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✦ Case report

A Case of Keratomalacia in Severe Vitamin A Deficiency

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Abstract

Vitamin A is a lipid-soluble vitamin essential for vision, playing a critical role in the function and health of the retina and cornea. While vitamin A deficiency is a common global health issue, it is relatively rare in the United States, typically occurring in the context of malnutrition or malabsorption syndromes. Xerophthalmia encompasses the spectrum of ocular manifestations associated with vitamin A deficiency, ranging from night blindness to keratomalacia. In this report, we describe a severe case of xerophthalmia manifesting as keratomalacia in a 42-year-old woman with short bowel syndrome. She presented with five weeks of progressive right eye pain, redness, and vision loss and further evaluation revealed undetectable vitamin A levels, attributed to malabsorption. This case highlights the critical importance of considering vitamin A deficiency in patients with corneal pathology and risk factors for malabsorption. Early diagnosis and treatment are crucial to prevent irreversible vision loss.

Introduction

Vitamin A, a fat-soluble vitamin essential for numerous physiological processes, plays a pivotal role in vision. Vitamin A is typically derived from the diet and is found in liver, butter, whole milk, and dark-leafy green vegetables.[1] In developing countries, vitamin A deficiency is largely due to inadequate dietary intake and nutrition. In developed countries, the etiology of vitamin A deficiency is often

secondary to an issue related to its metabolism and absorption such as liver, pancreatic, or intestinal pathology.[2] Low vitamin A levels have also been reported in patients with chronic alcohol use and associated cirrhosis.[3] Although vitamin A deficiency is rare in resource-rich countries, numerous cases of advanced-stage xerophthalmia have been reported in developed countries, including our case.[4-9] Globally, vitamin A deficiency remains a significant health concern leading to grave vision and life-threatening consequences.

Xerophthalmia describes the scope of ophthalmic manifestations of vitamin A deficiency and is a prominent cause of preventable blindness worldwide.[10] The active form of vitamin A is termed retinol, as it is vital for retinal function.[1] Intraocularly, vitamin A contributes to the generation of rhodopsin, the photosensitive visual pigment in rods which are critical for night vision.[2,11] The cornea, the clear front part of the eye, is vulnerable to vitamin A deficiency. Vitamin A is essential for maintaining the health of the corneal epithelium, preventing desiccation, and ensuring the proper function of the tear film. The deficiency disrupts the regenerative capacity of the corneal epithelium, leading to keratomalacia characterized by corneal thinning, inflammation, and compromised structural integrity.[2,12] If left unaddressed, vitamin A deficiency can led to irreversible ocular damage and vision loss. The corneal changes observed in keratomalacia are indicative of the stark consequences of vitamin A deficiency on ocular health. In addition to corneal pathology, deficiency-related damage may extend to other ocular structures, impacting overall visual function.

Xerophthalmia progresses through various stages, with the earliest clinical manifestation presenting as night blindness, a condition characterized by difficulty seeing in low-light conditions. As xerophthalmia advances, more drastic manifestations can occur, including corneal xerosis, corneal ulceration, and keratomalacia, which involves disruption of the corneal epithelium due to scarring, ultimately resulting in blindness.[2] Herein, we report an extremely critical case of xerophthalmia with an unusual presentation in a patient with keratomalacia from vitamin A deficiency secondary to malnutrition from short bowel syndrome. We aim to raise awareness and further characterize the clinical and ocular features of this extremely rare condition in resource-rich areas.

Case description

A 42-year-old woman with history of Graves' disease and alcohol use disorder presented to the emergency department with five weeks of progressive right eye (OD) pain, redness, and decreased vision. On initial examination, uncorrected visual acuity was hand motion OD and 20/30 in the left eye (OS). Intraocular pressure was normal in both eyes (OU). Slit-lamp examination OD revealed highly inflamed conjunctiva with diffuse injection, as well as exceptional corneal ectasia with 360-degree thinning at the limbus, a small superotemporal descemetocele, and diffuse stromal haze (Figure 1). The anterior chamber appeared shallow with the iris diffusely apposed to the corneal endothelial surface, but Seidel sign was negative. There was no posterior view. B-scan ultrasonography demonstrated no vitritis and an attached retina OU. OD examination was remarkable for peripheral superior and inferior corneal pannus with superonasal corneal neovascularization (Figure 2).

Further questioning of the patient revealed pertinent past surgical history including a surgical complication from the repair of an enterocutaneous fistula, which required multiple revisions and ultimately resulted in short bowel syndrome. The patient had been on total parenteral nutrition (TPN) until two years ago, when she was transitioned to enteral nutrition due to recurrent line infections.

