International Journal of Basic & Clinical Pharmacology
Bandyopadhyay S et al. Int J Basic Clin Pharmacol. 2026 Mar;15(2):381-384
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20260442

Case Report

Dasatinib induced perinephric hematoma in a patient with chronic myeloid leukemia: an uncommon adverse event of Dasatinib therapy

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Received: 27 December 2025
Accepted: 13 February 2026

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ABSTRACT

Dasatinib, a second-generation tyrosine kinase inhibitor (TKI) used in chronic myelogenous leukemia (CML) and Ph-positive leukemias, is known for adverse effects such as myelosuppression, gastrointestinal disturbances, fluid retention, rashes, and bleeding diathesis. This report presents a rare case of Dasatinib-induced perinephric hematoma in a 60-year-old woman with BCR-ABL–positive CML. Shortly after initiating Dasatinib, she developed frank hematuria, and CT-KUB revealed a large right perinephric hematoma with active bleeding from right renal artery branches, requiring embolization. No alternative etiology for the hemorrhage was identified. Discontinuation of Dasatinib and supportive management—including blood transfusion and intravenous fluids—led to gradual hematoma resolution without recurrence. A Naranjo score of 7 indicated a probable drug-related adverse event. This case emphasizes the need for clinicians to recognize rare but serious bleeding complications of Dasatinib, which may occur despite normal platelet counts and normal coagulation parameters, likely due to impaired platelet function.

Keywords: Dasatinib, Perinephric hematoma, Bleeding diathesis, Tyrosine kinase inhibitors, Naranjo score

INTRODUCTION

Chronic myeloid leukemia (CML) is a myeloproliferative disorder defined by the Philadelphia chromosome (Ph) and its BCR-ABL fusion gene, which drives uncontrolled proliferation through multiple signaling pathways. Dasatinib, a second-generation TKI, is 325-fold more potent than imatinib against BCR-ABL, active across all CML phases and Ph+ ALL, and competitively inhibits multiple additional kinases, including members of the SRC family, c-KIT, PDGFR-α/β, and ephrin receptor kinases.

Clinical trials confirm superior hematologic and cytogenetic responses, including in newly diagnosed and imatinib-resistant or -intolerant CML. Despite its efficacy, Dasatinib carries a distinct toxicity profile, most commonly causing myelosuppression, gastrointestinal disturbances, fluid retention and rash.[1] Rare but significant bleeding complications have been reported in few case reports affecting sites such as the gastrointestinal tract, central nervous system, and soft tissues, prompting concern over Dasatinib's impact on platelet function and vascular integrity.[2-5]

This report presents a rare case of Dasatinib-induced perinephric hematoma, contributing to the limited but growing body of evidence around this adverse effect. Recognition of such complications is essential for risk stratification, clinical monitoring, and timely intervention, especially given Dasatinib's expanding use in frontline therapy and in refractory settings.

CASE REPORT

A 60-year-old woman arrived at the emergency department in a confused and drowsy state with intermittent low-grade fever, anorexia and generalized weakness. On general examination, she was febrile (99°F), a blood pressure of 110/70 mmHg and other vitals were

stable. She had no icterus and pallor. Systemic examination revealed palpable splenomegaly, but no signs of meningeal irritation or focal neurological deficits. Her Glasgow coma scale was E3V4M6. Rest of the systemic examination was unremarkable. She did not have any background comorbidities or family history of leukemia.

She was admitted and Initial lab investigations revealed a markedly elevated white blood cell (WBC) count of 50,900/µl with a leucoerythroblastic picture in peripheral blood smear, normal haemoglobin (13 g/dl) and normal coagulation profile. C-reactive protein (CRP), procalcitonin, and arterial ammonia levels were within normal range. Neuroimaging (computed tomography (CT) and magnetic resonance imaging (MRI)) revealed no significant intracranial pathology. This lowered the probability of metabolic or infective causes of encephalopathy.

Blood and urine cultures were sterile. Given the persistent altered mental status, a lumbar puncture was performed. CSF analysis showed mildly elevated protein (111 mg/dl, normal: 15-45 mg/dl), normal glucose, and a mildly increased WBC count (40, 100% lymphocytes). No infectious etiology was found, as CSF GeneXpert for tuberculosis and rapid viral panels for Herpes simplex virus and Cryptococcus were negative.

She was conservatively treated with IV fluid and IV antibiotics, but her fever persisted with progressively increasing WBC count. In high suspicion of leukemia, Bone marrow evaluation was done revealing a hypercellular marrow with myeloproliferative features, and molecular testing (polymerase chain reaction) confirmed BCR-ABL fusion, establishing the diagnosis of chronic myeloid leukemia (CML). Dasatinib (100 mg tablet once daily) was initiated as first-line therapy as it has better CNS penetration.

Within a week of starting Dasatininb, she developed right flank hematoma and new onset gross hematuria with abdominal pain. CECT kidney, ureter and bladder (KUB) revealed a large right perinephric hematoma and pseudoaneurysm arising from segmental arteries of right renal artery branch (Figure 1). Subsequent angiography identified an active hemorrhage from a posterior division of the right renal artery, which was promptly embolized. Her hemoglobin dropped drastically from 12 to 6.7 g/dl. Lab tests showed markedly elevated amylase and lipase levels with rising serum creatinine. Dasatinib was stopped immediately. She needed multiple PRBC transfusions, and she was treated conservatively with IV fluids, IV antibiotics, and pain control.

To explore other causes of hematuria and bleeding, vasculitis screening was done (C-ANCA and P-ANCA), which came negative. Platelet count, INR, PT, and aPTT remained within normal limits. With continued conservative care, her condition gradually stabilized, hemoglobin levels improved and no further bleeding episodes were observed. A repeat abdominal CT scan showed resolving perinephric hematoma.

