Ocular artery thrombosis as an initial presentation of a prothrombin G20210A mutation

Occlusion de l’artère centrale de la rétine révélant une mutation G20210A du gène de la prothrombine

C. Parc*, E. Tiberghien, V. Pierre-Kahn

Service d’ophtalmologie, hôpital Foch, 40, rue Worth, 92150 Suresnes, France

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SUMMARY

The G20210A mutation in the prothrombin gene is an established risk factor for venous thrombosis. There is controversy as to the role played by this mutation in arterial thrombotic disease. We present the case of a 56-year-old man who presented with a central retinal artery occlusion of the left eye. Evaluation revealed hypercholesterolemia, smoking, and heterozygosity for the prothrombin G20210A mutation. The literature concerning hereditary thrombophilia and retinal artery occlusion was reviewed. The synergistic effect of multiple risk factors is emphasized. Screening for hereditary thrombophilia should be considered, regardless of patient age. The prothrombin G20210A mutation may be associated with central retinal artery occlusion.

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MOTS CLÉS

Mutation G20210A ; Occlusion de l’artère centrale de la rétine ; Prothrombine

Résumé

La mutation G20210A du gène de la prothrombine constitue un facteur de risque connu de thromboses veineuses. Son rôle dans la survenue des pathologies thrombotiques artérielles est controversé. Nous présentons le cas d’un homme de 56 ans ayant présenté une occlusion de l’artère centrale de la rétine de l’œil gauche. Le bilan a mis en évidence une hypercholestérolémie, un tabagisme modéré et une mutation hétérozygote G20210A du gène de la prothrombine. La littérature concernant les thrombophilies héréditaires et les occlusions de l’artère centrale de la rétine a été revue. L’effet synergique des risques facteurs

* Corresponding author.
E-mail address: c.parc@hospitafoch.org (C. Parc).

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Introduction

Central retinal artery occlusion (CRAO) is an acute event, often leading to irreversible loss of vision. It is caused primarily by emboli originating from atheromatous plaques in the carotid arteries or a cardiac source [1]. We evaluated a 56-year-old man with CRAO and found no thromboemboli or cholesterol emboli, but did find the G20210A mutation in the prothrombin gene.

The G20210A mutation in the prothrombin gene is an established risk factor for venous thrombosis [2], and there is controversy as to the role played by this mutation in arterial thrombotic disease and atherosclerosis [2].

Case report

A 56-year-old man presented with acute loss of vision in the left eye. He had a history of transient loss of vision of the same eye 5 years prior, for which he commenced long-term aspirin therapy. Ophthalmologic examination revealed visual acuity to be 20/20 in the right eye and finger counting in the left eye. In the left eye, a relative afferent pupillary defect was present. The anterior segment was normal. Fundoscopic examination showed whitening of the retina at the posterior pole with a cherry red spot (Fig. 1). A presumptive diagnosis of CRAO of the left eye was made. Delay in arteriovenous transit time was observed with fluorescein angiography. Doppler ultrasonography of the carotid arteries and of the orbits was normal. Both transthoracic and transesophageal echocardiographic examinations were negative for the presence of valvular disease, cardiac thrombi, aortic arch plaques, or a patent foramen ovale. Computed tomography angiography of the cerebral vasculature was normal. The patient was evaluated for a systemic etiology to explain the local thrombotic event, including testing for the common vascular risk factors and for thrombophilias. He was found to have two vascular risk factors: moderate hypercholesterolemia and a history of cigarette smoking. The triglyceride level was normal, and he did not have hypertension. Glycemic control was normal. A complete blood count was performed with normal results. Screening for thrombophilia included tests for protein C, protein S, free proteins, antithrombin III, circulating anti-coagulant, anticardiolipin antibodies, activated protein C resistance, thermodatable methylene tetrahydrofolate reductase (MTHFR), fasting plasma homocysteine, and factor V Leiden and prothrombin G20210A polymorphisms. The only abnormality found was a heterozygous mutation for prothrombin G20210A. There were no features of autoimmune disease, such as arthritis, oral ulcers, or systemic vasculitis.

The patient was discharged home with the same visual acuity. His INR was maintained at 2–3. After 20 months of follow-up he had no evidence of recurrent thromboembolism.

