Case Report: Vitamin A Deficiency and Nyctalopia in a Patient with Chronic Pancreatitis

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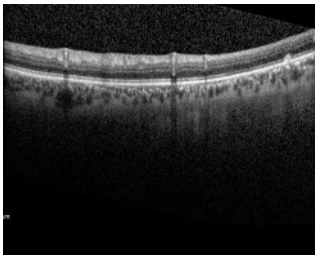
SIGNIFICANCE: Vitamin A deficiency is a known concern in developing countries, but it is often overlooked in developed regions. A history of conditions causing alimentary malabsorption should be considered when patients present with complaints of nyctalopia.

PURPOSE: A case of vitamin A deficiency with nyctalopia in a patient with chronic pancreatitis including pertinent diagnostic testing, treatment, and management is presented. The intent is to draw attention to the condition as a differential diagnosis for nyctalopia due to increased prevalence of conditions causing malabsorption.

CASE REPORT: A patient with a history of chronic pancreatitis and pancreatic tumor presented with symptoms of nyctalopia and xerophthalmia. Given his systemic history, testing was ordered to determine serum vitamin A levels and retinal function. After results had confirmed depleted vitamin A levels and diminished retinal function, treatment with both oral and intramuscular vitamin A supplementation was initiated to normalize vitamin A levels and improve retinal photoreceptor function. Subjective improvement in symptoms was reported shortly after beginning supplementation, and ultimately, vitamin A levels and retinal function showed improvement after intramuscular treatment.

CONCLUSIONS: Detailed case history and a careful review of systems along with serum vitamin A testing and, if available, electroretinography to assess retinal function can help to make a definitive diagnosis. With appropriate comanagement with the patient's primary care physician, it is possible for those with nyctalopia to begin vitamin A supplementation and regain retinal function.



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Vitamin A deficiency can result from malnutrition, impaired vitamin A metabolism, or malabsorption of vitamin A. The earliest and most common ocular manifestation of nutritional deficiency is nyctalopia, or night blindness. The fat-soluble essential vitamin plays a critical role in maintaining the conjunctival and corneal epithelium, as well as retinal pigment epithelial cell integrity and phototransduction of retinal cells.[1] Ocular findings in vitamin A deficiency include Bitôt spots, conjunctival and corneal desiccation, and multiple yellow-white peripheral focal retinal pigment epithelium defects.[2] A case of vitamin A deficiency with nyctalopia in a patient with chronic pancreatitis along with diagnostic testing, treatment, and management is presented. No identifiable health information was included in this case report.

CASE REPORT

A 61-year-old white man presented to the Veterans Affairs eye clinic with complaints of increasing difficulty seeing faces and inability to adequately perceive objects in dim light. The patient's medical history was positive for chronic pancreatitis diagnosed in 1991, hypertension, asthma, and diabetes mellitus type 2 diagnosed in 1997 (Fig. 1). The best-corrected visual acuity was measured in moderate illumination, and the result of the manifest refraction was similar to the uncorrected visual acuity, 20/30, measured binocularly.

Distance subjective refraction:
Right eye: plano –0.50 × 090 20/30–
Left eye: +0.50 –1.00 × 105 20/30+

Upon examination, mild cortical and nuclear sclerotic cataracts, mild nonproliferative diabetic retinopathy along with scattered yellow-white flecks in the midperipheral retina, and macular mottling were noted in both eyes. Humphrey visual field 30-2 SITA Fast was performed, and there was no field loss upon repeated testing, albeit with poor reliability indices throughout, from January 2013 to February 2015. Macular spectral-domain optical coherence tomographic scans showed retinal pigment epithelium disruption.

Systemic medications taken at the time of presentation included albuterol, pancrelipase, cyanocobalamin, fentanyl, gabapentin, glucagon, insulin, lisinopril, mesalamine, omeprazole, and oxycodone, none of which are particularly known to cause the patient's entering complaint of nyctalopia. In addition, the patient reported the use of over-the-counter vitamin A supplements. Despite subjective improvement in night vision with over-the-counter vitamin A supplements, the patient's concern for lung cancer risk due to β-carotene and his smoking status led him to discontinue using the vitamins. Although visual acuity remained at 20/30, the patient's own report of improved quality of vision in dim lighting prompted an order for serum vitamin A level testing to confirm suspicion of low levels of vitamin A (Table 1), and electroretinography testing was scheduled with the intention of objectively determining deficient visual function.