Subsequent evaluation revealed an undetectable vitamin A level (<5 mcg/dL) along with multiple other nutritional deficiencies. The combination of her slit lamp examination findings, undetectable vitamin A level, and short bowel syndrome, led to the ultimate ophthalmic diagnosis of keratomalacia in the setting of extreme vitamin A deficiency. She was admitted to the hospital for TPN and aggressive vitamin A supplementation was initiated to correct her deficiency and prevent further ocular deterioration. Ultimately, this patient's care was transferred to a drug rehabilitation facility due to her history of alcohol and substance use. The details of the patient's substance use history could not be obtained.

Long-term implications for patients with vitamin A deficiency, particularly those with underlying gastrointestinal issues, necessitate a comprehensive treatment approach. Managing the underlying conditions contributing to malabsorption, as seen in this case with short bowel syndrome, is crucial for preventing recurrence of deficiency-related complications. This case highlights the critical importance of early diagnosis and intervention in vitamin A deficiency and underscores the need to consider it as a potential cause of corneal pathology in patients with nutritional compromise.

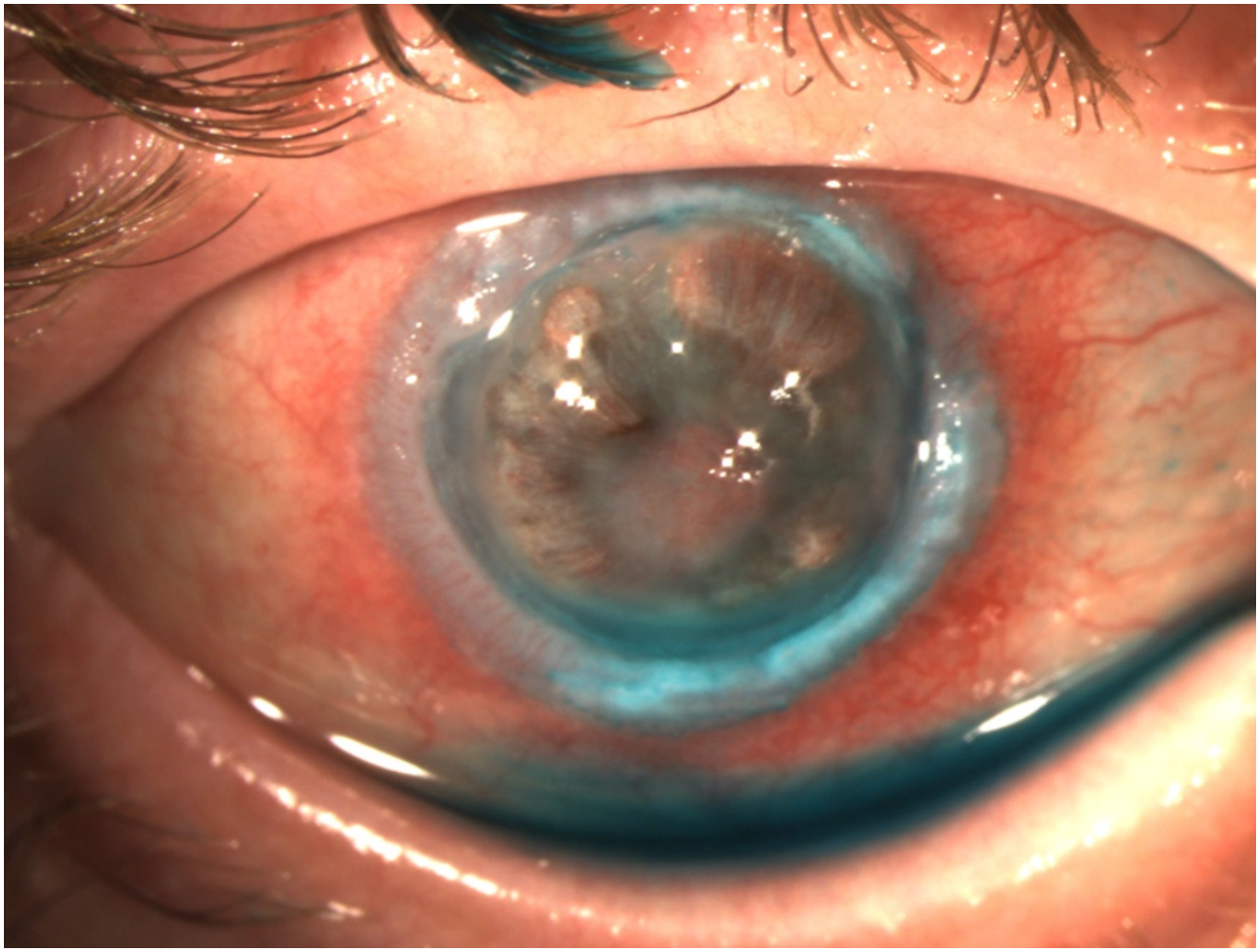

Figure 1. External photograph of the right eye demonstrating marked conjunctival inflammation with diffuse injection, corneal ectasia characterized by 360-degree limbal thinning, a superotemporal descemetocele, and diffuse stromal haze.

