

33. Eye (central retinal vein thrombosis) and factor F V Leiden

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Q: "I am in my late forties and have recently been diagnosed with heterozygous factor V Leiden. It began with an eye problem (extreme blurriness) and I saw a retinal specialist who diagnosed central vein occlusion. He felt it may not be a clot, but the anatomy of the vein and artery: they are touching, creating pressure in the vein and a subsequent leak from increased pressure. I have stopped estrogen therapy. I am taking one ASA daily, but now the hematologist suggests maybe Coumadin®. No doctor seems to have an answer about what caused this eye problem and how to handle the FVL. I do not know to whom to listen.

A: Unfortunately, little has been studied about central retinal vein thrombosis, and there are no answers to many of the important questions. Judging from venous blood clots in other anatomic areas, such as the deep veins of the legs, estrogen therapy and factor V Leiden may play a role in causing central retinal vein thrombosis, and aspirin may not be beneficial. The role of warfarin (=Coumadin) has not been examined and is unclear.

Thrombosis in the retinal veins is often thought to occur due to pressure of the overlying artery onto the vein, leading to compression of the vein, decreased blood flow in the vein, and then thrombosis. The role of factor V Leiden in causing central retinal vein thrombosis is not clear. Several studies have shown that there is no association between factor V Leiden and central retinal vein thrombosis [Blood Coag Fibrinol 1998;9:617-622; Retina 1998;18:308-315], one study suggested that there might be an association [Br J Ophthalmol 1996;80:203-208]. It appears fair to conclude, that the role of factor V Leiden in this disorder is not clear, but that it is probably not a major risk factor. Known risk factors for retinal vein thrombosis are:

- high blood pressure;
- elevated homocysteine levels [Ann Intern Med 1999;130:78];
- family history of high blood pressure or stroke;
- blood disorders causing "hyperviscosity", a condition in which the blood is too thick and the blood flow is slowed (such as polycythemia vera, multiple myeloma)
- increased intraocular pressure;
- possibly diabetes mellitus.

At the time of acute central retinal vein occlusion there is often associated bleeding into the retina. It is mainly the bleeding that causes the visual loss. Since the blood can be absorbed, there may be improvement of vision over the weeks and months following the event. From a theoretical point of view, a "blood thinner" such as warfarin may worsen the bleeding and therefore the visual loss. And indeed, a small study suggested that warfarin may be detrimental [Nippon Ganka Gakkai Zasshi Acta Societatis Ophthalmologicae Japonicae;1995:99:955-8]. Heparin or warfarin is therefore usually not given in this condition. However, good controlled studies examining heparin or warfarin in this disorder have, not been performed. Anecdotal evidence indicates that warfarin may be beneficial in some patients. The role of heparin and warfarin clearly needs to be examined in a prospective, controlled study. The role of Aspirin or Plavix has also not been examined. Since the clotting problem is in the veins, Aspirin and Plavix are unlikely to be very effective in improving symptoms or preventing recurrences (see Q/A 35). The risk of recurrence of central retinal vein thrombosis has, to my knowledge, also not been studied.

Comment: Realizing that we lack a lot of data, this is what I do in clinical practice, when I see a patient with central retinal vein thrombosis. I obtain the following laboratory tests:

- antiphospholipid antibodies (= anticardiolipin antibodies and lupus anticoagulant)
- factor V Leiden
- prothrombin 20210 mutation
- protein C activity
- protein S activity and total and free antigen
- fasting homocysteine levels
- serum viscosity
- complete blood count (CBC)
- sedimentation rate

At present, in most patients with central retinal vein thrombosis, I do not recommend warfarin (= coumadin). However, I consider warfarin in the patient who has clearly positive antiphospholipid antibodies and no other risk factors for the thrombosis, particularly if that patient has had recurrent central retinal vein thrombosis.

References:

1. Blood Coag Fibrinol 1998;9:617-622
2. Retina 1998;18:308-315
3. Br J Ophthalmol 1996;80:203-208
4. Ann Intern Med 1999;130:78
5. Nippon Ganka Gakkai Zasshi Acta Societatis Ophthalmologicae Japonicae;1995;99:955-8