

Case Report

Branch Retinal Artery Occlusion Associated with Hyperhomocysteinemia: Case Report

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Abstract

Introduction

Elevated plasma homocysteine is a risk factor for cardiovascular, cerebrovascular and peripheral vascular disease. We report the case of a young patient with branch ocular artery occlusion due to hyperhomocysteinemia.

Patients and methods

A19-year-old patient without significant medical history, presented for sudden, painless perception of black shadow in superior visual field of right eye since one day. Ophthalmologic examination revealed default hemi upper visual field in the right eye, best-corrected visual acuity 10/10 P2 on both eyes. Anterior segment exam was normal in both eyes, while the right fundus revealed normal disc with white ischemic retina encroaching the foveolar avascular zone around the infero-temporal vascular. Fluorescein angiography confirmed delayed filling of the right branch retinal artery occlusion.

Results

A work-up was performed, including: a full lipid profile, serum electrolytes, erythrocyte sedimentation rate, C reactive protein, a complete blood count (leukocytes, platelets, hemoglobin were normal), a coagulation work-up (prothrombin time/partial thromboplastin time, protein C, protein S, antithrombin III, factor V Leiden were normal), c-antineutrophil cytoplasmic antibody, antiphospholipid antibodies and antinuclear antibodies were negative, and finally cardiology studies (cardiac echo, carotid Doppler) and neurology (brain MRI) were ordered and came back normal. Otherwise, plasma homocysteine was moderately high, at 21.66 $\mu\text{mol/L}$. The patient was treated with platelet aggregation inhibitors and vitamin supplements and the condition was successfully controlled.

Conclusion

High plasma homocysteine is a risk factor for retinal vascular occlusive disease so it may be useful to measure homocysteine in the management of these patients.

Keywords: Branch retinal arterial occlusion; Homocysteine; Hyperhomocysteinemia; Vitamin B₁₂

Introduction

Retinal vascular diseases occur rarely in young patients. More than 90% of cases occur in people older than the age of 50 years and as many as 70% of patients have arterial hypertension, cardiovascular atherosclerotic disease, or diabetes mellitus [1]. Elevated plasma homocysteine is a recently recognized vascular risk factor for thrombosis and vascular diseases [2]. It is also shown to be a significant risk factor for retinal vascular occlusions [2]. Here we describe a young man with occlusion of branch retinal artery associated with homocysteinemia.

Case Report

A19-year-old patient without significant medical history, presented with sudden, painless and permanent perception of black shadow in superior visual field of right eye since one day. Ophthalmologic examination revealed default hemi upper visual field in the right eye, best-corrected visual acuity 10/10 P2 on both eyes. Anterior segment examination was unremarkable with normal pupillary reactions. Intraocular pressures were 12 and 13 mmHg OD and OS with applanation tonometry, respectively. Fundus examination revealed normal disc with white ischemic retina encroaching the foveolar avascular zone around the infero-temporal vascular in the right eye (Figure 1). Ophthalmologic examination was totally normal in the left eye. Fluorescein angiography showed a delay in the filling of inferotemporal artery in the right eye and capillary non-perfusion corresponding to the area of retinal whitening seen clinically (Figure 2). Visual field examination showed a default of the hemi upper visual field in the right eye (Figure 3). He was diagnosed as a branch retinal artery occlusion. There was no history for any sign of autoimmune diseases. The patient's family history was negative for thrombotic events. Physical examination and chest X-ray revealed no evidence of malignant disease or any other pathology. Haematological and cardiological consultation together with some laboratory tests (Table 1) including complete blood count, serum lipids and cholesterol, prothrombin time/partial thromboplastin time, erythrocyte sedimentation rate, fibrinogen, complement factors C3 and C4, antithrombin III, protein C activity, protein S antigen, activated protein C resistance, folate, vitamin B₆, serum vitamin B₁₂ levels, rheumatoid factor, antinuclear antibodies, c-Antineutrophil Cytoplasmic Antibody (cANCA), antiphospholipid antibodies and the factor V Leiden, were ordered and came back normal. Otherwise, the serum homocysteine level was found to be 21.66 $\mu\text{mol/l}$ (normal range: 0-12 $\mu\text{mol/l}$).

The patient was treated with platelet aggregation inhibitors and vitamin supplements (vitamin B₆: 300 mg/day, vitamin B₁₂: 60 mg/day and vitamin E: 200 mg/day) and the condition was successfully controlled. At the subsequent visits, the white retinal edema had disappeared but the lost of the visual field persisted (Figure 4-5). The serum homocysteinemia was nearly normalized (14.52 $\mu\text{mol/l}$).

