



**Figure 2.** Post-transplant liver nodular regenerative hyperplasia. **A:** Two regenerative nodules compressing hepatocytes. A portal area (bottom right) shows moderate fibrosis. (HE, 400x). **B:** Note the absence of inflammatory cells on the boundary between regenerating and compressed hepatocytes. (HE 1000x). **C:** Reticular fibrosis in the compressed areas, revealed by the Gomori's staining (400x).

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## Incidence of factor v leiden and prothrombin G20210A in patients submitted to stem cell transplantation

Factor V Leiden (FVL) and prothrombin G20210A are the most common defects associated with thrombophilia. The purpose of our study was to define the incidence FVL and prothrombin 20210A in a population of patients with hematologic malignancies submitted to high dose chemotherapy and stem cell transplantation and verify the role of these mutations in the development of thrombotic complications during and after transplantation

Sir,

Factor V Leiden (FVL) and prothrombin G20210A are the most frequent mutations associated with inherited thrombophilia. They are fairly common in the general population and exert a substantial risk of development of thromboses during a subject's lifespan. The prevalences of FVL and prothrombin G20210A are 5% and 2%, respectively, in Caucasians<sup>1</sup> and 1.8% and 2.8%, respectively, in the general Italian population.<sup>2,3</sup> The relevance of these mutations prompted us to investigate their prevalence and significance in thrombotic complications after stem cell transplantation (SCT) in patients with hematologic malignancies.

Sixty-nine consecutive patients referred to our Transplant Unit were screened for FVL and prothrombin G20210A mutation. Protein C, S and ATIII deficiency, and antiphospholipid antibodies were excluded in this series of patients. The patients' characteristics are shown in Table 1. Donor-recipient pairs were studied before allogeneic SCT in order to avoid bias from post-transplantation chimerism.<sup>4</sup>

Fifty-four patients are alive after a median follow-up of 31 months (range 10-69). Two out of 69 patients (2.9%) were heterozygotes for these thrombophilic mutations, one for FVL (1.4%) and one for

**Table 1. Characteristics of the patients.**

Patients	69
M/F 32/39	
Median age (range)	41 (17-62)
Diseases	
AML	22
NHL	15
HD	10
MM	17
CML	3
ALL	1
Rabdomyosarcoma	1
Conditioning regimens :	
BuCy2	32
Ida+BuCy2	1
BuMel	21
BEAM	10
ThioMelFlu	5
Type of transplantation:	
allogeneic SCT	23
autologous SCT	46

prothrombin G20210A (1.4%). The overall crude incidence of deep venous thrombosis (DVT) during and after SCT in this series was 4.3%.

Two episodes of DVT and 1 episode of pulmonary embolism (PE) were recorded. One of these episodes of DVT was felt to be related to the indwelling central venous catheter (CVC). This patient with acute myeloid leukemia developed thrombosis of the left subclavian vein, ipsilateral to the CVC, during the recovery phase after alloSCT. Fatal PE was diagnosed post-mortem in a patient with Ph+ acute lymphocytic leukemia one year after transplantation. Venooclusive disease (VOD) was observed in only 1 patient (1.4%).

In this study the prevalence of both FVL and prothrombin G20210A mutations was 1.4%, this being comparable to the prevalences in a general Italian population.<sup>2,3</sup> In patients developing VOD after SCT, Duggan *et al.*<sup>5</sup> found an increased risk of VOD in patients who were heterozygous for prothrombin G20210A but not in those heterozygous for FVL. In our series the incidence of VOD was too low to allow any conclusion, according to the survey by Carreras.<sup>6</sup> Interestingly a high incidence of VOD has been recently observed in female patients submitted to SCT receiving norethisterone.<sup>7</sup> This study comes from Sweden where the incidence of FVL is even higher than in other Western countries. The two patients in our series carrying the mutations did not develop thrombotic complications before, during or after transplantation; one of them developed a DVT when she started hormone replacement therapy (HRT) during long-term follow-up. Use of oral contraceptives, omitted in our female patients during transplantation,<sup>8</sup> adds to the risk of thrombosis in patients with inherited thrombophilia.

The overall incidence of thrombotic complications in our series was 4.3% and this result is comparable to that observed by Sgarabotto *et al.*<sup>9</sup> but inherited thrombophilia was present in only 1 out of the 3 patients who developed thrombotic complications.

We consider that comprehensive screening for inherited thrombophilia is not justified before SCT and is not cost-effective. The incidence of thrombotic events including VOD is low in this population and comparable to that in non-transplanted patients. In contrast, when HRT is being considered for a young female with early menopause induced by chemoradiotherapy, accurate investigations for inherited thrombophilia should be carried out in order to avoid thrombotic complications.

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### Key words

Factor V Leiden- Prothrombin G20210A- VOD- stem cell transplantation-thrombosis

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