Plasminogen activator inhibitor-1 4G/5G polymorphism and dyslipidemia with branch retinal artery occlusion in a young lady

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Abstract:
Branch retinal artery occlusion (BRAO) leads to obstruction of blood flow in the distribution of the affected vessel giving rise to ischemia and reorganization of the retinal layers. It is a very rare diagnosis and the etiological risk factors of BRAO are not clear in the young population. Various hypercoagulable states leading to thrombosis appeared to be more responsible. Here, the authors present an interesting case of a 25-year-old female patient with BRAO accompanying with plasminogen activator inhibitor-1 (PAI-1) 4G/5G gene polymorphism and dyslipidemia together, for the first time. There was a history of sudden painless blurred vision in her right eye 3 months ago. Her visual acuity was 20/20 in both eyes at the admission. Fundus photo, red-free photo, optical coherence tomography images of 3 months ago revealed BRAO in the right eye. Fundus exam and images taken at the 3th month confirmed the recovery of retinal edema. Attenuation of inferotemporal retinal artery still mildly appeared. Applied confrontation fields showed a visual field defect corresponding with affected area. Ophthalmologists are advised to be aware of the importance of PAI-1 4G / 5G gene polymorphism and dyslipidemia conditions besides the other genetic mutations and thrombophilic markers regarding BRAO in young patients.

Keywords:
Branch occlusion, dyslipidemia, plasminogen activator inhibitor, polymorphism, retinal artery

Introduction
Branch retinal artery occlusion (BRAO) leads to obstruction of blood flow in the distribution of the affected vessel giving rise to ischemia and reorganization of the retinal layers. It is a very rare diagnosis, and the etiological risk factors of BRAO are not clear in the young population. Various hypercoagulable states leading to thrombosis appeared to be more common in younger patients.

Here, the authors present an interesting case of a 25-year-old female patient with BRAO accompanying with plasminogen activator inhibitor-1 (PAI-1) 4G/5G gene polymorphism and dyslipidemia together, for the first time.

Case Report
A 25-year-old female patient who had sudden painless blurred vision in her right eye 3 months ago admitted to the clinic. Her visual acuity was 20/20 (LogMAR 0.00) in both eyes. Intraocular pressures were 16 and 14 mm Hg in the right and left eyes, respectively. Pupils were round and reactive in both eyes without evidence of the relative afferent pupillary defect in either eye. Biomicroscopy of the anterior segments were unremarkable. Dilated fundus exams revealed mildly attenuation...
and tortuosity of retinal arteries in both eyes. Three months ago, in the right eye fundus photo; intensive, extensive pallor and retinal edema in the lower quadrant of the retina due to inferotemporal BRAO was seen [Figure 1a]. No embolic plaques were noted. The red-free photograph of the right eye greatly accentuates the retinal whitening and attenuation of the inferotemporal retinal artery [Figure 1b]. Optical coherence tomography of the right eye showed normal foveal contour with inner retinal ischemia and thickening, with shadowing of the photoreceptors and retinal pigment epithelial layer consistent with an acute inferotemporal BRAO [Figure 1c]. Fundus examination and images taken in our clinic during the 3rd month confirmed the recovery of retinal edema in the right eye [Figure 2a]. Attenuation of the inferotemporal retinal artery still mildly appeared [Figure 2b]. Applied confrontation fields (standard automated perimetry, program test 30-2) showed a visual field defect corresponding with the affected area in the right eye and normal visual field in the left eye. Informed consent was taken from the patient to report this case.

There was no history of smoking, migraine, systemic, infectious disease, malignancy, trauma, medication, or surgery. Cardiological and neurological evaluations were reported as normal in another center. The results of magnetic resonance imaging of the brain and orbita, electrocardiogram and echocardiography, Doppler ultrasound imaging of the carotid arteries were normal. Evaluation for potential stroke factors revealed no suggestive family history.

No ocular therapy was offered. The patient was advised to go to hematology. Blood investigations including complete blood count with erythrocyte sedimentation rate, platelet count, coagulation profile, prothrombin/activated partial thromboplastin time, autoimmune markers, antiphospholipid antibody, protein C and S levels, enzyme-linked immunosorbent assay for human immunodeficiency virus, and serum homocysteine were all within normal limits. However, she had dyslipidemia in her lipid panel. In her genetic screening, there was only a PAI-1 4G/5G polymorphism, but not the other (Factor V Leiden, methylenetetrahydro-folate reductase, prothrombin G2010A) mutations.

Discussion

This is the first case reported as BRAO accompanying with PAI-1 4G/5G polymorphism and dyslipidemia together.

BRAO accounts for 38% of acute retinal artery obstruction cases. The incidence of retinal artery occlusion in patients under the age of 30 years has been estimated at <1 in 50,000 outpatients. Multiple factors may cause BRAO in the retina. Frequent etiologies include hypercoagulable states, hyperhomocysteinemia, vasculitis, emboli from cardiac valvular disease, and other risk factors such as smoking, use of oral contraceptives, and vasospasm such as in a history of migraine. In this patient, there was no history of smoking, migraine, systemic, infectious disease, malignancy, trauma, any medication, or surgery. The etiological risk factors of BRAO are poorly understood in younger individuals. Various hypercoagulable states leading to thrombosis appeared to be more common in younger patients.

PAI-1 is a serine protease that inhibits the plasminogen activator in the proteolytic cascade of plasmin. The balance of coagulation and fibrinolysis systems is regulated by the 4G/5G polymorphism of the PAI-1 gene, which alters the plasma concentrations of PAI-1. The genetic tendency to thrombosis due to PAI-1 4G/5G was well known. Genetic association
of thrombophilia-related gene polymorphisms in the development of visible cilioretinal artery as physiological vasculogenesis in the retina was shown.\textsuperscript{[3]} An association between increased risk for retinal vein occlusion and PAI-14G/5G polymorphisms\textsuperscript{[4]} and the relation between 4G/4G and 4G/5G genotypes and the thrombosis in vessels of internal organs\textsuperscript{[5]} were also reported, but there is no publication about BRAO accompanying with PAI-1 4G/5G polymorphism and dyslipidemia together.

Obesity is associated with the changes of PAI-1.\textsuperscript{[3]} PAI-1 polymorphisms accompany dyslipidemia in obese children was mentioned in the study of Kinik \textit{et al}.\textsuperscript{[6]} In another study, hyperlipidemia rate was found 15.6\% in retinal artery occlusion in the Indian population.\textsuperscript{[7]} This patient was an overweight female living a bit immobile and had also dyslipidemia.

Here, the condition is evaluated as transient BRAO due to PAI-1 4G/5G polymorphism and dyslipidemia together for the first time. The ophthalmologists should be aware of the importance of PAI-1 4G/5G gene polymorphism and dyslipidemia conditions besides the other genetic mutations and thrombophilic markers regarding retinal vascular occlusions in young patients.

**Declaration of patient consent**
The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**
There are no conflicts of interest.

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