Case report

EJO European Journal of Ophthalmology

European Journal of Ophthalmology
2022, Vol. 32(1) NP254–NP257

DOI: 10.1177/1120672120970112
journals.sagepub.com/home/ejo
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Ophthalmologic evaluation in vitamin-E deficiency: A case report

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Abstract

A 41-year-old woman has come to our attention complaining of decreased visual acuity and monocular diplopia associated with upper and lower limb hypoesthesia. Malabsorption syndrome with vitamin A and E deficiency developed after a bariatric biliopancreatic diversion. The clinical ophthalmological signs and symptoms improved after oral vitamin supplementation therapy. The past medical history is essential in the case of a patient complaining of visual symptoms compatible with vitamin deficiency in order to detect the cause and to start a prompt therapy to avoid irreversible neurological and visual sequelae. The clinical features of our case closely resemble other cases described in the literature of patients affected by vitamin A and E deficiency secondary to malabsorption syndrome.

Keywords

Optic neuropathy, neuro ophthalmology, diseases of the ocular surface, cornea/external disease, diseases of the ocular surface: nutritional disorders neuotrophic keratopathy, systemic drug retinal toxicity, retina, tear deficiency states

Date received: 22 April 2020; accepted: 9 October 2020

Introduction

Vitamin E (α-tocopherol) is one of the most important fat-soluble vitamins that acts as an antioxidant and free-radical scavenger; it is stored in the liver, muscle, and adipose tissue. Vitamin E (vit-E) deficiency is a condition unfrequently encountered in human beings since it occurs in rare diseases such as abetalipoproteinemia, isolated vit-E deficiency syndrome or as a consequence of abnormal fat absorption secondary to malabsorption syndromes and short bowel syndrome.[1] The antioxidant action of vit-E on free radicals has been widely described to prevent damage to central, peripheral nervous system and the retina, preserving them from ataxia, peripheral neuropathy, and vision loss.[2] Symptoms of deficiency may have an insidious onset, and diagnosis can often be delayed.[3] This report describes a 41-year-old woman with a documented prolonged vit-E deficiency who developed symptoms of peripheral neuropathy and visual field defect; oral replacement therapy improved visual symptoms, and it appeared to have prevented further deterioration.

Case description

This study was retrospective case report of a patient followed at the Clinica Oculistica, DiNOGMI, Ospedale Policlinico San Martino IRCCS, University of Genoa. The treatment followed the tenets of the Declaration of Helsinki. Written informed consent was obtained at the first visit both for data and for images.

A 41-year-old woman has come to our attention complaining of decreased visual acuity and monocular diplopia associated with bilateral hypoacusis, upper and lower limb hypoesthesia. In 2003, she was submitted to bariatric biliopancreatic diversion due to morbid obesity, followed by multiple abdominal surgeries because of recurrent hernias and intestinal malabsorption syndrome developed. Neurological examination evidenced mild dysarthria, upper and lower limb hypoesthesia, weak and symmetrical osteo-tendinous reflexes. No response to Babinski's sign

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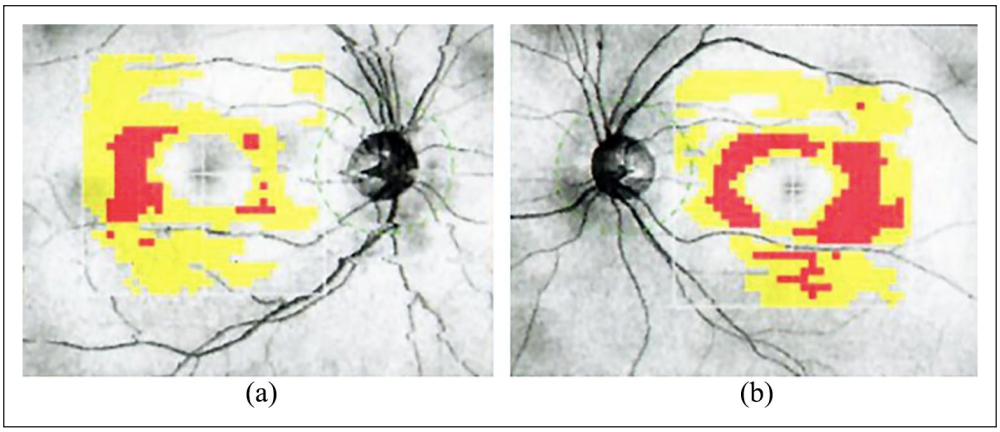

Figure 1. OCT reports of ganglion cell complex of the right (a) and left (b) eye; yellow background indicates GCC was in the lowest 5% of age-matched controls, red background indicates GCC was in the lowest 1% of age-matched controls.