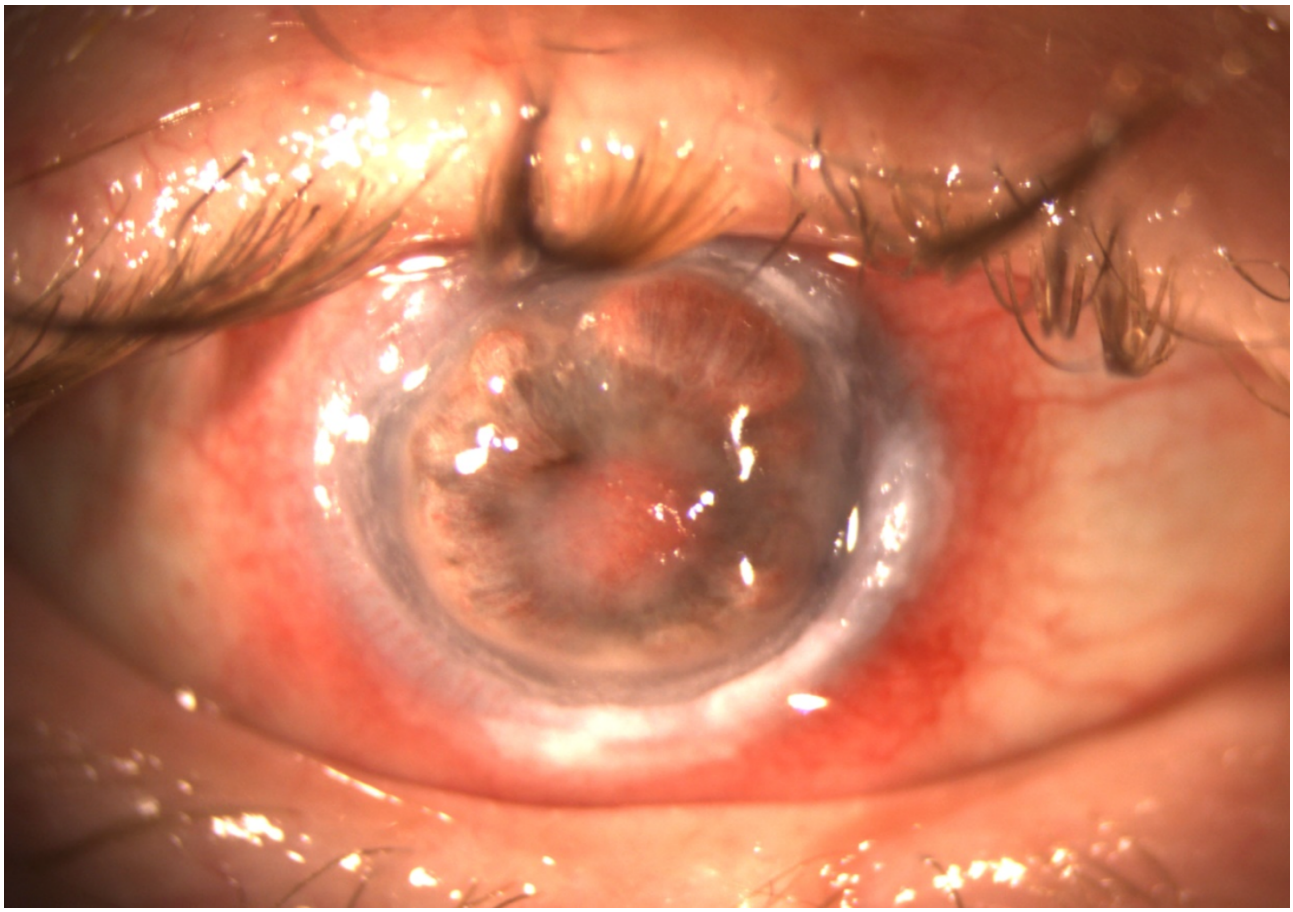

Figure 2. External photograph of the right eye showing peripheral superior and inferior corneal pannus with superonasal corneal neovascularization.

