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CLINICAL CASE REPORT

Xerophthalmia and acquired night blindness in a patient with a history of gastrointestinal neoplasia and normal serum vitamin A levels

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Abstract A 69-year-old male patient presented to our department with a 3-month history of nyctalopia. Reviewing of his general health revealed a history of gastrointestinal tumor treated with a modified WHIPPLE operation. Ocular findings at presentation included mild xerophthalmic features and nonspecific pigmentary retinal changes. A standard full-field electroretinogram (ERG) was obtained that showed normal photopic function and extinguished scotopic function. The ocular symptoms, the history and the ERG findings suggested vitamin A deficiency as a possible cause for his complaints. Serum vitamin A levels were subsequently requested, but the results were within normal limits. Despite the normal serum vitamin A levels, the patient was instructed to commence treatment with high doses of oral vitamin A supplements. One month after the onset of the treatment, the patient reported that his visual function has significantly improved, while repeat ERG testing revealed that scotopic function has improved to normal levels. This case highlights that in patients with acquired night blindness due to vitamin A deficiency, the ERG responses possibly represent a more sensitive marker compared to the serum levels of vitamin A.

Keywords Acquired nyctalopia · Vitamin A deficiency · Electroretinography · Serum vitamin A levels

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Introduction

Vitamin A (retinol) is a fat soluble vitamin with multiple biochemical roles in the human metabolism. In terms of the ocular metabolism, it is essential for conjunctival and corneal epithelial maintenance (necessary for conjunctival epithelial cell RNA and glycoprotein synthesis), retinal phototransduction (serves as a precursor of the photosensitive visual pigments), and retinal pigment epithelial cell viability [1]. Thus, vitamin A deficiency, most commonly as a result of malabsorption, malnutrition or due to liver disease, leads to significant dysfunction both at the ocular surface and at the level of retinal photoreceptors.

Night blindness is the main and earliest symptom in patients with vitamin A deficiency [2, 3]. Electroretinography (ERG) in such cases has shown that rod function is primarily affected, while cone function is preserved at least in the early stages of the condition [4].

Previous reports have demonstrated rapid recovery of visual function following parenteral administration of vitamin A supplements in patients with abnormally low serum vitamin A levels [5–7]. This case report presents a patient with night blindness and normal serum vitamin A levels who was successfully treated with oral vitamin A supplements, resulting in subjective visual recovery and objective restoration of scotopic function on ERG.

Case report

A 69-year-old male patient with a 3-month history of night blindness was referred for evaluation to the Medical Retina Department at the University of Crete. His ocular history and family ocular history were free. A general review of systems indicated a history of gastrointestinal tumor 8 years ago, managed with surgical resection of duodenal segments and parts of the pancreas. At the time of presentation, the patient was only receiving sorafenib tablets (a multikinase inhibitor that decreases tumor cell proliferation). Communication with his medical oncologist revealed that the malignant disease was stable for the last few years, and also that upon administration of this medication, diarrhea and weight loss were present for a short period that made them to modify (decrease) the dose of the cancer medication.

Best-corrected visual acuity (BCVA) was 20/25 with +0.50D and +0.50D/−0.25D × 175 in the right and left eye, respectively. Confrontation visual fields were full in both eyes, and external examination showed that eyes were orthophoric. Pupils were round and reacted normally to light. Slit lamp examination of the ocular surface showed moderate blepharitis and foamy secretions in the bulbar conjunctiva in both eyes (Fig. 1). Keratinised plaques were observed adjacent to the limbus. The cornea and anterior chamber were clear. The lenses showed 1+ nuclear sclerosis in each eye. Ocular pressures were normal in both eyes.

