Mesenteric venous thrombosis (MVT) is a rare disorder that involves the mesenteric, splenic, or portal veins. It is characterized by abdominal pain, tenderness, and sometimes hypercoagulable states or cancer. A recent novel mutation in the Janus kinase 2 (JAK2) gene involving a gain-of-function substitute of valine to phenylalanine at position 617 (JAK2 V617F) has been discovered to be prevalent in patients with mesenteric vein thrombosis and myeloproliferative disorders. This article reports a patient who presented with mesenteric vein thrombosis and relatively normal peripheral blood counts. He was diagnosed with essential thrombocythemia after he tested positive for the JAK2 V617F mutation. (J Vasc Surg 2010;52:205-7.)

CASE REPORT

A 65-year-old man presented with abdominal pain of 1-week duration. The pain was periumbilical and constant, although exacerbated in the postprandial period, and accompanied by abdominal fullness and anorexia. There was no history of nausea, vomiting, or diarrhea. The patient had a history of type II diabetes mellitus, hyperlipidemia, and chronic kidney disease, with a baseline creatinine level of 1.4 mg/dL. He had no history of deep venous thrombosis or thrombophilia.

On physical examination, he was afebrile and his vital signs were normal. He was not in acute distress, and his sclerae were icteric. His abdomen demonstrated mild tympany and mild diffuse tenderness but no peritoneal signs. Laboratory analysis showed levels of hemoglobin at 13.6 mg/dL, white blood cell (WBC) count of 11,600 mm³ with 8.25% neutrophils, and the platelet count was 685,000/mm³. After initial fluid resuscitation, his platelet count returned to within normal reference ranges (450,000/mm³). The remainder of his blood chemistry values, including amylase and lipase, were within normal reference ranges.

After prehydration, an intravenous contrast-enhanced computed tomography scan at admission revealed hepatosplenomegaly, with an 8 × 7-cm mass at the inferior border of the spleen containing a fluid density surrounded by a chronic, thin-walled, nonenhancing capsule that was thought to be liquefaction due to infarction of the spleen. There was complete thrombosis of the portal and splenic vein, with involvement of the proximal segment of the superior mesenteric vein (Fig). He was admitted, anticoagulated with unfractionated heparin, and placed on bowel rest.

A 10F pigtail catheter was inserted into the splenic fluid collection, and 140 mL of bloody fluid was aspirated. Gram stain of the aspirate revealed +3 white blood cells but no microorganisms. No aerobic or anaerobic growth was noted from the aspirate after 5 days. Blood cultures obtained at the time of admission were likewise negative for growth.

A peripheral smear revealed normochromic, normocytic anemia with mild anisopoikilocytosis. The WBC and platelet counts were within normal reference ranges, and there was no peripheral evidence for myelofibrosis. He was tested for anticardiolipin antibody, isotypes immunoglobulin (Ig) G, IgM, and IgA, which were negative, and for JAK2 mutation, which was positive for Val617Phe (V617P) genotype.

A bone marrow aspirate revealed maturing trilineage hematopoietic components consisting predominantly of granulocytic cells. The cellularity of the bone marrow was approximately 60% (normal for a patient age 65 is about 45%). The myeloid (M)/erythroid (E) ratio was increased to approximately 8:1 (normal range, 2-4:1) and the megakaryocytes were increased in number. A diagnosis of myeloproliferative disorder (MPD) was made given the hypercellular bone marrow, the increased M:E ratio, and the increase in megakaryocytes. The presence of the JAK2 V617F mutation and the history of thrombocytosis were thought to be most suggestive of evolving essential thrombocytemia.

The patient was prescribed Coumadin (Bristol-Myers Squibb, Princeton, NJ) therapy with a goal international normalized ratio

JAK2 V617F mutation, mesenteric vein thrombosis, and myeloproliferative disorders

Christopher D. Owens, MD, MSc, San Francisco, Calif

Mesenteric vein thrombosis is a rare disorder that is often the first manifestation of a systemic condition such as a hypercoagulable state or cancer. In particular, myeloproliferative disorders can present as mesenteric vein thrombosis even in the setting of relatively normal peripheral blood counts. A recent novel mutation in the Janus activated kinase 2 (JAK2) gene involving a gain-of-function substitute of valine to phenylalanine at position 617 (JAK2 V617F) has been discovered to be prevalent in patients with mesenteric vein thrombosis and myeloproliferative disorders. This article reports a patient who presented with mesenteric vein thrombosis and relatively normal peripheral blood counts. He was diagnosed with essential thrombocythemia after he tested positive for the JAK2 V617F mutation. (J Vasc Surg 2010;52:205-7.)

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The patient was prescribed Coumadin (Bristol-Myers Squibb, Princeton, NJ) therapy with a goal international normalized ratio
of 2.5, and he was discharged from the hospital without further thrombotic events.

