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Letters to the Editor

The role of *JAK2* gene mutations in the etiologic diagnosis of splanchnic vein thrombosis

Key words: Splanchnic vein thrombosis. JAK2 gene mutations.

Dear Editor,

Two clinical reports, both related to the association of a portal or mesenteric vein thrombosis and an hereditary thrombophilic disorder, have been recently published in this journal (1,2). Both suggest the need, in this clinical setting, of performing a thrombophilic study including G20210A factor II gene mutation, factor V Leyden mutation, activated protein C resistance, lupus anticoagulant, anticardiolipin antibodies, protein C and S deficiencies, antithrombin deficiency and plasmatic homocysteine.

Nevertheless, the most frequent cause of splanchnic thrombosis, either portal thrombosis (PT) or Budd-Chiari syndrome (BCS), is not the existence of one of those thrombophilic factors, but the presence of an underlying myeloproliferative disorder (MPD). This entity does not seem to have been taken into account in any of the two clinical cases. The MPD, identified using conventional criteria, is present in about 30% of the cases of PT and 50% of BCS, being this percentage at least similar to that of the whole group of the aforementioned thrombophilic disorders (3). The identification of a MPD in these patients is of paramount importance since the management of this disease is completely different to that of the patients with an abdominal thrombosis without a MPD. However, in this clinical setting the clinical suspicion of a MPD is hampered since the splenomegaly and the anemia induced by hemorrhage may induce normal values in blood cellular counts. This might have been the situation in the case report presented by Chirinos et al. (1) in which hemorrhagic phenomena were the main clinical feature. Thus, it is necessary to routinely evaluate patients with splanchnic thrombosis to rule out an "occult" MPD.

An association between MPD and point mutations in the *JAK2* tyrosine kinase gene has recently been described (4,5). The first mutation to be described, the *JAK2V617F*, has been identified in 90% of patients with polycitemia vera (PV) and in 50% of those with essential thrombocytemia or idiopathic myelofibrosis (6). If the recently described exon 12 mutations are considered, *JAK2* gene mutations are present in virtually all patients with PV, thus constituting a sensitive diagnostic marker of the disease. This has led to a proposal for the modification of the WHO MPD diagnostic criteria, in order to include *JAK2* mutations as major diagnostic criteria (8).

Patients with a MPD and the *JAK2V617F* mutation have an increased risk of thrombosis compared to those without the mutation (6). The *JAK2* mutation even seems to confer some additional risk specifically for the development of splanchnic thrombosis, but not for the rest of locations (9). This mutation has been described in 40-50% of patients with BCS and in 17-36% of patients with PT (10,11). A recent study about patients that had developed a massive abdominal thrombosis leading to a visceral transplantation (liver or bowel) showed a 17% prevalence of the *JAK2* mutation (12). Therefore, in the clinical setting of a patient with splanchnic thrombosis, the detection of *JAK2* mutation may help to the identification of an occult MPD. For instance, in the study of Patel et al. (13) in patients with BCS, the *JAK2* mutation was positive in 24 out of 41 patients, none of them fulfilling the classical MPD diagnostic criteria.

The presence of another thrombophilic factor, as it occurs in these case reports, does not exclude the possibility of finding an associated MPD. In the report by Kiladjian et al. (14), 11% of patients with PT and *JAK2* mutation had an antiphospholipid antibody associated, 8% a protein S deficiency and 5% a factor II G20210A mutation. In the Prigminani et al. report (11), 32.3% of patients with a *JAK2* mutation had another associated thrombophilic disorder. Our group has also described a patient with a BCS who presented an association of the *JAK2V617F* mutation and a factor V Leyden mutation (15).

In conclusion, nowadays, in the etiologic diagnostic work-up of a splanchnic thrombosis, the detection of *JAK2* mutations and mainly the *JAK2V617F*, should be included, even in the presence of other possible etiologic factors and despite there is not any other laboratory parameter to suspect the presence of a MPD (14-16).

G. Plumé G, M. Bustamante-Balén M[1] and A. Vayá

Unit of Thrombosis and Hemostasia. Department of Clinical Biopathology. University Hospital La Fe. Valencia, Spain.
[1]Service of Digestive Medicine. Hospital Ribera. Alzira. Valencia, Spain

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