

## Case reports

# It is time to adopt a strategy of routine some thrombophilias screening in women with a confirmed history of venous thromboembolism or recurrent fetal loss

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Vascular disease in pregnancy is a rare event. Inherited risk factors for vascular disease include factor V Leiden, prothrombin, methylenetetrahydrofolate reductase point mutations and Antithrombin, protein C and S deficiencies. Recent studies suggest that there is also a link between these inherited thrombophilias and adverse pregnancy complications such as fetal loss as well as venous thromboembolism. Here we describe 2 young patients with cerebrovascular thrombotic events whose only risk factor was genetic thrombophilia. In patients, complete clinical evaluation and laboratory investigations, including a thrombophilia workup and full radiological assessment, were performed. Recently genetic thrombophilia was reported in association with venous thromboembolism and various complications of pregnancy. Although it is rare, thrombophilia must not be misdiagnosed.

**Key words:** Cerebral venous thrombosis, deep vein thrombosis, factor V Leiden, gestation, pregnancy losses.

## INTRODUCTION

Recent studies suggest that there is a link between thrombophilia and gestational vascular complications, as well as other complications such as pregnancy loss.

Approximately 50% of gestational venous thromboembolism (VTE) is associated with thrombophilia and this condition remains an important cause of maternal morbidity and mortality (De Stefano et al., 2006; Gumus et al., 2008).

There is substantial interest in examining whether heritable thrombophilias are also associated with adverse pregnancy outcomes, and whether this can be ameliorated by antithrombotic therapy (Bates, 2007). We present such two cases of venous thromboembolism and pregnancy losses in association with genetic thrombophilia.

## Case reports

We report on two young women with cerebral venous thromboembolism (CVT) resulting in significant morbidity and without a family history of venous thromboembolism.

The first case was a 36-year-old female patient with a prior history of recurrent late pregnancy losses. There was no other past medical, surgical, obstetric or gynaecological history of note.

The second case was a 31-year-old woman. She developed CVT at 28 weeks of gestation. Her past medical history included deep vein thrombosis (DVT) of the lower-extremity (four years ago) but at that time, the patient was not evaluated for hypercoagulable states and other extensive examinations did not reveal any known cause.

On the other hand, thrombophilia workup was performed (testing for functional deficiencies of protein C, protein S, and Antithrombin and antiphospholipid

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syndrome screen including IgG and IgM anticardiolipin antibody).

Genotyping of thrombophilia polymorphism was done: Deoxyribonucleic acid (DNA) was extracted from the sample according to the extraction protocol supplied by the manufacturer. Hybridization of the amplified product was then conducted.

Both patients were found to be homozygous for factor V Leiden, a condition undetected until CVT occurred. They were successfully treated with low-molecular weight heparin and antibiotics. The second case had a term vaginal delivery.

## DISCUSSION

Our patients suffered from a known abnormality of hemostasis associated with pathological thrombus formation caused by a mutation in the gene coding factor V, also known as factor V Leiden. A single point mutation results in the substitution of arginine (Arg) at position 506 by glutamine (Gln) (Saini et al., 2005).

Pregnancy is associated with changes in haemostasis, including an increase in the majority of clotting factors, a decrease in the quantity of natural anticoagulants and a reduction in fibrinolytic activity. These changes result in a state of hypercoagulability, are likely due to hormonal changes and increase the risk of thromboembolism (Thornton and Joanne, 2005).

The relationship between CVT and thrombophilia has been recognized (Trevor et al., 2010), but only recently it was understood that certain hemostatic factors affect not only VTE, but have also a direct effect on obstetric complications such as pregnancy loss (Robertson et al., 2005). The extent to which thrombophilia influences the risk of gestational pathologies remains somewhat uncertain. There is substantial interest in examining whether heritable thrombophilias are also associated with adverse pregnancy outcomes, and whether this can be ameliorated by antithrombotic therapy (Bates, 2007).

Severe thrombophilias (for example antithrombin deficiency, homozygosity for factor V Leiden and V Leiden/prothrombin mutation double heterozygotes) may have a higher absolute risk of pregnancy-associated thrombosis (Bates, 2007). Approximately 50% of gestational VTE are associated with thrombophilia (De Stefano et al., 2006; Gumus et al., 2008).

A recent study found that 3 of 19 (15.8%) women with homozygous factor V Leiden developed pregnancy-associated venous thrombosis (Martinelli et al., 2001). These at-risk women cannot be efficiently identified without adopting a strategy of routine testing (Merriman and Greaves, 2006).

## Conclusion

There is a link not only between inherited thrombophilias and VTE but also with adverse pregnancy complications. The lesson to be learned from these cases is that young patients who experience recurrent pregnancy losses should be tested for thrombophilia. Pregnant women may need to be screened based on the aforementioned factors. If detected immediate therapy should be started to avoid a devastating outcome.

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