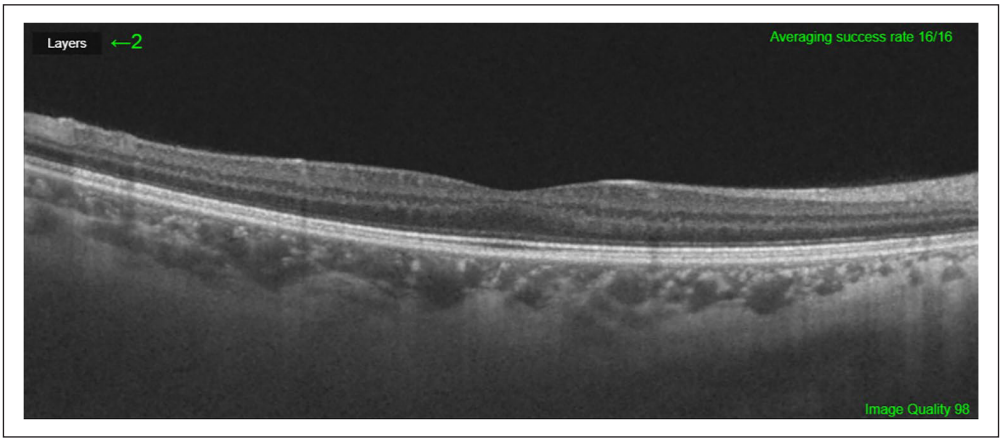

Figure 2. Minimal, aspecific focal hyperreflective RPE changes at the subfoveal and parafoveal area can be seen.

and positive Romberg sign were found. The psychological evaluation highlighted a mild cognitive impairment.

At the first ophthalmological examination, both eyes best-corrected visual acuity (BCVA) was 20/32 with research (i.e.: small eye movements), intraocular pressure (IOP) was 14 mmHg at Goldman applanation tonometer, Ishihara plates response was 1/17 (demonstration plate). Anterior segment evaluation showed superficial punctate epithelial defects in the left eye. Both eyes showed otherwise clear cornea, deep anterior chamber, and clear lens. Pupils were regular, the light reflex was normal, and no anisocoria was present.

Extraocular muscle motility showed convergence deficit, version, and ductions within the normal limits, no extraocular muscle weakness. The indirect ophthalmoscopy of both eyes revealed mild temporal pallor of the optic nerve.

During the first ophthalmological visit, a SITA-fast visual field testing 30-2 was also performed, and showed a centro-cecal scotomata, but unfortunately, this visual field was characterized by an extremely low reliability. Since VF testing was inaccurate due to lack of compliance of the patient, we preferred to perform optical coherence tomography (OCT) since the higher sensitivity and specificity of the latter.

Therefore, an OCT by TOPCON 3DwideH was performed and showed in both eyes thinning of the retinal thickness associated with ganglion cell loss (Figure 1). Furthermore minimal, aspecific focal hyperreflective RPE changes at the subfoveal and parafoveal area was present at the OCT (Figure 2).

Laboratory tests were then requested, and they showed a normocytic normochromic anemia (ferritin decreased, MCV, MCH, and MCHC within normal limits). Also, vit-E deficiency was observed and vitamin A (vit-A) level was at the lower limit of normal. In contrast, vit-B12 and folate were normal. The patient did not refer previous vit-B12 and folate deficiency. HCV Ab, HbsAg, and Treponema (s-TPHA) were negative.

The patient was also submitted to magnetic resonance imaging (MRI), which highlighted hyperintense signals of the white matter in the frontal region of both hemispheres and the cerebellum of supposed vascular etiology. After neurological evaluation, motor and somatosensory evoked

potentials and spine MRI were requested, and they did not show any abnormalities. Other investigations included transcranial doppler-ultrasound, echo-color doppler supra-aortic vessels, electroencephalogram (EEG), and they were within limits.

The patient has been treated with oral supplementation therapy with Retinol 30000 U.I. + Tocoferol acetate 70 mg once daily for 2 weeks. The therapy has been stopped for 1 month to avoid the risk of toxicity and restarted later for one more week. At the end of the treatment, laboratory tests showed a level of vit-A within the normal limits whereas level of vit-E was increased but still lower than normal. However, the patient reported improvement in visual acuity in both eyes associated to the disappearance of monocular diplopia and complete resolution of the scotoma. The ophthalmological examination showed a BCVA of 20/20 without research in both eyes, and a resolution of the corneal epithelial defects.

The patient was referred to a dietitian to develop a specific treatment plan to meet patients' nutritional needs.

Conclusion

Biliopancreatic diversion is a surgical procedure performed in patients affected by morbid obesity that leads to a decrease in hunger, increase satiety, and diminished calorie absorption. One of the drawbacks of this procedure is that malabsorption of calories can lead to lipid-soluble vitamin malabsorption. Malabsorption syndrome has been widely described in literature after bariatric surgery procedure; therefore, the medical team must be aware of it before complications occur.[4,5] The diagnosis of malabsorption syndrome can be overlooked and delayed because of its slow evolution and subtle symptoms at the beginning; therefore, any patients complaining of neurological and ophthalmological symptoms should be tested for vitamin levels.[6] McCarron et al. described that the duration, chronic versus short term, of malabsorption syndrome could be related to the clinical features of vit-E deficiency. Besides, the healing process from axonal and photoreceptor damage may be considerably limited after a chronic vitamin deficiency, especially in older people.[3]

Donaldson and Fishler showed a case of a patient who underwent first bariatric surgery in 2000 and subsequently LASIK surgery in 2008. After 2 years the patients showed corneal melt and she was treated without improvement, after months she admitted noncompliance with nutritional supplements.[7] Also Giannaccare et al. showed two cases of steril corneal perforation secondary to vitamin A deficiency after biliopancreatic diversion with duodenal switch.[8] These authors outlined in these case reports how important are nutritional supplements after bariatric surgery. Serum vitamins level dosage should be always monitored in these patients to avoid serious sight-threatening complications.

