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CASE REPORT | LIVER

Vitamin A Deficiency Screening in Patients With Chronic Alcohol-Associated Liver Disease: Implications for Liver Transplant Candidates

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ABSTRACT

Chronic liver pathologies may lead to vitamin A deficiency (VAD) through impairment of vitamin A absorption, storage, and distribution. VAD can contribute to ocular pathologies, and in the article, we present 2 patients with alcohol-associated cirrhosis admitted for liver transplant presenting with nonhealing central corneal epithelial defects in the eye without other known ocular pathologies. Low serum vitamin A levels were detected in both patients. Vitamin A supplementation eventually helped corneal epithelial healing within days/weeks. We suggest that VAD be screened for in all liver transplant candidates even before ocular symptoms present. This may prevent more severe VAD ocular sequelae.

KEYWORDS: vitamin A deficiency; screening; liver transplant; alcohol-associated liver disease

INTRODUCTION

Fat-soluble vitamin A is packaged into chylomicrons in the small intestine and transported to the liver, where it is stored in hepatic stellate cells and subsequently distributed to the tissues.[1] The liver is part of the bile system, which supports absorption of the fat-soluble vitamins. Hepatic stellate cells store 40%–90% of the total body pool of vitamin A.[2] Furthermore, to allow for distribution to other organ systems, the liver produces the retinol binding protein 4.[3] Thus, pathologies impacting hepatic function can interfere with vitamin A metabolism.[1]

The aldehyde form of vitamin A, retinal, binds to opsin to form rhodopsin, a pigment found on rods and cones, which contributes to phototransduction.[4] Vitamin A plays a vital role in regulating the growth, development, and differentiation of epithelial cells crucial for maintaining the health of the ocular surface.[5] Ophthalmic manifestations of vitamin A deficiency (VAD) include nyctalopia, Bitot spots, corneal/conjunctival xerosis, keratomalacia, and corneal ulceration/perforation.[6–8] We present 2 cases of ocular manifestations of VAD secondary to chronic alcohol-associated cirrhosis and their response to vitamin A supplementation.

CASE REPORT

Two liver transplant candidates with scleral icterus were seen by ophthalmology for unilateral corneal ulcers. The first patient was a 31-year-old man with alcohol-associated cirrhosis. He developed a large central corneal epithelial defect without infiltration in the left eye immediately before being admitted to the hospital for liver transplantation. Slit-lamp examination showed a large corneal epithelial defect, spanning nearly the entire cornea, characterized by a round and slightly elevated margin. No infiltration, edema, or opacity was observed (Figure 1). The right eye's ocular surface and cornea were unremarkable. The rest of the eye examination was unremarkable.

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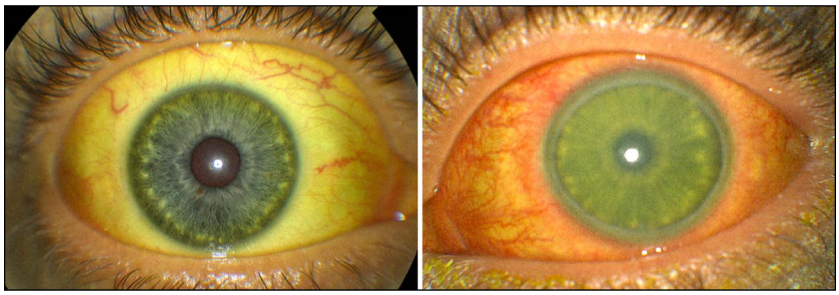

Figure 1. Unilateral corneal ulcer and large central epithelial defect in the left eye (right image; defect highlighted by fluorescein staining diffusely spread over the cornea of the eye) in a 31-year-old man with alcohol-associated cirrhosis with no sign of ocular xerosis. Serum vitamin A of 10.7 ug/dL (normal range: 20.1–62.0 ug/dL). Ocular surface in his right eye (left image) was unremarkable with no sign of xerophthalmia.

The second patient was a 28-year-old man with alcohol-associated cirrhosis. While in the hospital, he developed irritation, redness, and blurry vision in the right eye. Right eye examination revealed a large central epithelial defect with irregular margin but no infiltration, edema, or opacity. His left eye also showed significant punctate epitheliopathy without corneal epithelial defect or infiltration. The rest of the eye examination did not reveal any significant findings.

Neither patient displayed any identifiable risk factors for corneal ulcer or erosion, such as contact lens use. None of the eyes displayed conjunctival/corneal keratinization or xerosis. Both patients denied experiencing night blindness.

