to chemotherapy. No differences were found in the length of time until TPN was started in any group. Recovery of the neutrophil count to over 500 cells/mm^3 occurred at day 16.7±3.2, 16.9±3.1 and 20.3± 2.3 in the GLN, WP, and DXM groups, respectively. There were no significant differences in the incidence, severity or duration of GI toxicity (Table 1), nor in serum proteins during this study (Table 2). Their concentration decreased significantly in the three groups from day 1 to day 14. Gln levels did not differ among the three groups, nor did they change during the treatment.

In conclusion, our results do not prove the usefulness of oral Gln for preventing GI toxicity associated with chemotherapy for autologous hematopoietic transplantation in AHT. The timing and the dosage of oral Gln should be reassessed to find more evidence of clinically significant results. After considering the results published with parenteral and oral GLn supplements, it could be argued that parenteral Gln may be more efficacious than oral Gln, but a comparative trial to test this hypothesis has not yet been performed.

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A boy with venous thrombosis, homozygous for factor V Leiden, prothrombin G20210A and MTHFR C667T mutations, but belonging to an asymptomatic family

We evaluated a 9-year old boy presenting with deep venous thrombosis who was homozygous for factor V Leiden, prothrombin 20210A and methylenetetrahydrofolate reductase C677T mutations. All of his relatives who were either triple- or double-heterozygotes were asymptomatic. This observation indicates that thrombophilia is a complex genetic disorder and there is great deal more to be learned about this disease.

Sir,

Familial thrombophilia is a complex genetic disorder often caused by the joint action of two or more mutant genes. Individuals with these combined genetic defects are at higher risk of thrombosis than those with a single gene mutation.[1] Double-heterozygosity for factor V Leiden (FVL) and G20210A in the prothrombin gene (PT 20210A) is the most common combination.[2,3] Moreover, we have recently demonstrated, by both linkage and association studies, that the C677T polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene has a direct effect on homocysteine levels, suggesting that this polymorphism might be a genetic risk factor for thrombosis.[4] Here, we present the case of a 9-year old boy who presented with a first episode of idiopathic right popliteal deep venous thrombosis (objectively confirmed by Doppler ultrasound). This boy had never been exposed to any environmental risk factors for thrombosis. Plasma laboratory studies for thrombophilic disorders showed only a 1.3 pathologic value for resistance to activated protein C ratio (Coatest APC resistance Kit from Chromogenix) according to Dahlbäck *et al.*[5] Genetic analysis of this patient (individual IV-1 in Figures 1A and 1B) showed triple-homozygosity for FVL, PT20210 and C677T MTHFR mutations. Figure 2 shows the genetic status of these three mutations in the rest of the family members. It is important to note that the parents of the propositus were first cousins (Figure 2). Significantly, none of his relatives had a history of venous or arterial thrombosis, despite the fact that his mother and grandmother had had two and three pregnancies and deliveries, respectively, and his grandfather had died from lung cancer. Therefore, the combined carrier state in this family is apparently not associated with a high risk of venous or arterial thrombo-