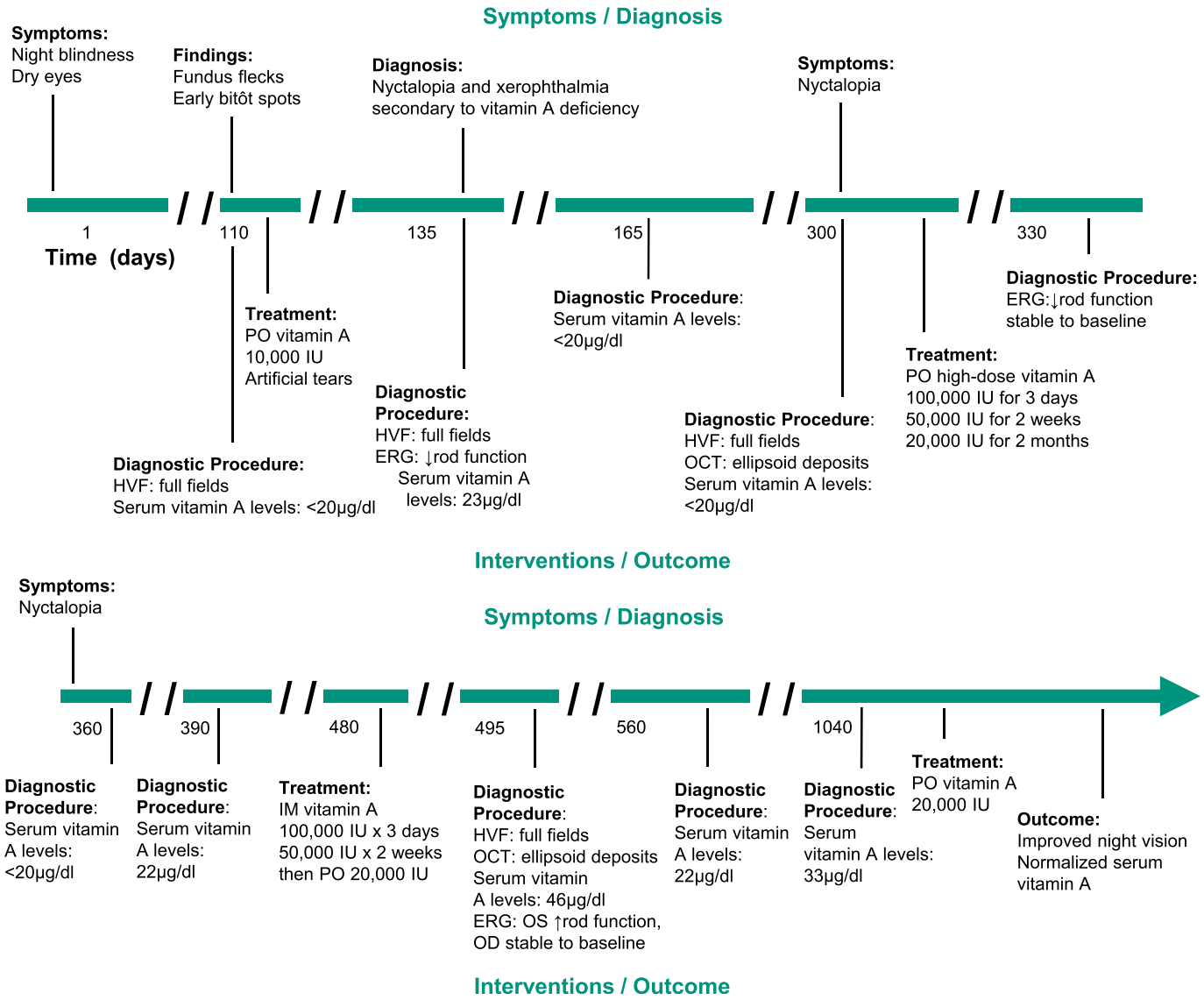


FIGURE 1. Clinical timeline: 61-year-old white man diagnosed as having nyctalopia secondary to vitamin A deficiency and treated with oral and intramuscular supplementation. ERG = electroretinogram; HVF = Humphrey visual field; IM = taken intramuscularly; OCT = optical coherence tomography; PO = taken orally; ↓ = decreased; ↑ = increased.

