committed to multiple hematopoietic lineages. In contrast, Cambier et al provided evidence in another PV patient who developed CML that the PV and CML originated from distinct clones. Our findings indicate that both the JAK2V617F mutation and BCR-ABL1 can occur concurrently in both CFU-GM and BFU-E and that JAK2V617F occurs before the acquisition of BCR-ABL1.

The clinical phenotype of myeloproliferative neoplasms frequently evolves over time. Although this progression can be enhanced by the use of chemotherapeutic agents, it represents the natural clonal evolution of these malignancies. The development of CML in PV occurs much less frequently than myelofibrosis or acute myeloid leukemia, but should be considered in patients with PV who develop extreme leukocytosis. The contribution of BCR-ABL1 to disease progression appears to be greater than that of JAK2V617F, because these patients display a clinical phenotype that is consistent with CML rather than PV. These clinical observations represent an example of clonal evolution in which the initial genetic event is a mutation leading to the activation of a tyrosine kinase (JAK2), which is then followed by either a second genetic event leading to the acquisition of a fusion protein resulting in activation of another protein kinase (BCR-ABL1) or by homologous recombination resulting in JAK2V617F-homozygous HPCs that lack BCR-ABL1. Subsequently, the JAK2V617F-heterozygous HPCs with BCR-ABL1 can also undergo homologous recombination and become homozygous for JAK2V617F.

To the editor:

Hemichorea in a patient with JAK2V617F blood cells

Chorea has been reported in patients with polycythemia vera (PV). JAK2V617F is a molecular marker used for the diagnosis of PV. Occasionally, patients have insufficient clinical criteria to establish a diagnosis of PV or only possess some disease features without having overt hematologic manifestations. We present a case of an elderly woman with subacute hemichorea who was found to have normal hematologic profile and JAK2V617F+ hematopoiesis. Hemichorea completely resolved after therapeutic phlebotomy and hydroxyurea therapy.

A previously active, healthy 87-year-old woman experienced an episode of dizziness and a week later dysarthria and facial asymmetry. An MRI/MRA of the brain was unrevealing. Three weeks later, she developed involuntary movements of the left arm, face, and leg that progressively worsened in intensity and frequency. Neurologic examination revealed left hemichorea with motor impersistence and “milkmaid’s grip.” Chorea was activated by rapid alternating movements and walking. There were no signs of Parkinsonism or dystonia.

Palpable splenomegaly was absent on examination. Blood work was notable for a hemoglobin of 15.6 g/dL, hematocrit of 44.2%, WBC count of 8.6 $\times$ 10$^9$/L, platelet count of 281 $\times$ 10$^9$/L, mean corpuscular volume of 95.7 fl, normal iron studies, and a serum erythropoietin of 12.7 mIU/mL. Her peripheral blood JAK2V617F granulocyte allele burden was 35% as determined by allele-specific PCR. The patient refused a BM biopsy.

*X.W. and J.T. contributed equally to this work.

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References


The patient was phlebotomized to a hematocrit less than 42% and started on daily hydroxyurea 500 mg and aspirin 81 mg. Treatment with venesection and hydroxyurea achieved resolution of chorea within 4 weeks.

Neurologic complications have been reported in up to 80% of untreated PV patients. PV-associated chorea (PVC) has been reported as the presenting complaint, primarily in older females, which typically involves the orofaciolingual and appendicular musculature and often resolves with phlebotomy or cytoreductive therapy. The exact mechanism underlying PVC is not known and there are no specific neuroimaging abnormalities or pathologic findings.

Chorea in this patient represents a possible forme fruste of an MPN in that the patient’s clinical features did not allow for a definitive diagnosis of PV even though she was JAK2V617F+. A similar situation has been documented in patients who present with splanchnic vein thrombosis and are found to be JAK2V617F+. These patients lack overt signs of an MPN and in some cases have normal BM morphology. More than 50% of such JAK2V617F+ patients with splanchic vein thrombosis eventually develop clinical features of MPN.

Based on this report, patients over the age of 50 years presenting with chorea should be tested for JAK2V617F even if they have a normal hematologic profile. This case highlights the possibility that chorea might represent a forme fruste of an MPN that will be responsive to venesection and cytoreductive therapy. The natural history of an unclassifiable JAK2V617F+ MPN presenting with neurologic complications is not yet known and will require further study.

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References

To the editor:

No cross-resistance after sequential use of romiplostim and eltrombopag in chronic immune thrombocytopenic purpura

Romiplostim and eltrombopag (a synthetic fusion peptidobody and a nonpeptide molecule, respectively) are second-generation thrombopoietin mimetics/agonists that are structurally dissimilar to thrombopoietin and do not induce the formation of autoantibodies.

They have been recently approved for the treatment of relapsed/resistant immune thrombocytopenia (ITP) and both are able to improve the production of new platelets, which, in this disease, are reduced by binding of antiplatelet antibodies to BM megakaryocytes. What is still not completely clear is whether these agents are cross-resistant. We describe herein 2 ITP patients who received eltrombopag as salvage therapy after they had become resistant to romiplostim.

A 58-year-old man was diagnosed in November 2007 with recurrent ITP after several lines of treatment, including steroids, high-dose immunoglobulins, cyclosporine, and rituximab. All of these therapies had induced significant responses but these were of brief duration. In June 2010, the patient’s platelet count dropped to 6000/µL and he was started on weekly subcutaneous administrations of romiplostim progressively increased from 1-4 µg/kg of body weight (Figure 1A). A complete response was achieved. However, 8 weeks later, a rapid decline of the platelet count occurred and further increasing romiplostim up to 10 µg/kg was not effective. After an episode of subdural bleeding, the patient underwent splenectomy, initially refused, in October 2010. A
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