CASE REPORT

# Dry eyes — vitamin A deficiency is a differential diagnosis not to be missed: a case report

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## Abstract

We describe a 53-year-old woman who presented with dry eye disease with poor vision in both eyes secondary to vitamin A deficiency.

*Key words: Cornea; Dry eye syndromes; Night blindness; Vitamin A deficiency; Xerophthalmia*

## Introduction

Dry eye is classified as aqueous deficient or evaporative or a combination of the two. In a multi-center study of >1800 Chinese adults aged 18 to 45 years, 41.4% were diagnosed with dry eye disease. Most of them had evaporative dry eyes caused by a reduced tear film break-up time; only about 25% had aqueous deficiency based on the Schirmer test. We present a case of dry eye disease with low vision in both eyes secondary to vitamin A deficiency.

## Case presentation

In December 2018, a 53-year-old Chinese woman was referred to our clinic with a 2-year history of bilateral dry eyes, corneal erosions, and blurring of vision. Her vision was worse at night. The patient had no family history of night blindness. The ocular dryness could not be resolved despite hourly instillation of preservative-free artificial tears. In 2014, she had hematuria secondary to urinary tract infection and bilateral renal stones. In 2015, the patient had undergone bilateral mastectomies for breast cancer (T1aN0M0), after which she declined hormonal therapy and opted for traditional Chinese medicine treatment. She was in remission since then.

On examination, corrected visual acuity in both eyes were 6/200 despite pinhole correction. Slit-lamp examination revealed the presence of whitish plaque-like lesions with crisscrossing lines over the nasal and temporal bulbar conjunctiva (**Figure 1**). The ocular surface appeared dull with marked conjunctival xerosis. Fluorescein staining revealed severe erosions of both corneas. The patient was very sensitive to light during examination. Fundal examination revealed diffuse pigmentary changes in the peripheral retinas of both eyes. Schirmer's test showed normal levels of aqueous tear production.

Differential diagnoses of dry eyes and depositions of keratin on the ocular surface include keratoconjunctivitis sicca, with or without underlying autoimmune diseases such as Sjögren syndrome, systemic lupus erythematosus, and thyroid disorders. Results of serological tests were negative for anti-nuclear antibodies, anti-neutrophil cytoplasmic antibody, and anti-double stranded DNA antibodies. Serum thyroid stimulating hormone was within normal levels. Cicatricial conjunctivitis such as Stevens-Johnson syndrome and atopic keratoconjunctivitis may also give rise to a keratinized surface, but patient had no history of generalized skin eruption or rash or ocular itch (a hallmark feature in ocular atopy). Neoplastic causes such as ocular surface squamous neoplasia may be a masquerade, but simultaneous bilateral involvement is rare unless in immunocompromised individuals.

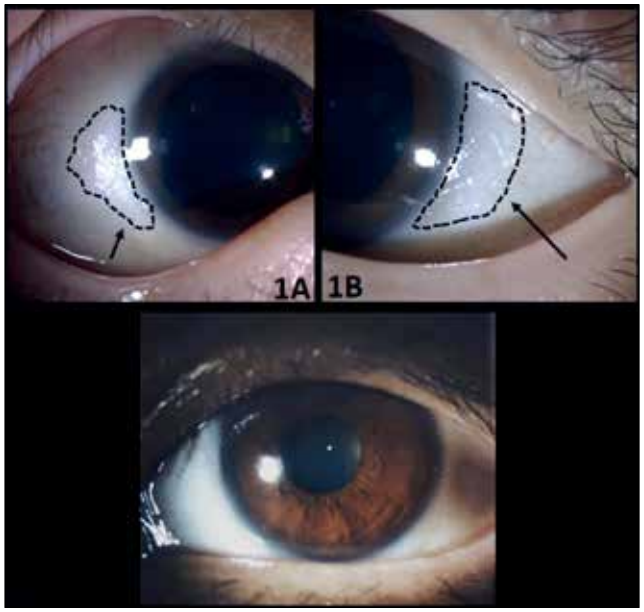


**Figure 1. (a) The presence of Bitot's spots on the interpalpebral conjunctiva. (b) Disappearance of Bitot's spots and restoration of the normal luster of the ocular surface after vitamin A supplementation.**

Results of automated perimetry were unreliable, as the patient could not identify or fixate on the target. Full-field electroretinogram revealed both delayed and reduction in the amplitudes of a and b waves following a light stimulus in both light and dark adaptation, with a diminished 30-Hz flicker response (**Figure 2**). All these suggested a generalized rod and cone dysfunction in both eyes. Vitamin A deficiency with xerosis and night blindness was suspected. Blood test revealed a borderline reduction in serum zinc level at 10.0 (normal range, 10.7-18.0) μmol/L and reduced vitamin A level at 26 (normal range, 38-98) μg/dL. A nutrition history revealed that the patient had avoided vegetables, eggs, melons, and milk in diet owing to 'irritable bowels'. She was counselled on change in diet and use of oral vitamin supplementation, but she refused the latter.

