Case report

Combined Branch Retinal Vein and Artery Occlusion in Toxoplasmosis with Hyperhomocysteinemia, and Mutation of Factor V Leiden

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Abstract

Background: The aim of this study was to assess the combined branch retinal vein and artery occlusion in Toxoplasmosis with hyperhomocysteinemia, and mutation of factor V Leiden.
Material and Methods: An 18 year old boy complained of low visual acuity and pain in his right eye for one week. Diagnosis of the patient was done with optic papillitis, low vitreous inflammation, and toxoplasma gondii antibody IgG. Measurement of homocysteine revealed hyperhomocysteinemia is the boy. Moreover, heterozygosity of a mutation of factor V Leiden; FVL (coagulation factor V gene) was also observed in the case.
Result: The patient was diagnosed with branch retinal vein and artery occlusion with hyperhomocysteinemia and mutation of factor V Leiden. The patient was underwent intravitreal injection of bevacizum (IVB), and PRP laser due to severe retinal ischemia and extensive NVD. The patient was treated with sulfamethoxazole (800 mg), trimethoprim (160 mg), and corticosteroid (1- 1.5 mg/kg/day). Vitamin B6 (100 mg/daily), acid folic (5 mg daily), and vitamin B12 (112 mg/daily) were also added to the treatment for 8 weeks. After treatment, the assessment of plasma homocysteine showed that the level of homocysteine was normal.
Conclusions: This is the first report of combined retinal branch vein and artery occlusion in toxoplasmosis with hyperhomocysteinemia and mutation of factor V Leiden.

Keywords: Branch Retinal Vein; Branch Artery Occlusion; Hyperhomocysteinemia; Mutation of Factor V Leiden; Ocular Toxoplasmosis.

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Introduction

Toxoplasmosis is the leading cause of infectious posterior uveitis (IPV) [1, 2], and accounts for 80% of cases in some areas. It is a recurring necrotizing retinitis, and progressive disease with vision-threatening complications, including choroidal neovascularization, and retinal detachment, as well as glaucoma [3]. The prevalence of ocular toxoplasmosis in Japan, Colombia, Thailand, and the United States was 1.8 %, 39.8 %, 22.2 %, and 8.4 %, respectively [4].

The most common cause of IPV in non-immunocompromised individuals is Toxoplasma gondii infection[5]. T. gondii infects a significant portion of the global population, with up to one-third of people affected, and it is the primary cause of infectious uveitis, which is inflammation within the eye. In certain countries, up to 50 % of all cases of posterior uveitis in a specific population are attributed to toxoplasmosis[6]. In addition, according to literature, Toxoplasma gondii is a leading cause of zoonotic infection, leading to pneumonia, pericarditis, neurologic disorders, and uveitis in immunocompetent hosts [5].

The genetic structure of T. gondii is more intricate than the previously proposed three-strain hypothesis, and unusual genetic variations in the parasite might contribute to different clinical outcomes of toxoplasmosis in various geographical regions. Furthermore, specific genetic variants have been linked to the severity of the disease's symptoms [6]. Furthermore, the importance of Toxoplasma gondii infection in patients with ocular disease has been recognized according to the clinical and etiological findings.

Toxoplasmic retinochoroidit is often due to a self-limiting course can lead to an irreversible visual loss chiefly when the optic nerve head and macula are involved. Vascular involvement usually involves segmental or diffuse sheathing produced by the deposition of antigen-antibody complexes in the vessel wall as well as by localized mononuclear cells infiltrates[1]. Although retinal vein occlusion may happen, artery obstruction is a rare process [5, 7]. Therefore, the current study aimed to introduce a case with combined branch retinal vein and artery occlusion in toxoplasmosis and hyperhomocysteinemia, and mutation of factor V Leiden.

Case Presentation

An 18 year old boy complained of low visual acuity and pain in his right eye for one week. He had no positive family history. Moreover, he had no history of drug use or family history. All CBC tests except WBC (3.9×10^3/ul) were in normal range. Vitamin B12 level was 298.8 pg/ml (normal range: 197-771 pg/ml), and homocysteine level was 59 micmol/L (normal range: 5-15 micmol/L). CRP and ESR were in normal range. The level of IgG, and IgM was 195.8 (>11 positive), and 0.22 IU/ml, respectively. B2 microglobulin, HBV DNA and HIV type 1 RNA was negative. Immunology test, including anti-phospholipid antibody (IgG), anti-phospholipid antibody (IgM), anti-cardiolipin antibody (IgG), and anti-cardiolipin antibody was negative. Protein C, and protein S assays were in normal range. The coagulation test, including factor X was 133% (normal range: 70-120 %), and APCR (leiden factor) was 80 sec (normal range > 120 S). The heterozaygous Factor 5 leidan G1691A was observed in the boy. In addition, prothrombin G20210A mutation was reported normal. Homocysteine level was assessed by HPLC method and reported normal.