Faint yellow-white flecks in the midperipheral retina consistent with vitamin A deficiency were found upon fundus examination, and deposits in the ellipsoid zone consistent with these findings were seen on spectral-domain optical coherence tomography imaging (Fig. 2). Early signs of conjunctival Bitôt spots were observed upon biomicroscopy (Fig. 3). Baseline electroretinogram revealed decreased amplitude of the scotopic (rod) waveforms (Table 2) with normal photopic (cone) responses consistent with other documented reports of nyctalopia. After thorough examination and ancillary testing, the patient was diagnosed as having vitamin A deficiency–associated nyctalopia and xerophthalmia due to a history of chronic pancreatitis, which resulted in malabsorption of vitamin A. Initially, the patient was prescribed artificial tears for relief of dry eyes associated with xerophthalmia and was eventually treated with silicone punctal plugs. In June 2013, baseline vitamin A serum level laboratory testing was ordered, and the patient's primary care physician was alerted for the initiation of daily oral vitamin A supplementation shortly thereafter (10,000-IU daily dosage).

Despite the patient's reports of subjective improvement in night vision early on, repeat testing of serum levels showed persistently subnormal levels of vitamin A. After the second consecutive set of low serum level results, the patient's vitamin A dose was doubled to 20,000 IU. At this point, electroretinogram testing was repeated, and the results were similar to baseline testing, indicating subnormal rod responses even with 20,000-IU dose of oral vitamin A supplementation. Next, high-dose oral vitamin A was initiated in June 2014 with a 100,000-IU pulse for 3 days, 50,000 IU for 2 weeks, and 20,000 IU for 2 months. Still, only marginal improvement was shown in November 2014 laboratory results, and it was determined that parenteral supplementation of vitamin A would be necessary.

TABLE 1. Serum vitamin A levels and concurrent dosages of vitamin A supplementation demonstrate minimal improvement before intramuscular injection

Date	Serum vitamin A levels (μg/dL)	Vitamin A supplementation
6/6/13	<20	None
6/21/13	23	10,000 IU PO
7/12/13	<20	10,000 IU PO
6/26/14	<20	20,000 IU PO
8/12/14	<20	High-dose vitamin A PO initiated on 6/26/14
		100,000 IU for 3 d
		50,000 IU for 2 wk
		20,000 IU for 2 mo
11/18/14	22	20,000 IU PO
1/12/15	<20	20,000 IU PO
2/20/15	46	Intramuscular vitamin A initiated 2/2/15
		100,000 IU × 3 d
		50,000 IU × 2 wk
4/17/15	22	20,000 IU PO
8/2/16	33	20,000 IU PO

Maintenance therapy of 20,000 IU given orally was initiated after normalization of serum levels. The reference range was 38 to 106 μg/dL. No current serum vitamin A level data are available after last result in 2016. PO = oral administration.

The pharmacy initially experienced delays in obtaining intramuscular vitamin A because of discontinuation of production in the United States. The patient continued his 20,000-IU oral course until he was able to initiate intramuscular injections in February 2015. Subsequent testing within 3 weeks of starting treatment showed normalized serum levels (Table 1). On the same day that serum testing was done, a third electroretinogram was completed. Results of this subsequent electroretinogram showed slightly increased amplitude of the scotopic electroretinogram waveform. Unfortunately, the right eye electroretinogram waveform remained stable to baseline (Table 2). The patient is currently on a maintenance dosage of 20,000 IU daily. The combined evidence of improved scotopic electroretinogram results and the dramatic increase in serum levels show promise for the patient's visual prognosis.

