To the editor:

Imatinib therapy in a patient with suspected chronic neutrophilic leukemia and FIP1L1-PDGFRA rearrangement

A 54-year-old man with no significant past medical history presented with skin rash. Complete blood count showed a white blood cell count of 64 × 10^9/L (63% neutrophils, 2% eosinophils), hemoglobin 14 g/dL, and platelet count 166 × 10^9/L. Bone marrow evaluation showed a hypercellular marrow with marked granulocytic hyperplasia (Figure 1). There was no increase in marrow eosinophils or fibrosis. No dysplasia was identified. Conventional cytogenetics showed constitutional inv(9). Testing for BCR-ABL rearrangement and JAK2V617F mutation was negative. The patient was diagnosed with chronic neutrophilic leukemia (CNL) and treatment with hydroxyurea was initiated. Subsequently, array comparative genomic hybridization demonstrated monoallelic interstitial deletion of chromosome 4q12. This was confirmed by interphase fluorescence in situ hybridization (FISH) analysis using a probe set that detects loss of fusion by FISH at 3 months was negative. The patient continues to be treated with imatinib 100 mg daily for >1 year with no recurrence of skin rash or leukocytosis.

Imatinib is approved for treatment of patients with FIP1L1-PDGFRA fusion-positive myeloid neoplasms. These patients typically present with peripheral blood eosinophilia. Cools et al described this entity as an interstitial deletion of chromosome 4q12 that leads to the juxtaposition of the FIP1L1 gene to the PDGFRA gene. The resultant fusion product, FIP1L1-PDGFRA, results in constitutive activation of the tyrosine kinase PDGFRA and is amenable to therapy with imatinib. Baccarani et al reported achievement of complete hematologic response with imatinib in all patients with FIP1L1-PDGFRA fusion and the responses were durable.

Our patient presented with characteristic diagnostic features of patients with CNL (neutrophilic leukocytosis, hypercellular bone marrow with granulocytic hyperplasia, and absence of dysplasia). Although the patient did not present with eosinophilia, FIP1L1-PDGFRA fusion was tested because of the presence of skin rash and, remarkably, the test was positive. To the best of our knowledge, this is the first case of a FIP1L1-PDGFRA fusion without eosinophilia that responded to tyrosine kinase inhibitor therapy. There is a recent report of FIP1L1-PDGFRA fusion without eosinophilia in a patient with monoclonal gammopathy; however, the response to imatinib was not reported. Imatinib response in a patient with CNL has also been reported previously; however, the molecular mechanism for the response was not elucidated. The diagnosis could easily have been missed in our patient because he did not present with eosinophilia. Establishing the correct diagnosis significantly altered the treatment management because FIP1L1-PDGFRA fusion is extremely sensitive to imatinib. The 2008 World Health Organization classification lists “myeloid neoplasms associated with PDGFRA rearrangement” under “myeloid neoplasms associated with eosinophilia and abnormalities of PDGFRA,” indicative of a strong emphasis on the presence of eosinophilia. This is a report of a single patient, but because of the enormous therapeutic implications, we recommend that evaluation for FIP1L1-PDGFRA fusion should be considered for all patients with nonclassical myeloproliferative neoplasms. We evaluated 7 additional CNL patients who had stored samples for FIP1L1-PDGFRA fusion by FISH; however, all were negative. Recently, activating CSF3R mutations were identified in majority of patients with CNL. It is possible that CNL patients without CSF3R mutations (17% to 41% of cases) likely have alternate molecular pathogenic lesions leading to constitutive activation of other tyrosine kinases such as PDGFRA.

Nitin Jain
Department of Leukemia, MD Anderson Cancer Center,
Houston, TX

Joseph D. Khoury
Department of Hematopathology, MD Anderson Cancer Center,
Houston, TX
To the editor:

Spontaneous coronary artery dissection during hematopoietic stem cell infusion

Spontaneous coronary artery dissection (SCAD) is a rare event. Known risk factors include female gender, peripartum status, hypertension, cocaine, smoking, heavy exercise, collagen vascular disease, and cardiac catheterization. Clinical presentation may be indistinguishable from ST segment elevation myocardial infarction. To our knowledge, SCAD has not been described as an adverse event in relation to stem cell infusion.

Here, we report on a 61-year-old white female without any known history of coronary artery disease, who underwent a nonmyeloablative (Fludarabine and TBI 400 cGy)-matched unrelated donor bone marrow transplant for a purine analog refractory chronic lymphocytic leukemia. Her pre-transplant echocardiogram was normal, demonstrating an ejection fraction (EF) of 68% without any regional wall motion abnormalities. Due to donor preference, a bone marrow harvest was obtained.

The patient started complaining of intermittent chest pain and shoulder pain during the bone marrow infusion. Peak systolic and diastolic blood pressures were 168 and 106 mm Hg, heart rate of 220 beats per minute. An electrocardiogram remained unchanged and nondiagnostic in the presence of a known left bundle branch block. Troponin T serum concentration was elevated at 1.8 ng/mL (normal <0.01). A stat echocardiogram demonstrated akinesis of the apex and midventricular wall, and an EF of 27% suggestive of an acute coronary syndrome. A coronary angiogram demonstrated a dissection of the mid left anterior descending artery with thrombus formation and thrombotic occlusion of the distal left anterior descending artery (Figure 1). No coronary intervention was pursued but an intra-aortic balloon was placed for coronary perfusion support. She eventually had an uneventful recovery and continues to do well 3 months after her transplant with improvement in her EF (50% with improvement in wall motion abnormalities).

Figure 1. Coronary angiogram. Right anterior oblique cranial projection outlining the typical angiographic appearance of coronary artery dissection of the mid segment of the left anterior descending artery (arrow). Furthermore, it reveals an abrupt cutoff of the distal left anterior descending artery consistent with thrombotic occlusion (arrowhead).
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Nitin Jain, Joseph D. Khoury, Naveen Pemmaraju, Praveen Kollipara, Hagop Kantarjian and Srdan Verstovsek