**DISCUSSION**

Patients with MVT may present with a variety of clinical manifestations, depending largely on the extent of the thrombus, the size of the vessels involved, and the depth of bowel wall ischemia. Patients with subacute presentations, such as in this patient, often have periumbical pain that suggests an origin in the midgut, but full-thickness bowel ischemia is not likely. Once the diagnosis of MVT has been made, associated casual pathology should be sought. Inflammatory diseases such as pancreatitis and inflammatory bowel syndrome are usually easily detected by history, and postoperative states, cirrhosis, and trauma are obvious. However, in the absence of obvious etiology, hematologic states involving thrombophilia should be investigated (Table).

Many thrombophilic abnormalities are associated with gain-of-function mutations such as factor V Leiden, A20210G prothrombin, or clonal disorders involving the hematopoietic system such the MPDs. The diagnosis of thrombophilia is relatively straightforward, and the treatment is generally anticoagulation. The diagnosis of MPD, however, can be problematic at the time of acute thrombosis due to hemodilution, occult bleeding, and hypersplenism and therefore may delay appropriate cytoreductive therapy. This is especially pertinent because MPD is prevalent in patients who present with MVT.

The MPDs can be broadly classified into Philadelphia chromosome-positive (chronic myelogenous leukemia) and Philadelphia chromosome-negative (polycythemia vera, essential thrombocytosis, and myelofibrosis). Thrombosis and transformation to acute myeloid leukemia are the major causes of morbidity and mortality in these disorders. MVT is the first clinical manifestation in an estimated 25% to 78% of patients with newly diagnosed polycythemia vera or essential thrombocytosis and often occurs before a rise in peripheral blood counts. An accurate diagnosis of an MPD historically has been supported by expensive and invasive tests such as bone marrow biopsy and endogenous erythroid colony formation assessment.

Recently, a point mutation in the **JAK2** gene encoding a valine to phenylalanine change at position 617 has been found. The **JAK2 V617F** genotype confers constitutive tyrosine kinase activation (gain-of-function) in patients with sporadic MPDs. JAK2 is a cytoplasmic tyrosine kinase that transduces signals by growth factors such as erythropoietin in normal and neoplastic cells. This change in a single amino acid renders the JAK2 enzyme constitutively active, leading to unregulated proliferation of hematopoietic cell lines. The mutation can be detected in peripheral blood cells by a commercially available qualitative RNA-based, polymerase chain reaction sequencing assay (Speciality Laboratories, Inc, Valencia, Calif). This mutation is found in 95% of patients with polycythemia vera and in 50% to 60% of the patients with essential thrombocytosis and primary myelofibrosis. Patients with polycythemia vera or essential thrombocytosis and the **JAK2 V617F** genotype have a higher rate of thrombosis than patients with the wild-type counterparts. A recent meta-analysis has determined a 32% overall prevalence of the **JAK2 V617F** mutation in patients presenting with MVT. Therefore, these data suggest that patients with MVT, with no other precipitating etiology, should be screened for the presence of the **JAK2 V617F** mutation, because the finding of this mutation is diagnostic of an occult MPD.

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**Table. Prothrombotic disorders associated with mesenteric venous thrombosis**

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Relative frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antithrombin II deficiency</td>
<td>Rare</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>Rare</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>Infrequent</td>
</tr>
<tr>
<td>G1691A factor V (Leiden) mutation</td>
<td>Rare</td>
</tr>
<tr>
<td>G20210A mutation in prothrombin gene</td>
<td>Infrequent</td>
</tr>
<tr>
<td>MTHFR C677T gene mutation</td>
<td>Rare</td>
</tr>
<tr>
<td><strong>JAK2 V617F</strong> gene mutation</td>
<td>Frequent</td>
</tr>
</tbody>
</table>

**JAK2 V617F**, Janus-activated kinase gain-of-function substitute of valine to phenylalanine at position 617; **MTHFR**, methylenetetrahydrofolate reductase.
Conversely, the JAK2 V617F mutation is no more prevalent in patients with other venous thrombosis disorders such as deep vein thrombosis (DVT) or pulmonary embolism than in healthy control populations. A recent review reported that a JAK2 V617F mutation was found in two patients with recurrent arterial thromboembolism, both of whom were subsequently diagnosed with MPD. Although widespread testing for the mutation in patients presenting with DVT cannot be endorsed, testing for the JAK2 V617F mutation may be warranted for patients with refractory thrombotic events and an otherwise negative hematologic workup.

Why the JAK2 V617F mutation is so strongly associated with MVT but not in lower extremity venous thrombosis is unknown. It is possible that MPD affects the blood flow through the mesenteric venous bed and therefore makes this location particularly prone to thrombosis. It has been shown that platelets from patients with the JAK2 V617F mutation express P-selectin more easily than wild-type controls, which may contribute to thrombosis. Other possibilities include an association with the JAK2 V617F mutation and higher levels of peripheral erythrocytes and WBCs, thereby increasing blood viscosity.

CONCLUSIONS

The diagnosis of MVT may be the first manifestation of an occult MPD that can occur even in the setting of peripheral blood counts within the normal reference range where suspicion would otherwise be low. The JAK2 V617F mutation is present in about one-third of patients with MVT and is diagnostic of an MPD. Therefore, knowledge of this genetic association will permit prompt diagnosis, possibly without the need for unnecessary invasive tests such as bone biopsy, and allow for the timely initiation of cytoreductive therapy.

REFERENCES