The patient underwent intravitreal injection of bevacizum (IVB) and PRP laser due to severe retinal ischemia and extensive new vessels on

Table 1: Ocular examination of the boy

	OD	OS
BCVA	CF 3m	10/10
Refraction	- 0.25/-0.5*3	Plano/-0.25*2
Ocular motility	Normal	Normal
RAPD	++	Negative
Intraocular pressure (IOP)	12 mmHg	14 mmHg
Ant. segment	Normal	Normal
Funds	Disc: Blurred margin Macula: CWS Periphery & vessels: Retinal Hx & CWS in inferior	Disc: Round, pink, sharp margin C/Dr:0.5 Good fovea reflex periphery & vessels: NL pattern

the disc (NVD).

After diagnosis, the patient was treated with sulfamethoxazole (800 mg), trimethoprim (160 mg), and corticosteroid (1-1.5 mg/kg/day). Steroid started 24-48 hours after anti-toxo treatment established. Vitamin B6 (100 mg/daily), acid folic (5 mg daily), and vitamin B12 (112 mg/daily) were also added to treat for 8 weeks. After treatment, the assessment of plasma homocysteine showed that the level of homocysteine was normal.

Figure 1 shows the ocular parameters of the patient.

Fluorescein angiography (FA) frames of the eye are shown in Figure 2.

Fundus photographs after 3 weeks medication with sulfamethoxazole, trimethoprim (800/160), corticosteroid is shown in Figure 3.

Discussion

Ocular toxoplasmosis is a recurring and progressive retinitis with vision-threatening complications which may occur at any time during the clinical course [3]. It causes various retinal vascular changes, including branch retinal vein occlusion, periphlebitis, periarteritis, branch retinal artery occlusion, choroidal retinal anastomosis, periphlebitis, segmental retinal periarteritis, and perivascular sheathing [8].

The ocular toxoplasmosis diagnosis is often straightforward; but challenging cases may also happen [8]. After some time, the pigmentation mainly happens in the lesion margins[1]. In toxoplasmosis, vascular changes typically involve veins; however arteries may also be impacted especially in the Kyrieleis arteritis which is characterized by nodular periarterial plaques [1]. In the current study, the patient was diagnosed with optic papillitis, low vitreous inflammation, and toxoplasma gondii antibody IgG and a case with combined branch retinal vein and artery occlusion in toxoplasmosis was introduced.

Branch artery occlusion may result from direct artery compression by retinochoroiditis or by arteriolar contraction [1]. It may also be as the result of perivasculitis, which may lead to thickening of the artery wall, and