Fundus examination showed some nonspecific pigmentary changes, while the rest of the retinal

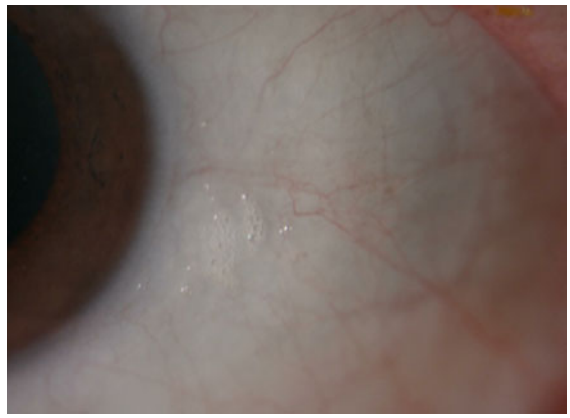

Fig. 1 Color photograph of the ocular surface showing foamy secretions adjacent to the limbus

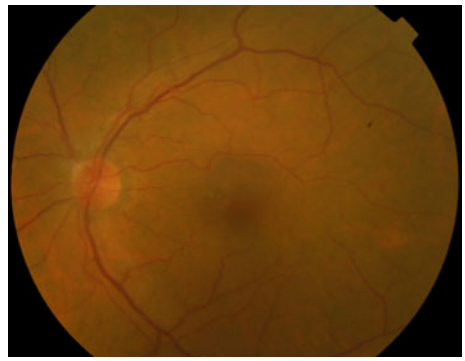

Fig. 2 Fundus photograph of the posterior pole showing nonspecific pigmentary changes

examination did not reveal any abnormalities (Fig. 2). Automated visual field (30-2) examination was performed and revealed normal peripheral boundaries. Full-field light-evoked electroretinography (ERG) was subsequently requested in an attempt to obtain objective information regarding the visual function of the patient. A computerized Primus 2.5 system (Tomey, Germany) that incorporated the ISCEV Standards [8] was used for recordings. ERGs were recorded using corneal silver-nylon thread DTL electrodes (DTLplus, Diagnosis LLC, Lowell, USA) draped across the limbus, as an active electrode. A 9-mm silver–silver chloride (Ag–AgCl) electrode (Biosense Medical, Chelmsford, UK) mounted at the ipsilateral outer canthus, used as a reference, while the earth electrode was placed on the forehead. Pupils were dilated with the use of tropicamide 1 % and phenylephrine 5 % drops. ERG data were acquired at

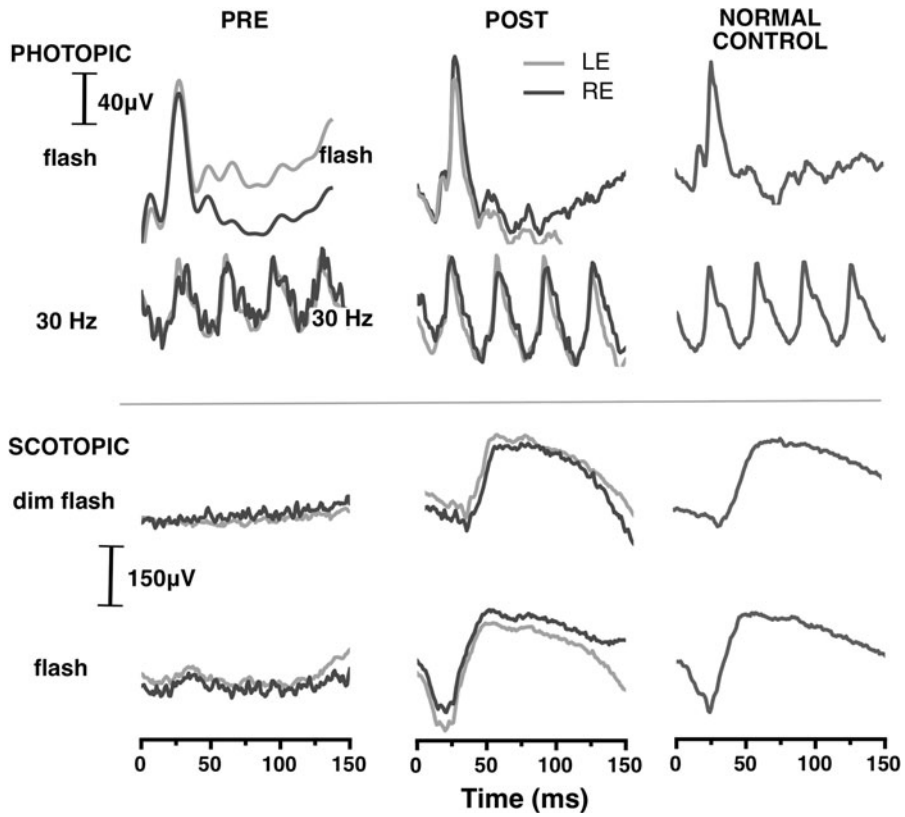

Fig. 3 Full-field light-evoked ERG waveforms (RE: *dark gray*, LE: *light gray lines*) at presentation (*left*) and 30 days (*middle*) following treatment with vitamin A supplements and from a normal control subject (*right*)