The abnormal midperipheral fundus findings are expected to resolve according to previous literature.[3,4] Modest improvement of rod function was shown in this case with follow-up electroretinogram testing, and the patient was able to subjectively report improvement in night vision after parenteral supplementation; however, normalized electroretinogram function has been found in previously documented cases.[3–7]

DISCUSSION

Vitamin A deficiency and resulting progressive night blindness are a common public health concern in the developing world. Lack of education, poor sanitation, and malnutrition contribute to the

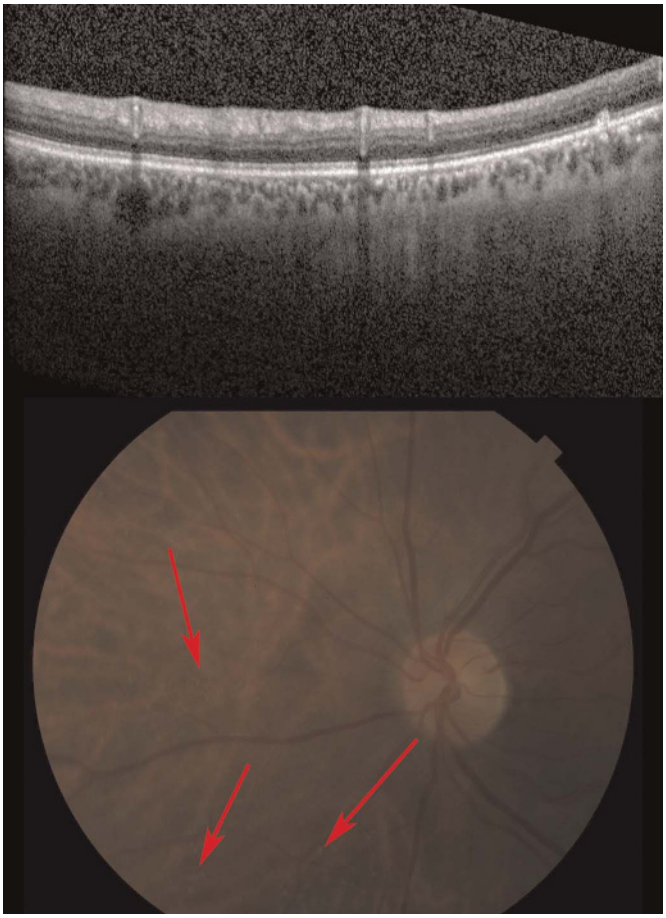


FIGURE 2. (Top) Spectral-domain ocular coherence tomography shows a jagged ellipsoid zone with focal hyperreflective deposits consistent in location with spots seen on fundus examination. (Bottom) Yellow-white granular lesions in midperipheral retina, characteristic of vitamin A deficiency retinopathy.

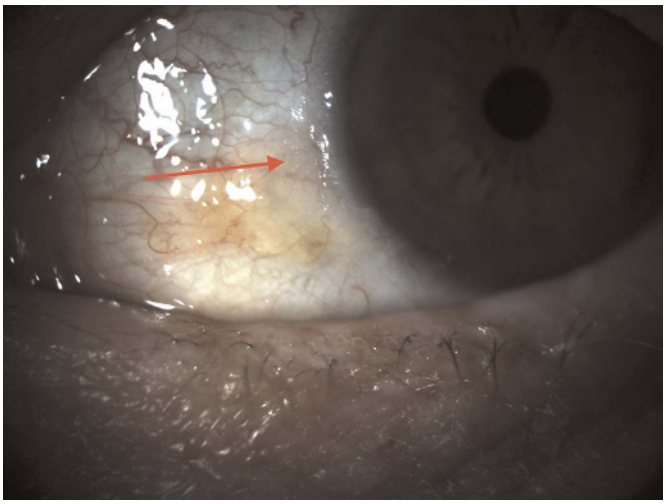
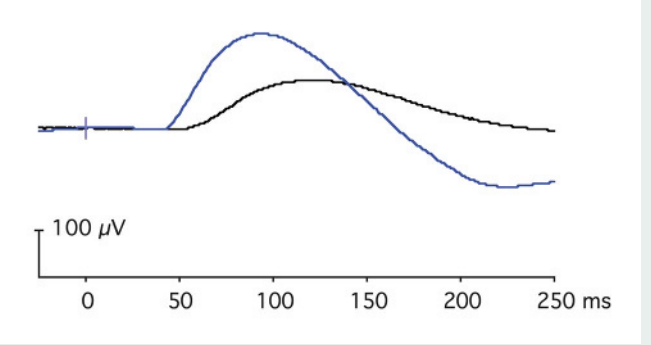


