

CLINICAL VIGNETTE

Portal and Mesenteric Vein Thrombosis in a Patient with JAK2 V617F Mutation

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Introduction

Venous thromboses are thought to occur due to a combination of factors, both acquired (immobility, malignancy, endothelial injury) and genetic.¹ Although portal vein thrombosis (PVT) is most commonly seen in the setting of cirrhosis, many patients develop PVT in the absence of cirrhosis due to a combination of other prothrombotic factors. The Janus kinase 2 (JAK2) V617 mutation has been implicated for its association with myeloproliferative disorders (MPD), and more recently for its potential role as an independent risk factor for portal and mesenteric vein thrombosis (PMVT).² We describe a case of a patient with JAK2 V617F mutation developing portal vein thrombosis in the absence of other significant risk factors for veno-occlusive disease.

Case Report

A 66-year-old African American male underwent routine laboratory evaluation, which revealed abnormal liver associated enzymes: AST 67 U/L, ALT 82 U/L, and alkaline phosphatase 197 U/L. His CBC was within normal limits. Iron studies and viral hepatitis screens were both within normal limits. Abdominal ultrasound revealed moderate splenomegaly (16.9cm spleen length) with a morphologically normal liver with no evidence of cirrhosis. CT abdomen with contrast revealed a partially thrombosed portal vein and proximal superior mesenteric vein as well as stigmata of portal hypertension including cavernous transformation of the portal vein, numerous portosystemic collaterals, and splenomegaly. Elevated liver enzymes persisted and MRI abdomen revealed a nonocclusive thrombus. The patient denied history of abdominal trauma, surgery, liver disease, or known prior thromboses. Laboratory analysis for hypercoagulability was positive for a heterozygous JAK2 V617 mutation with other tests including Factor V Leiden Mutation, prothrombin gene mutation, cardiolipin antibody, protein C and S antigens, and antithrombin III activity within normal limits. The patient was recommended to initiate anticoagulation with warfarin, both to address the current thrombus and prevent future thrombi given the patient's hypercoagulable state.

Discussion

We presented a rare case of a patient with JAK2 V617F mutation developing a portal vein thrombosis in the absence of overt MPD and local precipitating factors, such as cirrhosis or

malignancy. As described by a study by Kralovics et al,³ the JAK2 V617 mutation is considered a dominant gain-of-function mutation, which induces a cytokine-independent proliferative advantage in hematopoietic progenitors, mobilization of hematopoietic progenitors, and development of endogenous erythroid colonies that may lead to the development of MPD. This mutation is the most commonly seen mutation in myeloproliferative disorders such as polycythemia vera, essential thrombocythemia, and idiopathic myelofibrosis.³ However, cases like our patient's continue to demonstrate that the JAK2 V617F mutation is an independent risk factor of PMVT.

A study by Colaizzo et al² found that among patients presenting with PMVT, approximately 17% of patients carried heterozygous JAK2 V617F mutations. While 44% of these patients carried a diagnosis of MPD prior to the onset of the PMVT, the remainder did not. Furthermore, presence of the JAK2 mutation in the setting of venous thrombosis has been associated with increased likelihood of subsequent diagnosis of a myeloproliferative disorder.⁴ Together, such findings suggest that venous thromboses are often the first manifestation of occult MPD.

A meta-analysis by Dentali et al⁴ assessed the frequency of the JAK2 V617F in not only splanchnic vein thromboses, but also other thromboembolisms including deep vein thromboses and cerebral vein thromboses. The JAK2 V617F mutation was noted to be more strongly associated with splanchnic vein thromboses. Interestingly, in patients with venous thromboses at other sites, the JAK2 V617F mutation was no more common than in the general population. Although the mechanisms underlying these findings have not been fully elucidated, it has been hypothesized that the JAK2 mutation may affect the blood flow through the splanchnic venous bed.

Conclusion

Patients with PVT without known risk factors for thrombosis should be screened for acquired and hereditary thrombophilia, including the JAK2 mutations. Both the increased incidence of the JAK2 mutation in patients with PVT compared to other venous thromboses, and the commonly associated hypersplenism and portal hypertension, which can mask a preexisting MPD, justify this recommendation.⁴ Because presence of a JAK2 mutation represents a permanent

thrombotic risk factor, long-term anticoagulation is indicated in cases where the mutation is detected. Potential agents include vitamin K antagonists and direct oral anticoagulants (DOACs) such as rivaroxaban, apixaban, and dabigatran. Warfarin is the least expensive option, and the agent with the most experience in this setting. However, fluctuations in efficacy and safety with diet and interaction with other medications necessitates regular laboratory monitoring. DOACs circumvent the need for laboratory monitoring and have been used as safe, effective substitutes in the treatment of other venous thromboembolisms.⁵ Unfortunately, data regarding their successful use in PVT specifically are currently limited to case reports.^{6,7} Thus, the decision to use DOACs should be made on a case-by-case basis. Finally, successful detection of a JAK2 mutation warrants further surveillance for subsequent development of MPD with routine complete blood counts.

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