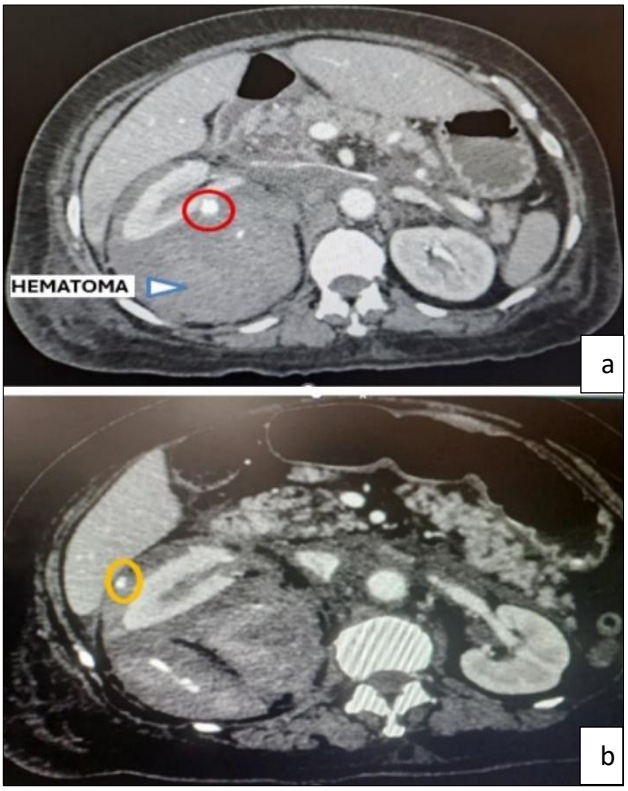

Figure 1 (a and b): CECT KUB- large area of perinephric hematoma compressing the right kidney, two rounded pseudoaneurysm noted arising from the segmental renal arteries at the medial cortex (midpole) (red circle) and lateral cortex (lower pole) (orange circle).

Dasatinib was discontinued and after her condition stabilized, Imatinib was started. She responded well to Imatinib. She reported no further episodes of bleeding and is under regular follow up with haematologist.

DISCUSSION

Bleeding associated with Dasatinib therapy is a recognized but incompletely understood complication. Dasatinib's broad inhibition of multiple kinases—including BCR-ABL, SRC family kinases (SFKs), c-KIT, PDGFR-β, and ephrin receptors—has been implicated in its hemorrhagic profile. Emerging evidence suggests that the causes of Dasatinib-induced bleeding are multifactorial, primarily involving platelet dysfunction rather than abnormalities in coagulation parameters.

Several mechanisms have been proposed. First, Dasatinib potently inhibits SRC family kinases (SFKs)—key regulators of platelet activation, including c-Src, Lyn, Fyn and yes—thereby impairing normal platelet signaling.[5] This affects early platelet activation pathways mediated by glycoprotein VI-Fc receptor γ-chain (FcRγ), GPIb-IX, and

integrins α2β1 and αIIbβ3.[6] Secondly, Dasatinib inhibits PDGFR-β, essential for pericyte function, vascular integrity, and angiogenesis; its blockade may weaken vessel walls, predisposing to bleeding. SFKs are also necessary for fibrin clot retraction, a process impaired by Dasatinib.[7,8] Additional contributing factors include low platelet counts, advanced disease phases, and disruptions in thrombopoiesis, as Dasatinib promotes megakaryocyte differentiation but impairs proplatelet formation.[9] In our case, common etiologies of perinephric hematoma like trauma, renal masses (like angiomyolipoma or renal cell carcinoma), vascular malformations, infections, vasculitis, coagulopathies, and iatrogenic interventions—were systematically excluded. She had no prior trauma or anticoagulant exposure; coagulation profile and platelet counts were normal. C-ANCA and P-ANCA for vasculitis were negative; cultures were sterile; and earlier imaging showed no renal mass, obstruction, stones, or vascular abnormalities. The convergence of these findings strongly supports Dasatinib-induced platelet dysfunction as the most plausible mechanism underlying this rare hemorrhagic complication. The Naranjo adverse drug reaction probability score was 7, indicating a probable causal relationship between Dasatinib and perinephric hematoma (Table 1).[10]

Table 1: Naranjo adverse drug reaction probability scale showing a score of 7 indicating probable adverse drug reaction.

Naranjo criteria	Score
Previous conclusive reports on this reaction	Yes (+1)
Did adverse event occurred after drug (Dasatinib) administration	Yes (+2)
Improvement on drug discontinuation	Yes (+1)
Did the adverse reaction appear when the drug was readministered?	Not done (+0)
Alternative causes ruled out	Yes (+2)
Adverse even confirmed by objective evidence?	Yes (+1), (CT KUB)
Was the drug detected in any body fluid in toxic concentrations?	Not done (+0)
Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	Not done (+0)
Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	No (+0)
Did the reaction reappear when a placebo was given?	Not done (+0)
Total	7 (probable adverse drug reaction)

CONCLUSION

Dasatinib can cause serious bleeding beyond the GI tract, and atypical sites such as the retroperitoneum or perinephric space should be considered when patients present with unexplained flank or abdominal pain, and haemoglobin drop following therapy initiation. Platelet dysfunction is a key mechanism, and bleeding may occur despite normal platelet counts and coagulation parameters. Clinicians must maintain high vigilance for atypical bleeding patterns in patients receiving Dasatinib, especially when no alternative cause is found.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Bandyopadhyay S, Pratihar S, Chandra SK, Dastidar AG, Sahu A. Dasatinib induced perinephric hematoma in a patient with chronic myeloid leukemia: an uncommon adverse event of Dasatinib therapy. Int J Basic Clin Pharmacol 2026;15:381-4.