Both patients had abnormal liver function tests such as low albumin and total protein levels (Table 1). Serum vitamin A levels were reported significantly low in both patients (10.7 ug/dL in the first patient and 14.9 ug/dL in the second patient; normal range: 20.1–62.0 ug/dL). Both patients were treated with oral/parenteral high doses of vitamin A. The corneal ulcer of the first patient healed with significant subepithelial haze/scar after several weeks of persistent epithelial defect complicated by exposure keratopathy and delayed healing because of a prolonged intensive care unit course after liver transplantation surgery. In the second patient, the epithelial defect healed within 1 week of initiation of treatment with vitamin A.

DISCUSSION

In our report, both patients were candidates for liver transplantation and presented with ocular surface disease associated with VAD that was related to their alcohol-associated cirrhosis because of malabsorption and liver failure mechanisms. VAD is more commonly seen in developing countries where malnutrition is prevalent. In developed countries, VAD is more likely caused by malabsorption rather than malnutrition. In the United States, organic malabsorptive disorders that may cause VAD include cystic fibrosis, chronic pancreatitis, celiac disease, inflammatory bowel disease, eosinophilic gastroenteropathy, small intestinal bacterial overgrowth, and bariatric surgery.[9–11] Nonorganic causes of VAD, such as history of severely restrictive diet, should also be considered.[12]

Chronic liver disease can be associated with a severe form of VAD because of 3 mechanisms: low dietary intake, malabsorption, and loss of hepatocytes.[13] Alcohol-associated cirrhosis may be more commonly associated with VAD than other etiologies such as viral-associated cirrhosis because of poor dietary intake and malabsorption.[14,15] Sohal et al[13] previously reported a patient with corneal ulcers secondary to alcohol-associated cirrhosis-induced VAD; however, they were unable to track corneal ulcer progression in response to vitamin A supplementation.

Table 1. Liver function tests and serum vitamin A level

	Patient no. 1	Patient no. 2	
AST (SGOT)	146	66	0–40 U/L
ALT (SGPT)	59	17	0–41 U/L
ALK PHOS	208	142	40–130 U/L
Total bilirubin	32.6	31.6	<=1.0 mg/dL
Total protein	4.3	3.6	6.0–8.3 gm/dL
Albumin	2.3	3.0	3.5–5.2 gm/dL
Vitamin A	10.7	14.9	20.1–62.0 ug/dL

ALT (SGPT), alanine aminotransferase; ALK PHOS, alkaline phosphatase; AST, aspartate aminotransferase; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamic-pyruvic transaminase.

Patients with advanced fibrosis and cirrhosis may experience a significant decrease in the number of hepatocytes responsible for the primary storage of vitamin A, leading to possible acute/subacute VAD.[14,15] This deficiency may first present in the eyes as an effect on corneal epithelial cells, which have a high rate of regeneration, before progressing to various stages of xerophthalmia, a more chronic condition seen in malnutritional form of VAD. Acute and nonclassical (nonxerophthalmic) ocular presentations associated with VAD such as corneal epithelial defects, corneal ulcers, keratomalacia, and perforation can easily be overlooked as being related to VAD because of the lack of typical ocular manifestation such as Bitot spots or conjunctival/corneal xerosis.[5–8]

Our cases further support vitamin A supplementation as an effective way to treat ocular pathology secondary to VAD. Bors and Fells treated a vitamin A–deficient patient with administration of intramuscular injection followed by oral supplementation of vitamin A. They observed a significant reduction in corneal ulcer size by half after 4 days of treatment.[16] Our second case documented a remarkable improvement within days of treatment with vitamin A. The treatment of VAD with ocular involvement requires high-dose vitamin A supplementation, preferably administered parenterally (intramuscularly) because of malabsorption in severe liver disease. The regimen used for our patients included 100,000 units/3 days, 50,000 units/14 days, followed by a maintenance oral dose of 10,000–20,000 units daily for up to 2 months. Regular monitoring of vitamin A levels and associated symptoms is important to prevent toxicity.

With a 70% prevalence of VAD in liver transplant candidates, prioritizing patients with severe liver disease is crucial for screening and supplementation. To achieve cost-effectiveness, a scoring system based on symptoms, history, and ophthalmological examination may guide serum testing. Patients with high scores albeit no apparent signs or symptoms would benefit the most because early vitamin A replacement can prevent VAD-related ophthalmic consequences.[17] Management of VAD before progression to severe ophthalmic sequelae, such as ulceration and perforation, can prevent damage to the eye and severe visual loss.[8]

DISCLOSURES

Author contributions: MH Dastjerdi was responsible for the collection of patient data. All authors contributed to project conception, interpretation of patient data, writing, and revising of the manuscript. MH Dastjerdi is the article guarantor.

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