

## Homocystinuria in a 14-year old girl manifesting as central retinal artery occlusion: A case report

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### Abstract

Central retinal artery occlusion (CRAO) is one of the causes of sudden loss of vision. Homocystinuria is an autosomal recessive inherited disorder and is characterized by increased levels of homocysteine in the urine and blood. We present a case of homocystinuria in a 14-year girl, presenting as CRAO with a family history of vascular thrombotic events. The patient did not have any local predisposing factors or prior history of thrombo-embolic episodes. Left eye fundus examination revealed a pale retina with sparing of cilioretinal artery. On examination Visual acuity of the right eye was 6/6 and left eye was completely blind with no perception of light. Homocysteine level on admission was 34.60umol/l. Patient was started on Rivaroxaban 10mg, Vitamin B6, Vitamin B12 and folic acid. On follow up examination after 2 months the visual acuity in the left eye was 6/9. The dramatic improvement in the visual acuity can be attributed to the sparing of the cilioretinal artery. Follow-up Homocysteine levels after two months of treatment was 12umol/l. Ophthalmologist should be aware of this rare manifestation of homocystinuria as CRAO as they can play an important role of diagnosing the underlying medical illness.

**Keywords:** Retinal Artery Occlusion, Homocystinuria, Visual acuity.

**DOI:** <https://doi.org/10.5455/JPMA.23704>

### Introduction

Central retinal artery occlusion is one of the causes of sudden profound loss of vision. CRAO has been previously reported in association with a number of systemic diseases including homocystinuria.<sup>1</sup> Homocystinuria is an autosomal recessive inherited disorder and is characterized by increased levels of homocysteine in the urine and blood. It has a broad spectrum of clinical manifestation and can present as developmental delay, marfanoid features, and ocular findings like ectopia lentis, osteoporosis and most

importantly accelerated atherosclerosis.<sup>2</sup> The mechanism by which Homocystin predisposes to thrombo-embolism is by upregulating prothrombotic factors.<sup>3</sup> Without treatment, there is a 50 percent chance of having a thrombotic event by the age of thirty.<sup>4</sup>

We present a rare case of homocystinuria in a 14-year girl, presenting as CRAO with sparing of cilioretinal artery and a family history of vascular thrombotic events. The patient did not have any local predisposing factors or prior history of thrombo-embolic episodes.

### Case Report

A 14-year-old girl presented with a sudden loss of vision in the left eye. Past medical and surgical history was unremarkable. Patient was a progeny from a second-degree consanguineous marriage. Family history was positive for multiple vascular thrombotic events in both the maternal and paternal family in young ages of 30s and 40s. Rest of the history was unremarkable. On examination Visual acuity of the right eye was 6/6 and left eye was completely blind with no perception of light. On pupillary examination, there was RAPD in the left Eye. Left eye fundus examination revealed a pale retina with sparing of cilioretinal artery (Figure-1 and Figure-2). Finding of lack of perception of light in the left eye could be explained by retinal oedema that develops as a result of retinal artery occlusion. Sparing of the cilioretinal artery meant that the prognosis for improvement in visual



**Figure-1:** Left eye fundus photo.

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Figure-2: Left eye fundus photo.

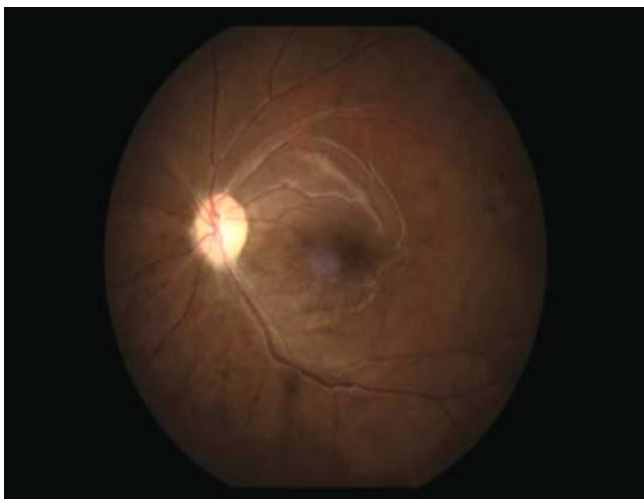


Figure-3: Follow-up left eye fundus photo.

