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CLINICAL SCIENCE

Influence of factor V Leiden on the development of neovascularisation secondary to central retinal vein occlusion

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Aims: To investigate if the presence of factor V Leiden has an influence on the prognosis in central retinal vein occlusion (CRVO).

Methods: 166 patients with CRVO were studied retrospectively. They were tested for factor V Leiden using DNA analysis. The presence of the mutation was studied in correlation with the development of neovascular complications 1 year after the thrombotic event.

Results: 56 of 166 patients (34%) developed neovascular complications after 1 year. In the patients who had the studied mutation 11 of 20 (55%) had developed neovascular complications after 1 year, compared to 45 of 146 patients (31%) in the group without factor V Leiden ($p=0.04$).

Conclusion: The presence of factor V Leiden seems to enhance the risk of developing neovascular complications in CRVO.

Glaucoma, hypertension, arteriosclerosis, and diabetes are factors that are well known to be associated with central retinal vein occlusion (CRVO). These conditions affect vascular flow or cause vascular wall abnormalities, thereby contributing to the development of CRVO.^{1–5}

Hereditary alterations in the coagulation/anticoagulation pathways can result in thrombophilia, increasing the risk for thrombosis.^{6–7} It is, however, debatable whether hereditary alterations in the coagulation pathway are aetiological factors for CRVO.

Activated protein C resistance is the most common genetic cause of venous thrombosis.⁶ A point mutation in factor V (factor V Leiden) renders it resistant to the normal inactivation by activated protein C. This “activated protein C resistance” produces a mild thrombophilic state. There are studies in the literature pointing towards an association between CRVO and factor V Leiden,^{8–12} though most of the evidence today indicates that factor V Leiden does not have a major aetiological role in CRVO.^{13–22}

After thrombus formation, independent of cause, a restoration of the venous lumen can occur spontaneously.^{23–24} We do not know the exact mechanism of this recanalisation, but it could be related to the balance of coagulation/anticoagulation.²⁵ We stated the hypothesis that even though factor V Leiden has not been found to be an important risk factor for CRVO, it may have a more important role during the recanalisation phase after the thrombotic event. We wanted to investigate if the factor V Leiden influences the prognosis in CRVO, and so studied the prevalence of factor V Leiden in relation to the development of neovascular complications after CRVO.

PATIENTS AND METHODS

Patients

A total of 190 consecutive patients with CRVO examined in the eye clinic of Lund University Hospital from 1994 to 2000 were invited to take part in the study; of these, 166 patients agreed to participate. Venous blood samples were collected after informed consent was obtained. Of the 166 patients, 86 were men and 80 were women. The patients were aged between 22 and 91 years (mean age 64 (SD 15) years).

All patients were followed for at least 1 year. This time was chosen as we know that the majority of the patients who develop neovascular complications after CRVO have done so within this time period.^{26–29} The end point was the development of neovascular complications or not, 1 year after the thrombotic event. Neovascular complications were defined as any retinal, disc, iris, or chamber angle neovascularisations. Clinical information was derived from the patient records.

DNA analysis

Preparation of genomic DNA from EDTA blood and determination of the factor V Leiden mutation (G to A at nucleotide position 1691), which causes activated protein C resistance, was performed as described earlier.³⁰

RESULTS

After a year 56 of 166 patients (34%) had developed neovascular complications. Factor V Leiden was present in 20 of 166 patients (12%). The patients with factor V Leiden did not significantly differ in age or sex compared to the patients without the studied mutation. The patients with factor V Leiden, 10 men and 10 women, ranged in age between 22 and 86 years (mean 58 years; median 64 years). The patients without factor V Leiden, 76 men and 70 women, ranged in age between 28 and 91 years (mean 65 years; median 68 years).

In the patients with factor V Leiden, 11 of 20 (55%) developed neovascular complications. In the patients without the mutation 45 of 146 patients (31%) developed neovascular complications ($p=0.04$; Fischer's exact test) (Fig 1). This gives an odds ratio of 2.7 (CI 95% 1.1 to 7.1).

DISCUSSION

In this study we have shown that the presence of factor V Leiden seems to increase the risk for neovascularisation secondary to CRVO.

The presence of factor V Leiden results in a mildly thrombophilic state. Although it has not been found to be an important risk factor for CRVO,^{13–22} it is possible that factor V Leiden may have a more important role in the recirculation phase after the thrombotic event. The mild predominance of coagulation over anticoagulation may contribute to a delayed

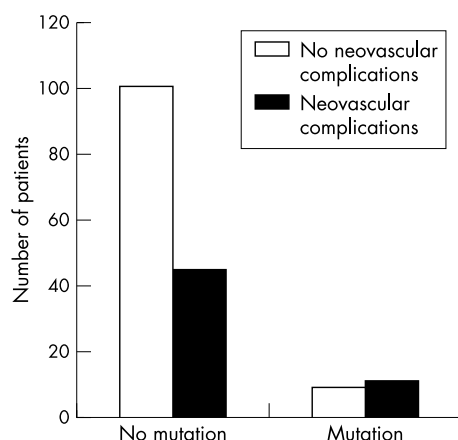


Figure 1 The presence of factor V Leiden correlated with the development of neovascular complication in CRVO. The result points towards an almost threefold risk of developing complications with the mutation present.

recirculation, and thereby possibly a more severe ischaemia resulting in a higher risk for neovascular complications. Our study points towards an almost threefold risk of developing neovascular complications after CRVO with factor V Leiden present. We have not seen other studies in the literature regarding factor V Leiden and the prognosis for CRVO.

As the presence of the studied mutation is independent of the time of the blood sample, this has enabled us to supplement the DNA tests independent of time for follow up. Since it is well established that the most important risk factor for the development of neovascular complications after CRVO is the extent of retinal ischaemia,^{2-29 31 32} it would have been of interest to see if the patients presenting with factor V Leiden mutation showed a more pronounced retinal ischaemia, as detected by fluorescein angiography, but a weakness of this study being retrospective is that this information is not complete. This would preferably be dealt with in another prospective study.

The incidence of neovascular complications in our patients during the first year after the thrombotic event is in accordance with earlier reports.^{26-29 31 32} The prevalence of factor V Leiden is also at the level expected in the normal population in the studied area,⁶ which confirms that factor V Leiden probably does not have an important aetiological role in CRVO, as pointed out earlier.¹³⁻²²

In conclusion, the presence of factor V Leiden seems to enhance the risk of developing neovascular complications in CRVO.

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