Two months after a change in diet, her vision improved to 18/200 bilaterally. Pinhole correction further improved the vision to 20/40. In March 2020, she eventually opted for vitamin supplement. In May 2020, she reported improvement in night vision, with resolution of photopsia, tearing, and eye discharge. In July 2020, her vision with spectacles improved to 20/40 and 20/30 in the right and left eyes, respectively.

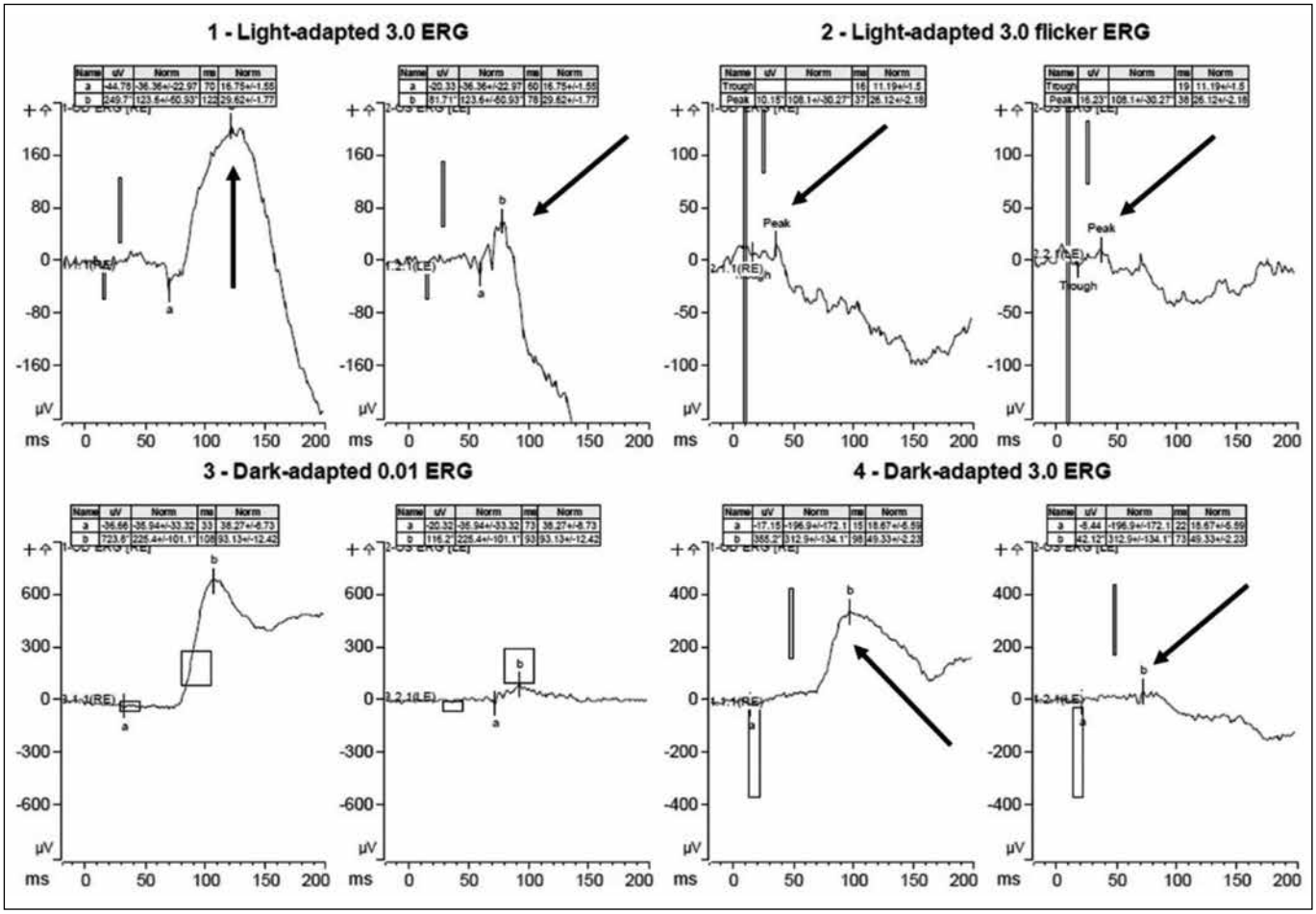


**Figure 2. Light- and dark-adapted full-field electroretinogram showing the delayed and reduced amplitudes of a and b waves after a light stimulus suggestive of a generalized dysfunction of rod and cone photoreceptors in right and left eyes.**

Examination revealed disappearance of punctate epithelial erosions on both corneas and restoration of a stable tear film with a break-up time of >5 s. Pigmentary retinopathy resolved in both fundi.

## Discussion

Vitamin A deficiency is a rare cause of dry eyes and a common cause of night blindness. Globally, vitamin A deficiency is the leading cause of preventable blindness in children in low-income countries.[1] In developed countries, vitamin A deficiency usually occurs in patients with bariatric surgery, pancreato-hepato-biliary surgery, bowel diseases, and psychiatric disorders with dietary restrictions. Xerophthalmia is an ocular complication of vitamin A deficiency.[2] Our patient had night blindness, conjunctival xerosis, Bitot's spots, and corneal xerosis, all of which are reversible upon treatment.

Vitamin A is fat-soluble micronutrients essential in the visual cycle.[3] These compounds include retinol, retinal, retinoic acid, and carotenoids; they can be found in animal liver, egg yolk, and vegetables. Vitamin A is responsible for the recycling of rhodopsin, a visual pigment found in rod photoreceptors accountable for night vision. Absorption, metabolism, hepatic release, transport, and tissue utilization of vitamin A rely on adequate zinc in the system.[4] Zinc regulates the metabolic conversion of retinol to retinal in the retina by mediating a zinc-dependent enzyme known as alcohol dehydrogenase. Conversely, severe vitamin A deficiency limits the absorption and lymphatic transportation of zinc by altering the synthesis of a zinc-dependent binding protein. Vitamin A and zinc have a synergetic effect in maintaining the structures of corneal and conjunctival epithelium.[5] Hypovitaminosis leads to a loss of goblet cells, which is an important source of glycoproteins that wet the ocular surface. This is followed by squamous cell metaplasia in the conjunctiva leading to xerosis and deposition of keratin in the perilimbal areas of the interpalpebral conjunctiva.

