preventive treatment of this complication is still controversial due to the higher risk of hemorrhage in the patients. Till now, there is no standard protocol of anticoagulant therapy in acute leukemia patients, except APL with high TLC or at high risk of developing all-transretinoic acid syndrome.[8,9] Although UFH and low molecular weight heparin (LMWH) are efficacious for the thromboembolism prophylaxis in acute leukemia patients, the risk of bleeding may significantly increase especially if platelet count is below 50×10^9/L.[9,10]

Hyperleukocytosis leading to end-organ dysfunction is far more common in AML than in ALL. Although the TLC may typically be higher in ALL, patients with AML are more likely to have serious complications and organ dysfunction related to high TLC. In AML, 5%–29% of adults and a little higher percentage in children will present with WBC $>50 \times 10^9$/L.[11] In a large study by cancer and leukemia Group B on patients with AML, 29% of patients had TLC $>50 \times 10^9$/L and 12% had TLC $>100 \times 10^9$/L.[12]

Hyperleukocytosis is associated with adverse prognosis in APL, which is largely due to severe coagulopathy in these patients. In hyperleukocytosis, leukopheresis is not recommended routinely[13] but may be used as a last choice in APL since it may deteriorate the associated coagulopathy.[13] Hyperleukocytosis is frequently seen in ALL even though clinical leukostasis is uncommon. High TLC is a clear adverse prognostic factor for overall survival in both pediatric and adult ALL patients. Similarly, its presence is related to adverse survival outcome in AML as well, especially if the leukocytes count is very high.[14] The fundamental pathophysiology of leukostasis was described initially in autopsy studies where patients with hyperleukocytosis were noted to have organ infiltration by leukemic cells, commonly in the lungs and brain.[15] Leukostasis in acute leukemia primarily complicates the pulmonary and central nervous system circulation and is associated with increased early mortality of both adults and children with the disease.[14,15] Renal vein is an uncommon site for thrombosis in AML, and consequently, there is a lack of literature on its management.[2] The present case of AML (FAB-M1) with hyperleukocytosis was complicated by the presence of thrombocytopenia. In the absence of thrombocytopenia, the treatment of such thrombi is started with standard anticoagulation with UFH/LMWH. The optimum anticoagulation in patients with hematological malignancies and thrombocytopenia is debatable, with studies favoring[16] as well as against[17] the use of LMWH. UFH has the advantage that it can be reversed easily unlike LMWH, but it has to be used with caution due to the risk of heparin-induced thrombocytopenia.

The decision for surgery in this case was itself a tough call as the patient had high-grade fever and a nonfunctioning, infected left kidney with a renal vein and IVC thrombus in the presence of thrombocytopenia. Looking retrospectively, it seems that early postoperative heparinization could have been beneficial in our patient, but persistent thrombocytopenia and consequent bleeding were a constant threat that had to be borne in mind, especially with surgical repair of IVC.

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Conflicts of interest

There are no conflicts of interest.

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