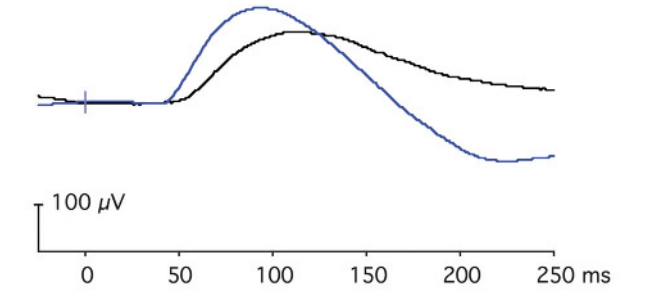
FIGURE 3. Early conjunctival Bitôt spots with subtle foamy appearance indicating initial signs of conjunctival xerosis.

TABLE 2. Dark-adapted 0.01 electroretinogram (rod response) baseline versus normal

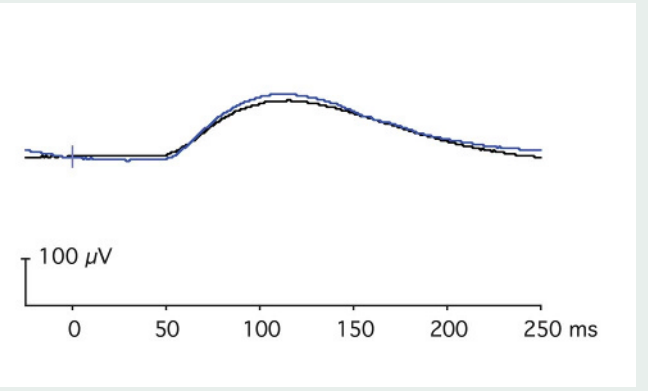
(A) Right eye baseline vs. normal
RE baseline ——— (black line)
Normal ——— (blue line)



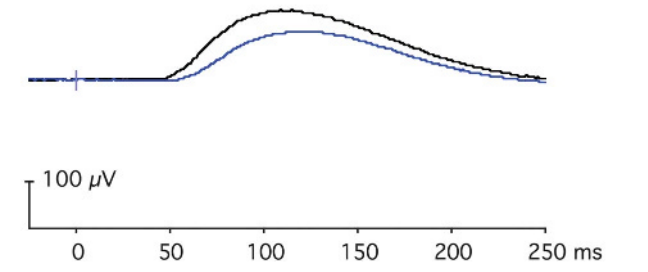
(B) Left eye baseline vs. normal
LE baseline ——— (black line)
Normal ——— (blue line)



(C) Right eye at follow-up vs. patient's baseline
RE follow-up ——— (black line)
RE baseline ——— (blue line)



(D) Left eye at follow-up vs. patient's baseline
LE follow-up ——— (black line)
LE baseline ——— (blue line)



(A) Comparing patient's right eye baseline testing (black) with a normal database (blue) shows significantly reduced rod function. (B) Comparing patient's left eye baseline testing (black) with a normal database (blue) shows significantly reduced rod function. (C) Comparing patient's right eye initial testing (blue) with follow-up testing after treatment (black) shows no significant change despite improved levels of serum vitamin A and the patient's subjective report of improved night vision. (D) Comparing patient's left eye initial testing (blue) with follow-up testing after treatment (black) shows measurable improvement in rod function. LE = left eye; RE = right eye.

prevalence of vitamin A deficiency. Xerophthalmia remains a leading cause of preventable childhood blindness in developing countries due to severe keratomalacia in those with highly depleted vitamin A stores.[7] In developed countries, the deficiency is attributed to alimentary malabsorption associated with chronic systemic conditions of the liver or pancreas, inflammatory bowel disease, and cystic fibrosis.[1–5] It is a common postoperative complication after bariatric surgery for obesity, which is increasing in popularity in developed countries. In addition, previous reports of malabsorption due to hepatitis C, alcoholic cirrhosis, Crohn disease, biliopancreatic diversion surgery, and nutritional deficiency have been published.[8,9] Vitamin A absorption occurs in the upper small intestine upon hydrolysis of retinol by the pancreas; therefore, any insufficiency in gastrointestinal or pancreatic function can lead to deficiency.[9]