acuity was good. A diagnosis of Central retinal artery occlusion in the left eye was made. Differential diagnosis for the underlying cause of CRAO included all thrombophilia's given the young age of the patient and family history of vascular thrombotic events. To search for the underlying cause of thrombophilia comprehensive Lab tests were ordered including a thrombophilia screen. Other investigations included, Full blood count, Erythrocyte Sedimentation Rate (ESR), C-reactive protein (CRP), PT/APTT, Protein C & S, Homocystiene levels, Carotid Doppler, ECG, ECHO, VDRL/RPR, TPHA, Factor V Leiden mutation, Anti-thrombin III deficiency, Anti-nuclear antibody (ANA), Thyroid Function Test (TFTs), vitamin B12 levels and Hb electrophoresis. All the lab tests were unremarkable except for elevation of homocystien

levels (34.60umol/l). Patient was started on Rivaroxaban 10mg BD for three months, Vitamin B6 50mg, Vitamin B12 2mcg and folic acid 400mcg to be continued indefinitely.

Based on the elevated homocysteine levels and family history of thrombotic events at an early age a diagnosis of homocystinuria was made.

On follow up examination after 2 months the visual acuity in the left eye was 6/9. The dramatic improvement in the visual acuity can be attributed to the sparing of the cilioretinal artery (Figure-3). Homocysteine level responded to vitamin B supplementation and follow-up homocysteine level was 12umol/l. No adverse or unanticipated events occurred during the follow-up.

Informed consent was taken prior to writing of this case report.

### Discussion

Hyperhomocystinaemia and homocystinuria due to deficiency of key enzyme like cystathionine beta-synthetase causes early onset Strokes, Myocardial infarctions and peripheral vascular disease. Hyperhomocystinaemia is a proven independent risk factor for vascular thrombotic disease.<sup>5</sup> Homocysteine can be metabolized via the transsulfuration pathway or the remethylation pathway, therefore a defect in the cystathionine beta-synthase or MTHFR can lead to elevated levels of Homocysteine. Moreover, a deficiency of folate, or vitamin B12, medical conditions like hypothyroidism, chronic renal failure and SLE are also associated with homocystinaemia.<sup>6</sup> There can be a considerable variability in the severity of complications ranging from diagnoses at routine family screening or newborn screening to life threatening complications like coronary artery occlusion and strokes.<sup>7</sup>

Supplementation with vitamin B6, Vitamin B12 and folic acid is required to suppress blood levels of homocysteine. In a recent review done by Marti- Carvajal et al reported that vitamin B supplementation has shown a beneficial effect in stroke patients by lowering homocysteine levels.<sup>8</sup> Transient monocular loss of vision is considered a Transient ischaemic attack (TIA) equivalent and retinal artery occlusion is considered stroke equivalent.<sup>9</sup> We started the patient on Rivaroxaban as a secondary prevention. Anti-coagulants may be administered after retinal artery occlusion but the therapeutic benefit is uncertain.<sup>10</sup> One study has reported improvement in retinal function in rats with coumarin derivatives.<sup>11</sup>

Central retinal artery occlusion is an expected complication of homocystinuria given the prothrombotic state the disease induces. CRAO associated with

homocystinuria has been previously reported. Two of the cases of CRAO associated with homocystinuria occurred due to local predisposing factors. One study describes the case of a 6-year-old boy who developed CRAO secondary to bilateral acute glaucoma due to his dislocated lenses. In another instance, post-operative CRAO developed after removal of dislocated lenses. In our case, there was no local predisposing factor for CRAO as the patient never underwent ocular surgery, lens was not dislocated and intra ocular pressures were normal. Yet in another 31-year-old lady, presenting with CRAO secondary to homocystinuria, there was a past history of unexplained thromboembolic phenomenon including deep venous thrombosis, peripheral limb ischaemia and multiple pregnancy loss.<sup>12-14</sup> Two case reports of bilateral central artery occlusion in homocystinuric patients have also been reported.<sup>12,15</sup> Our patient is probably the youngest and had no previous history of thromboembolic episodes and had presented with central retinal artery occlusion as the initial manifestation of the underlying homocystinuria. In our case the ophthalmologist played a pivotal role in the ultimate diagnosis of the disease that might have spanned multiple generations of the patient's family. However, we could not do a genetic family screening given the financial constraints and lack of resources.

## Conclusion

Ophthalmologists should be aware of this rare manifestation of Homocystinuria presenting as CRAO, even if there are no local signs such as ectopia lentis. In developing countries like Pakistan where there is no routine newborn screening or family screening for genetic diseases, it is mandatory that thrombotic events at a younger age like CRAO should prompt the ophthalmologist or the general practitioner to order a thrombophilia screen to diagnose underlying prothrombotic disorders.

**Disclaimer:** None to declare.

**Conflict of Interest:** None to declare.

**Funding Sources:** None to declare.

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