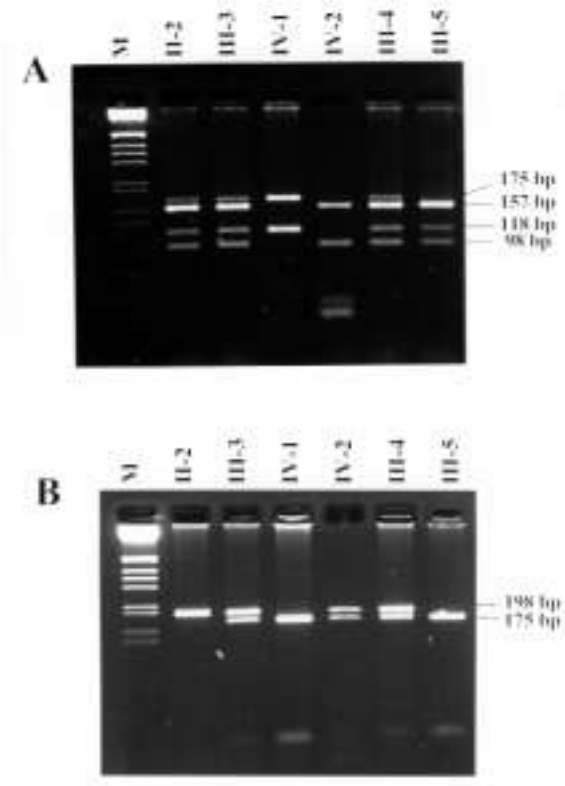

Figure 1. A. Familial segregation of the FVL and PT20210A mutations. A new Taq I site is introduced into the 175 bp amplified fragment when the FVL mutation is present, and a new Taq I site is introduced into the 118 bp amplified fragment when the PT20210A allele is present. These digestions yield two fragments of 157 bp and 18 bp for FVL, and 98 bp and 20 bp for the PT20210A. The smallest bands are out of the agarose gel. B. Familial segregation of the C667T MTHFR mutation. The 198 bp product was digested with Hinf I, yielding two fragments of 175 bp and 23 bp when the 667T allele was present. The small band is out of the agarose gel. M is the 1 Kb ladder molecular weight marker in both digestions.

sis, since only the triple-homozygous patient had experienced thrombotic disease. Two patients who were double-homozygotes for FVL and PT20210 mutations have been reported.[6,7] In one of these cases, the 34-year old propositus was the only family member with venous thrombosis, despite the fact that his double-heterozygote father died of myocardial infarction at the age of 57 and a son died from cotdeath.[6] The other case was a 18-year-old man with superficial thrombosis. His double-heterozygote father had a history of recurrent deep venous thrombosis and a sister had a saphenous vein thrombosis.[7] It has been reported[8] that double-heretozygous FVL-PT20210A subjects have an increased risk of thrombosis, presumably because of a synergistic effect between these two

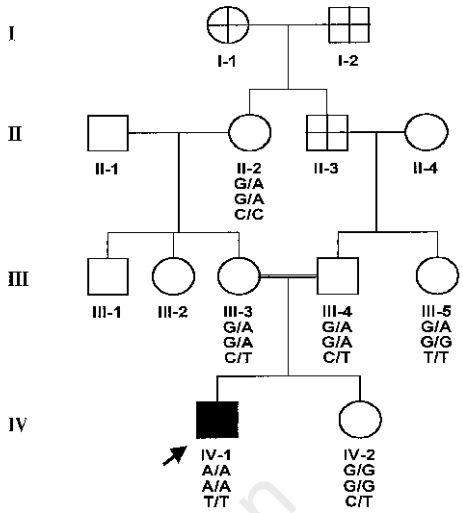

Figure 2. Pedigree of the reported family: the proband is indicated by an arrow. The genotype for FVL, PT20210A and C667T MTHFR mutations present in family members are also shown in descending order under his/her symbol. The solid-black symbol indicates thrombotic disease, and a cross inside the symbol indicates death.

mutations. This could explain the clinical manifestations in these patients, but these conjectures do not explain why our triple and double-heretozygous individuals were asymptomatic, whereas the double-heretozygotes (FVL-PT20210) in other families were reported to be symptomatic. It seems that there are unknown genetic risk factors for thrombosis in these families that do not cosegregate in our family. Further large cohort studies (case-control) will be required to investigate the interaction of these genetic factors with each other and with environmental factors. This family also illustrates an important medical problem that results when screening patients with venous thrombosis for thrombophilic factors. This problem is to recognize the potential risk in asymptomatic family members. Further studies, such as prospective studies in non-treated asymptomatic subjects with thrombophilic defects, should be carried out to give clear guidance on the optimum management of clinically unaffected carriers.

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