In the case presented, because of a history of pancreatic disease resulting in vitamin A malabsorption, it is possible that the patient's chronic condition warranted more aggressive initial vitamin A supplementation therapy to achieve notable serum level increase. It has been shown that parenteral vitamin A restoration, rather than oral supplementation, is highly effective in cases of malabsorption. In addition, iron and riboflavin supplementation, especially in patients with depleted vitamin A stores, can further enhance functional visual improvement.[10] Suggested initial therapies in previous studies have not been consistent, and it seems that initial therapy varies by patient and severity of condition. For example, the World Health Organization recommends an initial dose of 200,000 IU for 2 days and a repeat course 2 weeks later for adults and children older than 12 years, but symptom reversal has been achieved with lower doses and with varying lengths of treatment from 2 to 13 months.[7,8,11]

The affected mechanism involves retinal, the aldehyde form of vitamin A, which binds with opsin in rod photoreceptors to create rhodopsin. In the process of phototransduction, retinal is lost, necessitating a constant supply of the fat-soluble vitamin. Deficiency of this supply will lead to nyctalopia with associated decreased electroretinogram measurements and possible visual field changes.[1]

Vitamin A also aids in maintaining specialized epithelial cells. Loss of goblet cells, accompanied by squamous cell metaplasia in the conjunctiva, results in xerosis and the formation of perilimbal regions of keratinized conjunctival tissue known as Bitôt spots. Corneal xerosis and full-thickness necrosis of the cornea, known as keratomalacia, can occur and lead to visual impairment.[6,12–14] Retinopathy occurs in the midperipheral retina and presents as yellow-white fleck lesions or dots, which are focal pigment epithelium defects thought to be degenerated Müeller cell footplates.[2]

Retinal function is measured using electroretinogram, and studies have observed the selective effects of vitamin A deficiency upon rods and cones. Electroretinogram records action potentials produced by the retina when stimulated by light of varying intensities. The a-wave is the initial fast negative deflection that represents the photoreceptor response, and the b-wave is the slower, positive large amplitude deflection representing the cells, which compose the inner layers of the retina, including the bipolar cells and Müeller cells. Under scotopic conditions, to elicit a rod-driven response, a dim light stimulus is used as in a dark-adapted 0.01 electroretinogram. No a-wave is present in this instance, allowing the b-wave to indirectly represent solely the rod response. A dark-adapted 3.0 electroretinogram measures the combined responses derived from the photoreceptors—both rods and cones—and bipolar cells.[15] In vitamin A–deficient patients with nyctalopia, the absence of rod function along with delayed and reduced amplitude of cone responses is an expected finding.[16] Deterioration in rod function is more pronounced than that of cone function, which is consistent with electroretinogram findings in the case presented. Cones show more resistance to damage from vitamin A deficiency and often show little to no decreased function upon testing.[17–19]

CONCLUSIONS

For patients with complaints of gradual progressive night blindness with a history of pancreatitis or other systemic condition that increases susceptibility to malabsorption, consider vitamin A deficiency as a possible differential diagnosis. Despite its prevalence in developing regions, deficiency of the fat-soluble vitamin is easily missed in developed countries.[20] Thorough case history of symptoms and review of systems, with special attention to conditions that can cause lipid malabsorption, can prove to be instrumental in the diagnosis of vitamin A deficiency. Serum vitamin A level laboratory testing and electroretinogram provide definitive evidence of deficiency and reduced retinal function, respectively. The dosage and mode of vitamin A supplementation for the patient should be closely comanaged with the patient's primary care physician. With proper care and management, patients with vitamin A deficiency–associated nyctalopia are able to regain visual function and reverse signs of retinopathy with adequate supplementation.[4,21]

ARTICLE INFORMATION

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