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LETTER TO THE EDITOR

Molecular analyses in the diagnosis of myeloproliferative neoplasm-related splanchnic vein thrombosis

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Dear Editor,

Myeloproliferative neoplasms (MPNs) are characterized by proliferation of mature blood elements, progressive stromal alterations and/or evolution to acute myeloid leukemia. Significant morbidity and mortality are due to an increased risk of thrombosis, either arterial or venous [1]. Clinical manifestations may vary widely; in particular, venous thrombosis can occur not only in common sites, but also in unusual sites, including cerebral [2] or splanchnic district (SVT), the latter showing a prevalence ranging between 1 and 23 %.

As the occurrence of SVT can be related to MPNs in about half of the cases, the search for JAK2 V617F mutation should be performed in all SVT patients, even in the presence of normal blood cell counts [3, 4]. However, this mutation is not detectable in all MPN patients, rendering this biomarker far from being an optimal diagnostic test in SVT-related MPN cases. Regarding MPL, its mutations have been documented in a significantly lower number of SVT patients [5, 6]. Finally, after the description of calreticulin (CALR) mutations [7, 8], Turon et al. [9] and Haslam et al. [10] have recently evaluated their incidence in two cohorts of SVT patients of different etiologies, but they detected them in only 1.9% and in 0% of all cases, respectively.

To gain further insights, we retrospectively evaluated a consecutive series of 29 patients from our hospital between 1979 and 2013 with a diagnosis of MPN-related SVT.

All our cases were evaluated for JAK2 V617F and MPL mutations. In 27 patients out of 29, JAK2 V617F mutation was detected, and we also evaluated JAK2 allele burden: it varied widely and the median value was 27 % (range 4.8–97 %).

The two JAK2-negative patients were evaluated for MPL mutations, and one of them carried a rare mutant variant, W515K. In the other patient, CALR was subsequently evaluated but did not carry any mutation. All these features are reported in Table 1.

These molecular data are in line with previous findings in the literature and stress the critical role of searching for JAK2 V617F mutation in all SVT patients [3, 4]. However, this diagnostic test alone is not always enough: indeed, two patients of ours did not carry this mutation. As a consequence, in JAK2-negative cases, the next step should be to search for CALR and, if negative, also for MPL mutations, even though in the literature the latter have been reported in only 3.4 % of SVT cases [5, 6, 10].

Furthermore, our data show that JAK2 allele burden varies widely in MPN-related SVT patients, thus not representing a useful tool to distinguish between the different BCR-ABL1-negative MPNs. Regarding CALR mutations, in the only

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Table 1 Clinical and molecular features of 29 patients with MPN-related SVT

Features	Patients (n=29)
Age (years); mean	42
Male sex; *n* (%)	9 (31)
SVT subtype; *n*	PVT 23
	spVT 13
	MVT 7
	BCS 5
JAK2 V617F; *n* (%)	27 (93)
JAK2 allele burden (%); median	27
MPL W515K; *n* (%)	1 (3.5)
Triple negative; *n* (%)	1 (3.5)

PVT portal vein thrombosis, *spVT* splenic vein thrombosis, *MVT* mesenteric vein thrombosis, *BCS* Budd-Chiari syndromes

JAK2- and MPL-negative patient of ours, the CALR gene also resulted in being non-mutated, thus corroborating recent reports of a very low incidence of these mutations in SVT patients [9, 10]. Lastly, our data confirmed previous reports about the low frequency of MPL mutations in such patients [5, 6]; moreover, our case uncovered a very rare mutant variant of this gene, W515K, which was found in only 3 patients out of 305 in a recent meta-analysis [6].

Authorship AI, DC and UG interpreted the data and prepared the manuscript. EF and CA performed laboratory studies. AC revised the data and approved the manuscript.

Conflict of interest All authors disclose no conflicts of interest.

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