

Case 15-2006: The Budd–Chiari Syndrome and V617F Mutation in *JAK2*

TO THE EDITOR: The discovery of a V617F mutation in the Janus kinase 2 (*JAK2*) gene was a seminal advance in our understanding of the chronic myeloproliferative disorders (MPDs). Ostensibly, the recent Case Record by Chung et al. (May 18 issue)¹ was chosen to showcase the expression of this mutation in defining the cause of hepatic-vein thrombosis. However, although the expression of the V617F mutation identifies the presence of an MPD, it does not define the limits of the phenotype, and the absence of the mutation does not rule out an MPD.

The discussants focused on borderline thrombocytosis and World Health Organization criteria for the diagnosis of MPDs — criteria that have recently been discredited² — to suggest that essential thrombocytosis was responsible for the hepatic-vein thrombosis. Evidence that essential thrombocytosis causes hepatic-vein thrombosis is anecdotal, whereas polycythemia vera is a well-documented cause.³ Furthermore, V617F expression occurs in more than 90 percent of patients with polycythemia vera but in less than 50 percent of patients with essential thrombocytosis. Until proven otherwise, a hematocrit of 45 percent in a woman with ascites, splenomegaly, and hepatic-vein thrombosis suggests the presence of erythrocytosis masked by an expanded volume of plasma^{4–6} (Table 1). In this clinical setting, analyses of red-cell mass and plasma volume have diag-

nostic and therapeutic implications that an assay of a V617F mutation in *JAK2* cannot offer.

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TO THE EDITOR: Chung et al. classified the condition of their patient as “subacute-to-chronic Budd–Chiari syndrome” on the basis of the duration of symptoms; mesocaval shunting was subsequently performed. However, in our view, the classification of conditions as acute, subacute, and chronic lacks scientific foundation and should not be used as guidance for therapy.¹ We were surprised by the decision to perform surgical shunting rather than place a transjugular intrahepatic portosystemic shunt (TIPS). Two studies assessing the effect of surgical shunts on survival (after adjustment for prognostic factors) did not show either a favorable effect² or a beneficial outcome in a selected group,³ suggesting that operative mortality and morbidity swamp the benefit. The extremely positive results described by Orloff et al.⁴ are probably subject to selection bias, since the criteria for the selection of patients and the proportion of those patients who were not suitable for surgery were not mentioned. We would suggest that

Table 1. Hepatic-Vein Thrombosis and Masked Erythrocytosis in a 30-Year-Old Woman with a Hematocrit of 44.8 Percent and Polycythemia Vera.

Variable	Expected Value*	Observed Value	Multiple of Difference
Red-cell mass (ml)	1379	2847	2.1 times
Plasma volume (ml)	2232	3507	1.6 times
Total blood volume (ml)	3611	6354	1.8 times

* Data are from Pearson et al.⁶

TIPS, preferably with the use of covered stents, has surpassed surgical shunting in both efficacy and safety and should be considered as a first-line intervention.

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TO THE EDITOR: In the analysis of ascitic fluid in a patient with the Budd–Chiari syndrome, Chung et al. incorrectly state that “a high serum–ascites albumin gradient with low ascitic fluid total protein (<2.5 g per deciliter) is observed.” The total protein in ascitic fluid in patients with postsinusoidal portal hypertension, including the Budd–Chiari syndrome, is more than 2.5 g per deciliter owing to the preserved inherent “leakiness” of the hepatic sinusoidal membrane. Only late in the course of postsinusoidal obstruction, when significant fibrosis occurs, does the composition of the ascitic fluid begin to reflect the low total protein commonly seen in cirrhosis. Early recognition of an elevated total protein level in ascitic fluid is important clinically, since it can direct further diagnostic testing toward cardiac and vascular conditions and potentially obviate the need for liver biopsy.

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THE DISCUSSANTS REPLY: Drs. Murad and Janssen correctly point out that TIPS can be associated with excellent short-term outcomes in the management of the Budd–Chiari syndrome.¹ However, long-term follow-up will be required to assess the durability of this benefit. They also suggest a prognostic classification scheme with the use of sim-

ple, objective criteria that appear to correlate well with the outcome when the criteria are applied retrospectively.¹ Although this scheme is attractive, prospective studies are still needed to confirm the validity of these criteria. When the criteria are applied to patients with moderately advanced cases of the Budd–Chiari syndrome, such as our patient, improved survival was actually suggested for patients who underwent portosystemic shunt surgery. The team that was involved in the care of this patient thought that the durability of shunt surgery and its greater potential for improved survival justified this option as the first choice.

Dr. Spivak and colleagues correctly point out that a definitive diagnosis of polycythemia vera or essential thrombocythemia could not be made in this patient with the Budd–Chiari syndrome. We were not implying that essential thrombocythemia was the operative diagnosis but merely pointing out that thrombocytosis was the only overt hematologic manifestation. In the past, the diagnosis of polycythemia vera required the assessment of red-cell mass. However, many centers now follow the World Health Organization criteria, which permit the substitution of an elevated hemoglobin level (>18.5 g per deciliter for men and >16.5 g per deciliter for women) for the elevated red-cell mass.² In fact, our center no longer offers an analysis of red-cell mass as a diagnostic test, since it is no longer routinely ordered. With the availability of molecular markers of disease such as the V617F mutation in *JAK2*, the classification of myeloproliferative disorders will doubtless evolve toward more precisely defined disease entities.

Dr. Sheth is correct. The sentence regarding the analysis of ascitic fluid should have read, “a high serum–ascites albumin gradient with a high ascitic fluid albumin (>2.5 g per deciliter) is observed.”

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