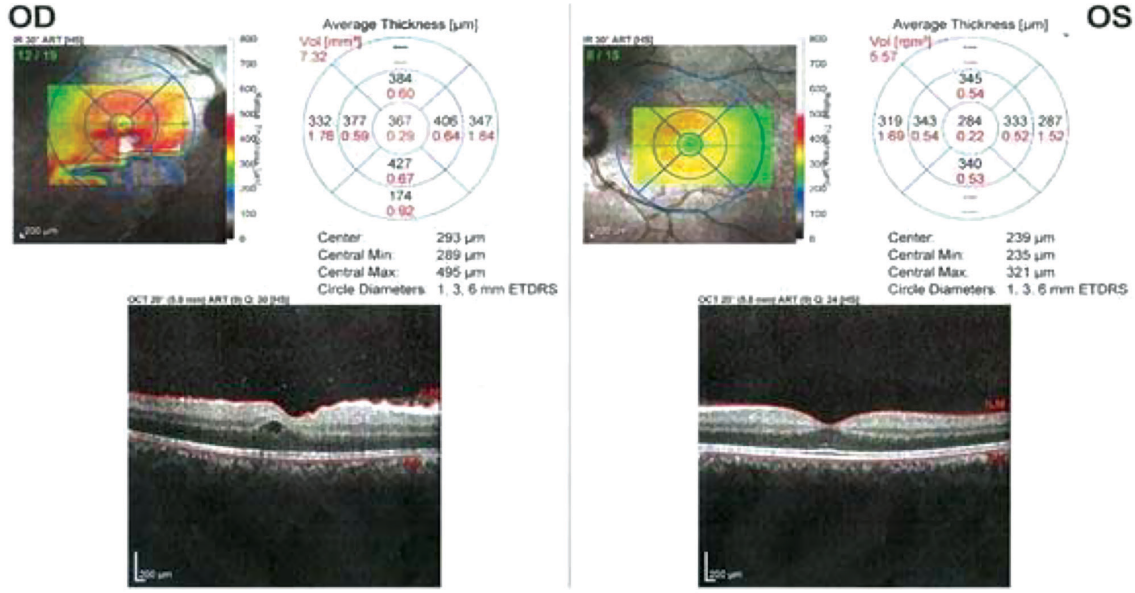

Figure 1: Ocular parameters of the patient

maculopathy, and impaired blood flow, as well as thrombosis [1]. When recurrence occurs, it usually involves the adjacent retina [9].

Chiang et al., revealed the branch retinal vein occlusion in a 17 years old patient in the pediatric population. They believed that diagnosis of toxoplasmosis should be considered in young patients with retinal artery occlusions which are associated with inflammation [5]. Fabio et al., also demonstrated the combined branch artery retinal vein and artery occlusion in toxoplasmosis [1].

Moreover, after measuring the plasma cysteine level, we observed hyperhomocysteinemia in the case. Hyperhomocysteinemia is one of the risk factors for several disorders such as ocular diseases. Association of hyperhomocysteinemia with eye diseases, including pseudoexfoliative glaucoma, retinopathy, cataract, optic atrophy, retinal vascular occlusion were also seen [10]. The metabolism of homocysteine happens via the transsulfuration to cysteine or the remethylation to methionine in the presence of enzymes with vitamins such as folic acid, vitamins B12 and B6 [11]. Moreover, supplementation with betaine reduces plasma level of homocysteine levels. It donates methyl group to homocysteine, and is metabolized to methionine [12].

Moreover, heterozygosity of a mutation of factor V Leiden; FVL (coagulation factor V gene) was also observed in the current case. Heterozygosity of a mutation of factor V Leiden causes the resistance to activated protein C and shows the most common reasons of inherited thrombophilia.

FVL may be a risk factor for venous thrombosis [13]. Moreover, the coinheritance of factor V Leiden and methylenetetrahydrofolate reductase defects increase the risk of venous thromboembolism [14].

Conclusion

In the current study, an unusual presentation of toxoplasmosis which is characterized by combined branch retinal vein and artery occlusion with hyperhomocysteinemia, and mutation of factor V Leiden was described. Therefore, immediate treatment may prevent a poor visual outcome.