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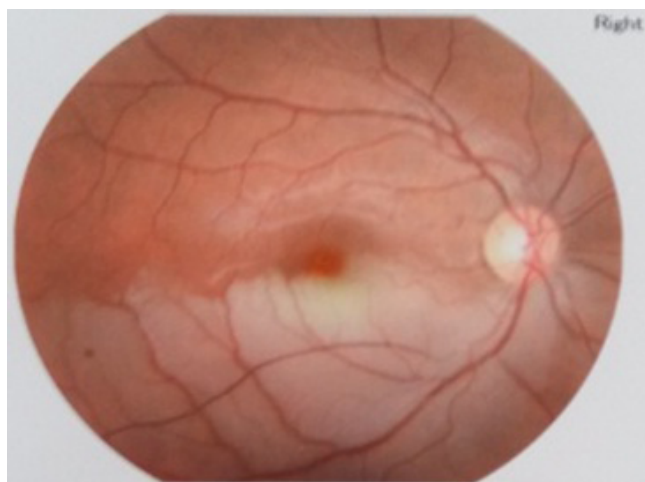


Figure 1: Fundus examination revealed retinal oedema, and whitening in the inferior temporal arcuate in the right eye.

Complete blood count
Serum lipids and cholesterol
Prothrombin time/partial thromboplastin time
Erythrocyte sedimentation rate
Fibrinogen
Complement factors C3 and C4
Antithrombin III
Protein C activity
Protein S antigen
Activated protein C resistance
Folate
Vitamin B ₆
Serum vitamin B ₁₂
Rheumatoid factor
Antinuclear antibodies
c-Antineutrophil Cytoplasmic Antibody (cANCA)
Antiphospholipid antibodies
Factor V Leiden

Table 1: Laboratory workup reported as normal.

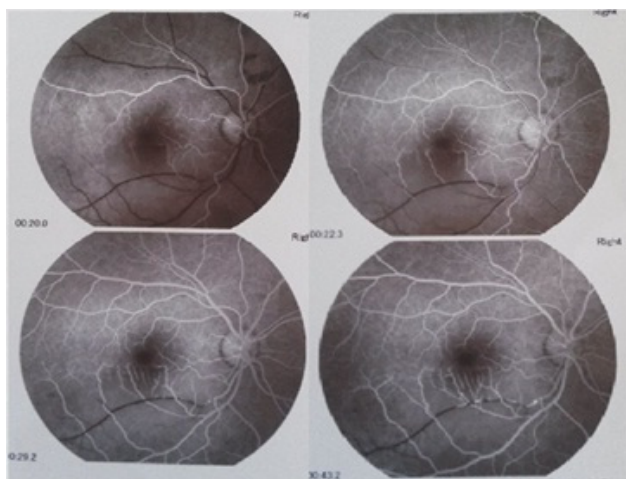


Figure 2: Fluorescein angiography showing a delay in the filling of inferotemporal artery in the right eye.

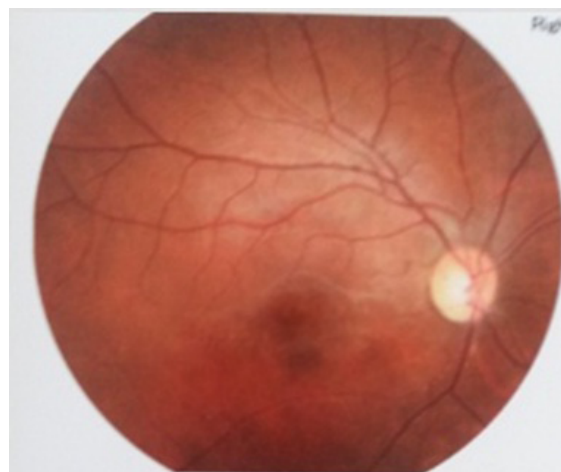


Figure 4: Fundus examination 4 months after treatment.

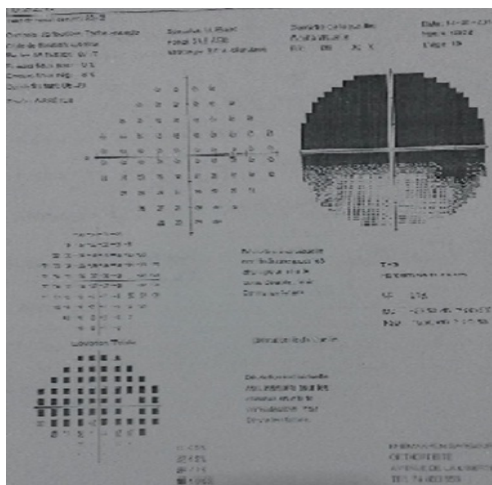


Figure 3: Visual field examination showed a default of the hemi upper visual field in the right eye.

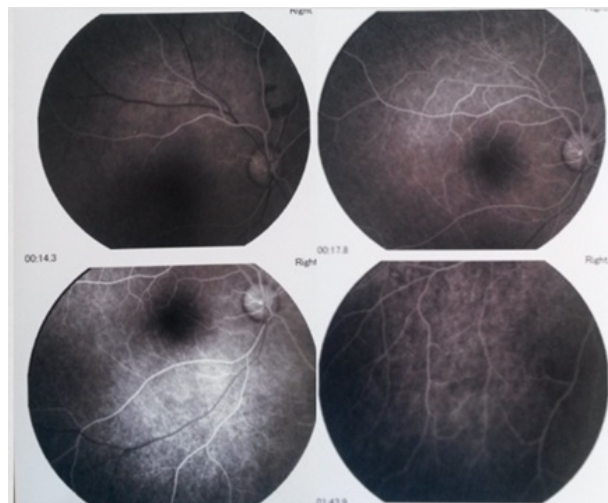


Figure 5: Fluorescein angiography 4 months after treatment.

