autoimmune disease and mouth ulcers in carriers.[4,5] Yet, a very recent report describes the occurrence of retinal lesions in patients as well as in carriers.[6] Thus a reliable screening of carriers of CGD may give us a better understanding of the natural history of non-infective manifestations of CGD and potentially provide new insights into the clinical spectrum of CGD, its pathogenesis and ways to treat it.

The diagnosis of CGD and carrier status routinely relies upon the demonstration of an absent or greatly diminished neutrophil respiratory burst. For initial screening,the NBT slide test is rapid and relatively simple. For confirmation, a quantitative test of the respiratory burst is deemed necessary.[7] Identification of the specific genetic subgroup for a patient is required for purposes of genetic counselling and prenatal diagnosis. Although this report of one case provides only limited information, it suggests that quantitative tests might fail to detect X-linked CGD carriers in late pregnancy. Production of reactive oxygen intermediates has been reported to be higher in pregnant women during the peripartal period than in early pregnancy or in non-pregnant women.[8,9] Accordingly, it is possible that an apparently normal oxidative burst activity might have been achieved in our 38-week pregnant carrier by enhanced activity of the normal population of cells. At any rate,whatever the mechanism(s) accounting for the present findings, we hope the information given here will alert the readers to the reliability of neutrophil function screening tests in identifying maternal CGD carrier status in pregnancy. These issues need to be investigated further in women throughout their pregnancies.

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Key words

X-linked CGD carrier, pregnancy, oxidative burst activity.

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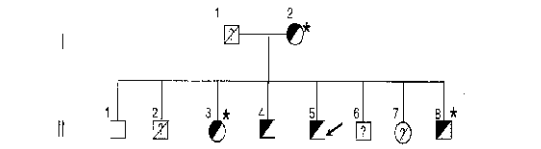
Factor V Leiden in absence of activated protein C resistance after orthotopic liver transplantation in a patient without thrombosis but with familial thrombophilia

There are reports that orthotopic liver transplantation may produce phenotypic correction of activated protein C (APC) resistance in patients with FV Leiden. We report the case of a factor V Leiden heterozygote with absence of APC reistance following an orthotopic liver transplantation. The patient suffered not thrombotic episodes prior to or after the transplant despite a strong history of familial thrombophilia.

Sir,

We report a heterozygous FV Leiden individual with absence of activated protein C (APC) resistance following orthotopic liver transplantation. APC resistance is associated with a mutation in factor V gene, named FV Leiden.[1,2] APC resistance is defined as a poor anticoagulant response of the patient's plasma to APC. Some patients with APC resistance do not have the FV Leiden, and this suggests the existence of an acquired APC resistance phenotype.[3] However, the existence of the FV mutation without APC resistance is a rare cause of discrepancy between the genotypic and phenotypic analyses.[4,5]

The propositus (II-5) (Figure 1) is a 48-year old man with a family history of thrombosis but with no personal history of deep venous thrombosis (DVT). He underwent orthotopic liver transplantation in 1994 because of alcoholic cirrhosis. Figure 1 shows the pedigree of the family. The father of the propositus (I-1) died at the age of 55 probably as a result of cerebral thrombosis. The mother of the propositus (I-2), aged 77, developed cerebrovascular ischemia at the age of 73. The propositus's sister (II-3) had a DVT at 29 in puerperium and one of his brothers (II-8) had a DVT and pulmonary embolism at the age of 37



Subject	Age (y)	thrombosis	(APTT-APC)/APTT ratio	APCr	FV Leiden	AT activity(%)	AT antigen (%)
I-2	77	CVD (73y)	1.80	+	+/-	45	56
II-1	57	No thrombosis	3.07	-	-/-	111	90
II-3	54	DVT (29y)	1.86	+	+/-	58	60
II-4	52	No thrombosis	1.96	+	-/-	73	73
II-5	48	No thrombosis	2.75	-	-/-	103	77
II-8	39	DVT+PE(37 y)	1.93	+	-/-	43	60
Normal			2.13-3.57	-	-/-	70-120	70-120

CVD=Cerebrovascular disease DVT= deep vein thrombosis PE=Pulmonary embolism

after acute pyelonephritis. The propositus (II-5) and four relatives (I-2, II-3, II-4, II-8) were identified as heterozygous carriers of FV Leiden. All of the FV Leiden family members except the propositus have APC-resistance. The relatives with thrombotic disease have combined heterozygous FV Leiden and antithrombin deficiency type I (I-2, II-3, II-8). The presence of other thrombophilic risk factors was excluded.

The modified APC-resistance assay was performed as reported elsewhere.[6] The FV Leiden mutation was studied as previously described.[7] Antithrombin antigen was measured by radial immunodiffusion. Antithrombin activity was measured using the Coamatic Antithrombin Kit (Chromogenix AB, Mölndal, Sweden).

Some cases of heterozygous FV Leiden subjects with phenotypic correction of APC resistance by orthotopic liver transplantation have been reported.[4,5,8] In one of them, the presence of FV Leiden did not result in thrombosis either before or after liver transplantation.[4] In other cases, the patients suffered thrombosis before or after liver transplantation, despite the phenotypic correction of APC-resistance.[5,8]

Our patient had no personal history of thrombosis and his relatives who have suffered thrombosis have combined FV Leiden and antithrombin deficiencies. Familial thrombophilia is considered a complex genetic disorder frequently caused by the segregation of two or more gene defects, and the thrombotic events are more frequent with two or more thrombophilic risk factors.

Coagulation FV is distributed between two blood pools (80% in plasma and 20% in platelets) and at the site of vascular injury the concentration of platelet FV is more than 600 times higher than that of plasma FV within the platelet aggregate.[9] Plasma FV is synthesized in the liver, but although the origin of platelet FV had been previously established as being endogenous synthesis in the megakaryocyte, recently, Camire *et al.*[8] showed that the majority of platelet FV is endocytosed by megakaryocytes from plasma.

Previous reports suggest that although liver transplantation may lead to the disappearance of APC-resistance in plasma, the platelet-derived FV Leiden can contribute to the persistence of the prothrombotic state.[4,5] However, because most of platelet FV is endocytosed by megakaryocytes,[8] we believe that the plasma correction of APC-resistance and the normalization of platelet FV after liver transplantation in a patient with FV Leiden could help to correct the prothrombotic state. In the cases of thrombosis after liver transplantation the presence of another thrombotic risk factor cannot be ruled out.

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Key words

Factor V Leiden, liver transplantation, familial thrombophilia.

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