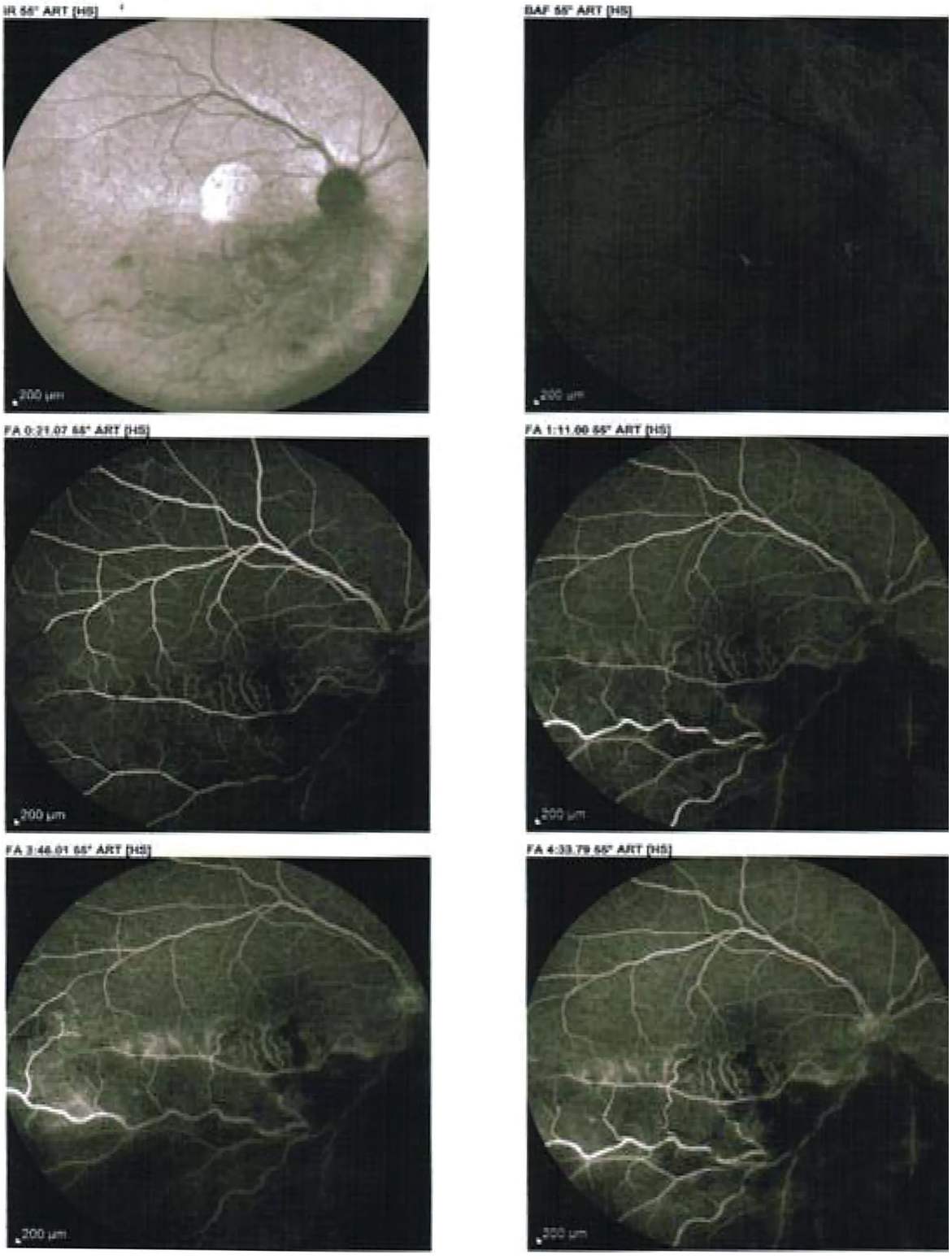

Figure 2: Fluorescein angiography (FA) frames of the eye before the beginning of treatment

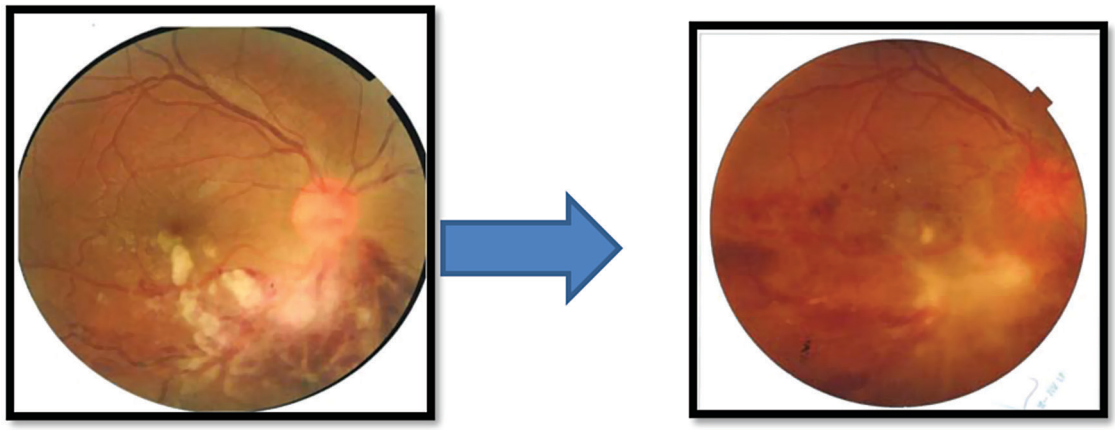

Figure 3: Fundus photographs of typical ocular toxoplasmosis after 3 weeks

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Footnotes and Financial Disclosures

Conflict of interest:

The authors have no conflict of interest with the subject matter of the present manuscript.