1,000 Hz and constrained by online band-pass filtering between 0.3 and 300 Hz and a gain of 5,000. Rod-specific response (to a 0.01 cd*sm^{-2} flash) was undetectable in both eyes, while bright flash scotopic ERG (mixed response to a 3.0 cd*sm^{-2} flash) was profoundly reduced to about 20–25 % of the normal (b-wave amplitude at 40 and 60 μV, for the RE and LE, respectively; lower limit of normal levels, 200 μV). Single flash photopic and 30 Hz flicker were within normal limits in both eyes (Fig. 3, left graphs).

The differential diagnosis included either vitamin A deficiency or an autoimmune type of retinopathy on the basis of the clinical examination and history. Serum vitamin A levels were requested that came back normal (0.47 mg/l, normal range 0.30–0.60 mg/l). Despite the surprising normal serum vitamin A levels and since the patient did not consent for repeat vitamin A serology, he was considered as having nyctalopia due to vitamin A deficiency. Therefore, he was instructed to commence treatment with oral vitamin A supplements (200,000 IU qd for 2 days and repeat the dose after 2 weeks).

On re-evaluation, 1 month after the onset of oral vitamin A treatment, the patient subjectively reported rapid visual recovery (soon after the onset of treatment), while repeat ERG testing showed normal scotopic function in both eyes (Fig. 3, middle graphs). Photopic ERG responses at both conditions (single flash and 30 Hz flicker) were also found improved compared to pre-treatment recordings. Patient's ocular examination was unchanged in comparison with his initial visit.

Discussion

Night blindness resulting from vitamin A deficiency involves multiple pathophysiologic mechanisms. These mechanisms may implicate any of the following: abnormal serum vitamin A (retinol) levels,

abnormal synthesis of retinol binding protein, low serum zinc levels (zinc dependent enzyme is involved in conversion of retinol to retinal) or simply impaired storage of vitamin A esters in the liver [9]. Although malnutrition (rare in developed countries) and malabsorption (in patients with history of gastrointestinal bypass surgery) present as the most straightforward causes for decreased serum vitamin A levels, the presence of simultaneous hepatic or renal disease can also interfere with the serum vitamin A levels [10, 11].

Vitamin A is released from the liver in association with a carrier protein, called retinol binding protein (RBP). In situations of severe protein or liver insufficiency, the release of the combined molecule declines. Additionally, patients with renal disease show increased levels of urinary RBP and normal serum vitamin A levels. Thus, serum vitamin A levels do not actually reflect total vitamin A stores [12]. In our patient, liver and renal function tests were both found normal.

The diagnosis of vitamin A deficiency is usually made by clinical findings, but can be supported by measurement of serum retinol levels (levels less than 20 μg/dl suggest deficiency), or the ratio of retinol to RBP (a molar ratio <0.8 suggests deficiency [13, 14]. In our patient, the serum vitamin A levels were found normal, thus rendering the clinical diagnosis questionable. Furthermore, the patient did not consent for repeat vitamin A serology testing, to confirm the initial surprising result. Apart from the history of bypass surgery, the drug induced functional diarrhea in our patient could also have contributed to any type of malabsorption. The decision to treat the patient with vitamin A supplements was based on the history, the xerophthalmic features of the ocular surface and on the electrophysiologic abnormalities, that demonstrated a functionally cone-isolated retina. Of note, cone responses were also decreased to a lesser extent at the baseline ERG, implying some milder cone involvement in vitamin A deficiency, as also suggested in previous studies [7, 15].

Some authors have suggested that the simplest and most inexpensive way of confirming the diagnosis is treatment [1, 16] with vitamin A, especially when electrophysiologic testing is not readily available or vitamin A serology is difficult to obtain.

In summary, the current report highlights that electrophysiologic testing is possibly a more sensitive marker in vitamin A deficiency cases in comparison with serological tests and that a successful response to treatment can be an indicator that the suspected diagnosis is correct.

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