Short communication

Hyperhomocysteinemia in chronic alcoholism: A case with retinal manifestations

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Abstract
Case report: An alcoholic patient with loss of vision in his right eye and a peripapillary hemorrhage, who then presented with a venous thrombosis. Blood analysis revealed hyperhomocysteinemia with coagulation parameters within the normal range. In the follow-up he developed a bilateral optic neuropathy.

Discussion: An increase in homocysteine levels is common in alcoholics, and it has been considered a vascular risk factor. Folic acid and vitamins B₆ and B₁₂ deficiency may lead to hyperhomocysteinemia, as they participate in its metabolism.

Conclusions: When presented with a retinal occlusive disease or ischemic optic neuropathy in young patients, coagulation disorders and elevated levels of homocysteine should be ruled out.

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Manifestaciones retinianas secundarias a hiperhomocisteinemia en un caso de alcoholismo crónico

Resumen
Caso clínico: Paciente alcohólico con disminución de agudeza visual en el ojo derecho, presentando una hemorragia peripapilar temporal superior y, posteriormente, trombosis de subrama venosa. La analítica mostró hiperhomocisteinemia con coagulación normal. En la evolución desarrolló una neuropatía óptica bilateral.

Discusión: La elevación de homocisteína es común en alcoholícos, considerándose un factor de riesgo cardiovascular. El ácido fólico y las vitaminas B₆ y B₁₂ participan en el metabolismo y su déficit puede incrementar sus niveles.


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Case report

A 39-year-old patient, a national from India, heavy alcohol drinker was seen for loss of visual acuity (VA) in his right eye (OD). Patient was a non-smoker and non-vegetarian.

VA was 0.6 in OD; patient had superior temporal peripapillary hemorrhage (Figs. 1A and 2A), with thickening of nerve fiber layer in temporal field as shown in optical coherence tomography (OCT) (Fig. 2E). Both, ocular fundus and left eye (OS) OCT were normal, with VA of 0.8 (Fig. 2B and E).

At 3 months, patient had an inferior-temporal vein small-branch obstruction in OD, while papillary hemorrhage disappeared completely. OS remained unaltered. Furthermore, we found petechial hemorrhages in his limbs.

Due to the occlusive vascular events, a complete set of laboratory tests including coagulation parameters was requested. Transaminases, lactate dehydrogenase and D-dimer were elevated. B6 and B12 vitamins were within normal limits and coagulation was also normal. As a result, a folic acid and plasma homocysteine evaluation was requested; the latter was 2 times above the limit value (29 μmol/l; upper limit: 15 μmol/l). Folate, however, was unaltered (4 ng/ml; lower limit: 2.33 ng/ml).

Six months after the first visit, VA decreased to 0.5 with temporal pallor and increased papillary cavitation (Fig. 1B). Fluorescein angiography showed no vascular obstructions, despite persistent hemorrhage adjacent to inferior temporal vein in OD (Fig. 1C). OS had slight pallor and increased cavitation with VA at 0.6.

One year later, the patient had visual field defects with VA 0.4 in OD and 0.5 in OS (Fig. 3). The optic nerve head shows changes related to optic neuropathy, with pallor and increased cavitation, with existing correlation with loss of nerve fibers as shown by OCT in both eyes (Fig. 2).

Visual evoked potential showed bilateral visual pathway axonal involvement with moderate latency (VEP-pattern), mild-moderate increase in latency and decrease in amplitude of P100 wave in both eyes without significant interocular or interhemispheric differences, suggesting bilateral optic neuropathy, possibly resulting from alcoholic toxicity and an ischemic mechanism.

Full-field electroretinography (ERG-Ganzfeld) showed no abnormalities in the latency of responses (bilaterally), although a possible functional impairment of the retina was not ruled out.

Coagulation parameters remain normal with elevated levels of plasma homocysteine (28.5 μmol/l). B1, B6 and B12
vitamins remained within normal limits, and folic acid assessment close to the lower limit (3.4 ng/ml).

**Discussion**

Hyperhomocysteinemia or mild to moderate elevation of plasma homocysteine may be caused by genetic determinants (tetrahydrofolate reductase thermolabile variant), lifestyle (high-protein diets, coffee or alcohol consumption) or some drugs (methotrexate). Prevalence in the general population is about 5%. Independent cardiovascular risk factor is considered, related to ischemic heart disease, atherosclerosis, strokes and venous thrombosis, including the central retinal vein or its branches, as well as non-arteritic

![Fig. 2](image1.png)

Fig. 2 – (A) Papillary hemorrhage in the right eye at baseline. (B) Optical disk without abnormalities in the left eye at baseline. (C) and (D) Pallor of temporal neuroretinal rim and increased cavitation in both optic discs at one year of follow-up. (E) OCT at baseline showing an increase in nerve fiber layer in temporal sector of right optic nerve, related to hemorrhage, and left eye within normal limits. (F) OCT showing decreased nerve fiber layer of retina in the temporal sector of both eyes, one year later.

![Fig. 3](image2.png)

Fig. 3 – Vision field, at one year of follow-up. (A) Nasal-inferior and paracentral defects in right eye. (B) Central defect in left eye.
anterior ischemic optic neuropathy and retinal arterial occlusions.\textsuperscript{3,4}

Folic acid and B\textsubscript{6} and B\textsubscript{12} vitamins participate in methionine–homocysteinemia metabolism, and their deficiency may cause an increase in homocysteinemia levels.\textsuperscript{5} Deficiency of these vitamins is common in chronic alcoholics, especially those with liver damage; this can lead to hyperhomocysteinemia and increased cardiovascular risk. This patient had occlusive retinal phenomena in OD, with high levels of homocysteine and folic acid at the lower limit of normal which, combined with an alcoholic-nutritional mechanism, appear to be the source of a bilateral optic neuropathy. Other cardiovascular risk factors such as hypertension, diabetes or tobacco were discarded.

Folic acid supplement has been suggested as a treatment for reducing plasma homocysteine in these patients.\textsuperscript{6} The patient refused this treatment and has not reduced his alcohol consumption; therefore, we expect a progression in successive visits, with greater loss of VA and optic nerve involvement.

In conclusion, due to retinal vascular occlusion or ischemic optic neuropathy in young patients without known cardiovascular risk factors, coagulation and increased homocysteine level abnormalities must be ruled out. Moreover, this patient was a chronic alcoholic, which increases the likelihood for abnormality of the two, and was unique in that coagulation was not affected despite hepatic impairment, and we only found hyperhomocysteinemia without significant effect of the metabolism’s cofactors.

### Conflicts of interest

The authors declare that they have no conflicts of interest.

### REFERENCES