Discussion

Branch retinal artery obstruction is a rare event, even less common than central retinal artery obstruction overall. Branch retinal artery obstruction is, however, more prevalent than central retinal artery obstruction in young patients [1]. Conditions that promote embolus formation in youth include atrial myxoma, mitral valve prolapse, rheumatic heart disease, and endocarditis [1]. Youth may also develop a hypercoagulable state secondary to hyperhomocysteinemia, factor V Leiden mutations, or antiphospholipid antibody syndrome [1].

Hyperhomocysteinemia is an established risk factor for vascular diseases including retinal vascular occlusion [3]. The exact mechanism by which high plasma concentrations of homocysteine induce arterial and venous thrombosis is still not clear. Endothelial injury by release of free radicals, creating an environment of hypercoagulability, and by modification of vessel wall is probably the key mechanism of thrombotic and atherosclerotic complications [2]. Weger et al., [4] found that the mean plasma homocysteine levels were significantly higher in patients with retinal artery occlusion compared with normal controls. Vine et al., [5] described hyperhomocysteinemia as a risk factor for retinal vascular occlusion in 74 patients. Martin et al., [6], by measuring the homocysteine levels in 70 patients with retinal vascular disease, conclude that hyperhomocysteinemia may be a risk factor for retinal vascular disease and could be simply and cheaply treated with folate and vitamins B₆ and B₁₂. Parchand et al., [7] found raised serum homocysteine levels in a patient presenting a primary branch retinal artery occlusion with idiopathic retinal vasculitis, aneurysms, and neuroretinitis syndrome. Furthermore, Coban-Karatas et al., [8] reported central retinal artery occlusion associated with hyperhomocysteinemia caused by methylenetetrahydrofolate reductase C677T mutation and high lipoprotein (a) level in a child. In our case, homocystinaemia was the only predisposing factor for artery occlusion. Thus, it may be useful to measure homocysteine in the management of premature retinal vascular diseases.

Differing mean plasma homocysteine values for healthy people from various countries have been reported that range from 6 µmol/L in Japan to 13 µmol/L in South Africa [9]. In 1997, Alfthan et al., [9] reported the mean plasma homocysteine concentrations in 13 different countries which ranged from 7.1 µmol/L in Germany to 10.7 µmol/L in Finland. Recent studies indicate that 15 to 30 percent of patients with premature occlusive vascular disease have moderately elevated total plasma homocysteine concentrations (higher than 15 µmol/L). A plasma homocysteine concentration exceeding 15 µmol/L defines hyperhomocysteinemia [10].

Moderate hyperhomocysteinemia (15-30 µmol/L) reflects impaired pathway of remethylation. The possible causes include deficiency of folic acid, vitamin B₁₂ or dysfunction of 5,10-Methyltetrahydrofolate Reductase (MTHFR). A point mutation of amino acid 677 (677 C → T) in MTHFR gene can cause alanine-valine substitution and is associated with reduced enzyme activity of MTHFR. This is the commonest form of genetic hyperhomocysteinemia [11]. Severe hyperhomocysteinemia (>100 µmol/L) may be caused by deficiency of homozygote Cystathionine β-Synthase (CBS), homozygote thermo-stable MTHFR, or enzymes catalyzing vitamin B₁₂ metabolism. Abnormal increase of plasma Hcy (>15 µmol/L) after a methionine load (100 mg/kg) may reflect impaired Hcy transsulfuration due to deficiency of heterozygous CBS or vitamin B₆ [12].

Patients with retinal vascular occlusive disease have also a significant excess of mortality from coronary and cerebrovascular diseases [13]. So it is assumed that by reducing the toxic effect of homocysteine on the blood vessels, the probability of further retinal and systemic vascular occlusion, and therefore the resulting morbidity and mortality will be reduced. Randomized clinical trials have shown that oral supplementation with the combination of folate, B₆, and B₁₂-vitamins substantially lowers circulating homocysteine levels [14]. If effective, the simplicity, availability, and presumably favorable side effect profile of hyperhomocysteinemia treatment with combined folate and oral B₆- and B₁₂-vitamin supplementation makes this an attractive addition to standard medical therapy for retinal vascular diseases and primary prevention of cardiovascular disease.

Further, some studies have demonstrated that hyperhomocysteinemia might be involved in the pathophysiology of many neuropsychiatric disorders, including brain atrophy, epilepsy, and Alzheimer's disease [15-18]. But homocysteinemia-lowering therapies from an early age are they effective at preventing neuropsychiatric disorders? Answer to this question remains novel area for further work.

Conclusion

Retinal vascular occlusions in young patient should be investigated throughout for embolic sources and any disease causing thrombophilia as well as local ocular conditions. We would like to stress on the investigation for homocystinaemia as a predisposing condition for the occlusion of branch retinal artery occlusion in the absence of other risk factors. The next question to be answered is whether homocysteine -lowering therapy contributes to the prevention of retinal vascular occlusion.

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