Vit-E (α-tocopherol) is a fat-soluble vitamin and liver, muscle, and adipose tissue are the main site of storage. It plays many essential functions in the body, such as immunomodulation, inhibition of platelet adhesion, and prevention of the propagated oxidation of saturated fatty acids in cellular membranes. Therefore, its antioxidant action on free radicals prevents damage to the central, peripheral nervous system and retina[3]; this because the brain is very rich in polyunsaturated fatty acids. Primate studies have demonstrated that vit-E deficiency results in a wide range of clinical features, including neurological manifestations due to peripheral axonopathy and spinocerebellar pathways' involvement,[9] hemolytic anemia, thrombocytosis,[10] and visual field defects.

In addition to visual impairment, our patient had normocytic normochromic anemia and neurologic symptoms such as upper and lower limb hypoesthesia, depressed osteo-tendinous reflexes, no response to Babinski's sign and positive Romberg sign. As it is possible to associate these clinical findings with vit-E deficiency, in our patient the anemia was probably due to multiple factors including the of iron deficiency as part of malabsorption syndrome and hemolysis as a consequence of erythrocyte membranes instability.

Regarding visual symptoms, it is crucial to highlight that retinal pigmented epithelium (RPE) is the leading site of vit-E storage; therefore, early manifestations of vit-E deficiency might be detectable through optical coherence tomography (OCT) examination, but in our patient OCT changes were mild and aspecific (Figure 2). On animal model, vit-E deficiency leads to the breakdown of photoreceptor outer segments in the retina, causing accumulation of lipofuscin in the RPE. Furthermore, it has been described that it prevents oxidative destruction of vitamin A stores which lead to additional damage to photoreceptors. In literature, there are few reports about ophthalmological manifestations of vit-E deficiency, and this may suggest that RPE as the leading site of storage, may play a role in preventing manifestations of vit-E deficiency damage. Despite this, our patient has come to our attention because of decreased visual acuity, central scotomata, and monocular diplopia together with some neurological symptoms.

OCT examination was performed with Topcon Triton DRI, and it showed a ganglion cell complex defect in both eyes associated with thinning of the inner retinal layers (nerve fiber layers, ganglion cells, inner nuclear layer), outlining a possible optic nerve damage. These anatomical anomalies, visible at the OCT, can be supported by the evidence of the lack of vit-E and might play a role in lipid peroxidation of the retinal ganglion cell membranes,

causing damage to themselves. Similar mechanism could take place in other part of the central nervous system causing the neurological symptoms. OCT examination has been performed earlier and repeated after the supplementation therapy. Retinal layers' thickness and anatomy have not recovered, however symptoms improved with treatment.

Regarding monocular diplopia, it often results from refractive media abnormalities such as cataract, tear-film abnormalities, corneal defects (e.g. diffuse epithelial punctate keratopathy) as in our case. It was clearly demonstrated that vitamin deficiency, especially vitamin A, can result in a wide range of corneal diseases, including superficial corneal defects.[11,12]

The disappearance of diffuse punctate keratopathy and the subsequent monocular diplopia after vitamin supplementation therapy would support the vitamin deficiency related pathogenesis. After oral supplementation therapy, vit-A and E dosage were requested, and they resulted in stability of vit-A levels while vit-E remained under the normal limits. McCarron et al. highlighted the same results to oral supplementation therapy. In their case in which they reported that the nutritional assessment over 10 years of vit A, C, B1, B6, B12 normalized with the therapy except for vit-E despite the treatment.[5]

In conclusion, the past medical history is essential in the case of a patient complaining of visual symptoms compatible with vitamin deficiency syndrome in order to detect the cause and to start a prompt vitamin supplementation therapy to avoid possible irreversible neurological and visual sequelae. This condition can be reversible in the early stages and younger patients. However, it could lead to severe complications in prolonged cases, which are characterized by inadequate response to therapy. This case report highlights the presence of a possible causative role of vitamin deficiency, especially vit-E and also vit-A, in visual and neurological manifestations.

Besides, ophthalmologists should be aware of specific ophthalmological findings that might represent an early manifestation of malabsorption syndrome, especially in patients who underwent a biliopancreatic surgery. For this reason, an ophthalmological evaluation should be required during the follow-up of these patients.

Acknowledgements

This work was developed within the framework of the DINOGMI Department of Excellence of MIUR 2018-2022 (legge 232 del 2016).

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

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