Diagnosing vitamin A deficiency relies on detailed clinical history taking and a blood test for serum level of vitamin A. In Hospital Authority, only serum zinc level test is available. Patients with suspected vitamin A deficiency are referred to private laboratories for a diagnosis. Causes of vitamin A deficiency include dietary insufficiency, defects in absorption (eg, chronic diarrhea, malabsorption syndrome, and bile salt deficiency), transportation (Kwashiorkor disease) or storage (liver disease) of vitamin A. Medication for xerophthalmia in adolescents and adults consists of three oral doses of vitamin A at 200 000 international units. The first dose should be given immediately on diagnosis, the second on the next day, and the third at least 2 weeks later. Women of reproductive age or during pregnancy should be given smaller doses unless the xerophthalmia is severe. In severe cases or patients unable to take oral medications, intramuscular injections of 100 000 international units of vitamin A is an alternative. Topical vitamin A ophthalmic ointment is not available in Hong Kong, but the ointment itself is inadequate to treat underlying systemic hypovitaminosis. Zinc supplementation is rarely required especially in developed countries. Children with zinc deficiency in resource-limited countries may benefit from zinc supplementation at 1-2 mg/kg/day for 4 to 6 weeks.

## Conclusion

Vitamin A deficiency is rare in developed countries. It can cause treatable ocular dryness and blindness. Workup for dry eyes should include a nutritional history for any food restrictions and a medical history for any relevant gastrointestinal tract disorders to reveal any underlying vitamin A deficiency.

## Author contributions

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

## Conflicts of interest

All authors have no conflicts of interest to disclose.

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## Ethics approval

The patient was treated in accordance with the Declaration of Helsinki. The patient provided informed consent for the treatment/procedures and publication.

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