Discussion

CRAO and branch retinal artery occlusion (BRAO) are frequently caused by thromboemboli or cholesterol emboli originating in atherosclerotic plaques of the carotid arteries, or by emboli originating in the heart [3]. Nearly one-half of patients will have cardiac pathology found by transthoracic echocardiography [4]. In our case, no embolic source was found.

Risk factors for CRAO include vascular risk factors, and this patient had two risk factors: hypercholesterolemia and smoking.

Causes of in situ thrombosis due to arterial wall disease were considered, in addition to potential inherited or acquired causes for local thrombosis. Screening for thrombophilia in patients with retinal artery occlusion in whom no embolic source is identified is advisable even when vascular risk factors are present because there appears to be an interaction between vasculopathic and thrombogenic risk factors [3].

Van Cott determined that an extended panel of laboratory tests improved the detection of a hypercoagulable state in ocular thromboses [5]. The prothrombin G20210A mutation and hyperhomocysteinemia were significantly more frequent in patients with ocular thrombosis compared to controls [5].
Mutations in certain genes of coagulation factors may lead to higher levels or an altered function of these coagulation proteins. As a result, these mutations might be risk factors for atherosclerosis and its clinical complications. The mutation was found in the 3′ untranslated region of the prothrombin gene. A G→A transition of nucleotide 20210 is associated with higher prothrombin clotting activity and a two- to four-fold higher risk for venous thrombosis [2].

The prothrombin G20210A mutation causes a procoagulant state and is well-known as a risk factor of central retinal vein occlusion [2]. Its role in the pathogenesis of retinal artery occlusion is still unclear [2]. Salomon et al. [3] found that five types of thrombophilia were found in 43% of patients with retinal artery occlusion in whom no embolic source was demonstrated by imaging examinations: the MTHFR C677T mutation, the factor V G1691A heterozygous mutation, a high titre of IgM antiphospholipid, lupus anticoagulant, and hyperhomocysteinemia. The prothrombin G20210A mutation was rare and was not a significant risk factor for thrombophilia in that study. In 2007, Marcucci et al. evaluated the cardiovascular and thrombophilic risk factors in patients with retinal artery occlusion [6] compared to a control group. The authors highlighted the increased prevalence of hypercholesterolemia, smoking, and the “thrombophilic burden” in patients with CRAO. Thrombophilic risk factors examined in that study were hyperhomocysteinemia, anticardiolipin positivity, lupus anticoagulant positivity, lipoprotein(a) greater than 300 mg/l, factor VIII greater than 150%, plasminogen activator inhibitor-1 greater than 15 IU/ml, and heterozygosity for factor II G20210A. Independent risk factors for CRAO were smoking, hypercholesterolemia, hyperhomocysteinemia and elevated lipoprotein(a) levels. The factor II G20210A was not found to be an independent risk factor for CRAO.

Ben-Ami et al. [4] reported that the prothrombin G20210A mutation should be added to the list of thrombophilic states implicated in CRAO.

The prothrombin G20210A mutation has been associated with the factor V Leiden R506Q mutation [7], but in our case, the prothrombin G20210A mutation was isolated, i.e., without any other thrombophilia. We found no other case of isolated prothrombin G20210A mutation in CRAO in the literature. Gerdes’ study suggested that the G20210A mutation contributes to the process of arterial wall thickening and is associated with the occurrence of ischemic events in a cohort of elderly persons with atherosclerosis [2]. The synergistic effect of multiple risk factors is emphasized [4].

The therapeutic approach suggested by Marcucci et al. included the treatment of hypercholesterolemia and smoking, and the introduction of an antithrombotic treatment, especially in patients with a combination of risk factors [6]. We found no evaluation of the efficiency of the therapeutic measures reported in the literature.

**Conclusion**

Screening for hereditary thrombophilia should be considered, regardless of patient age, in patients with retinal artery occlusion in whom no embolic source is identified. The prothrombin G20210A mutation, a genetic risk factor, may be associated with CRAO. Therapeutic measures should include antithrombotic treatment and the correction of cardiovascular risk factors.

**Conflicts of interest**

None.

**References**