Discussion

We present a rare case of vitamin A deficiency with profound ocular manifestations in Massachusetts in 2022. In the United States, cases of vitamin A deficiency are extremely rare in the general population, estimated to be 0.3% in 2013.[2] In resource-rich countries, vitamin A deficiency is more prevalent among specific populations, including individuals with gastrointestinal disease, chronic alcohol use, or restrictive diets, which may be seen in individuals with autism spectrum disorder.[10]

In the context of this case, the patient's history of short bowel syndrome resulting from surgical complications led to malabsorption, a common pathway for the development of vitamin A deficiency. This, coupled with the patient's history of chronic alcohol use most likely exacerbated their deficiency. In the rare occurrence of vitamin A deficiency in the United States, the incidence of keratomalacia, the most advanced stage of xerophthalmia, is exceedingly rare. Xerophthalmia has a grading system, which defines the lowest grade as night blindness and the later stages manifesting as corneal ulcers and keratomalacia. Night blindness is typically one of the earliest symptoms observed; however, in some cases, the later manifestations of the disease can occur without any preceding early signs.[10] Keratomalacia, as described in this case, is a severe and visually debilitating condition primarily associated with vitamin A deficiency. The rarity of this condition in the United States underscores its importance as a diagnostic consideration in patients with corneal pathology, especially those with underlying risk factors. The patient's history of Graves' disease, short bowel syndrome, and chronic

alcohol use provided a unique set of circumstances leading to the advanced and unusual presentation of vitamin A deficiency.

Our patient provided a rare and advanced presentation of xerophthalmia, which had progressed to stage X3B keratomalacia, characterized by liquefactive necrosis of the cornea.[10] Keratectasia, the progressive bulging and thinning of the cornea, was present in our patient and has been documented in advanced cases of vitamin A deficiency and can lead to serious vision impairment.[9] Our patient also presented with corneal xerosis which is illustrated as the dull and hazy appearance of the cornea and is secondary to goblet cell dysfynction (Figures 1 and 2).[10] If untreated, corneal xerosis can progress and result in corneal ulceration and melting, also called keratomalacia, which is a blinding condition. A corneal ulcer may evolve into a full-thickness corneal perforation, increasing the risk of descemetocele formation, which involves the herniation of Descemet's membrane through a corneal defect. Our patient presented with the most severe features of xerophthalmia including keratomalacia, corneal ulcers, and a descemetocele OD.

Vitamin A deficiency is well-documented in populations with chronic alcohol use, but recent reports have highlighted the complexities of vitamin A supplementation in these patients.[13] Ethanol has been found to enhance the hepatotoxic nature of retinol, complicating its administration in patients with chronic alcohol use.[13] Although vitamin A supplementation is crucial to correct the deficiency, its interaction with ethanol and narrow therapeutic window must be considered when developing treatment plans, especially in patients with alcohol use disorder.

In addition to our case, recent reports of xerophthalmia demonstrate the important link between vitamin A deficiency and alcohol use in developed countries.[9,14] These reports illustrate a need to prevent and better identify vitamin deficiencies in substance using populations to prevent such advanced ocular pathology from occurring. It is imperative to obtain thorough social histories and provide patients with resources to address substance use disorders. As in our case, referring patients to appropriate drug rehabilitation centers is necessary to prevent devasting consequences of malnutrition secondary to substance use such as keratomalacia.

Vitamin A deficiency may be overlooked in adults and in developed countries such as the United States due to its rarity. However, this case illustrates that keratomalacia due to vitamin A deficiency is an important consideration for the differential diagnosis in patients with corneal pathology, even in regions with low prevalence. Early diagnosis and prompt intervention are crucial to prevent irreversible damage to the cornea and maintain visual function. Healthcare providers should remain vigilant in recognizing this potentially sight-threatening condition, particularly in patients with risk factors for nutritional compromise. Obtaining a thorough surgical, nutritional, and social history is imperative to identify important risk factors for the condition. Furthermore, this information is vital to cultivating a comprehensive and effective treatment plan, catered to addressing both the deficiency and underlying contributing factors. In patients with substance use disorders as in our case, referring the patient to a drug rehabilitation center is essential to better prevent future malnutrition secondary to substance use.

Conflicts of interest

The authors declare no potential conflicts of interest.

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Authors' contributions

- **Jonathan Deck**: Conceptualization, Formal analysis, Writing (original draft and preparation), Visualization
- **Athena Cohen:** Writing (review and editing)
- **Joseph Raevis:** Investigation, Resources
- **Jae Young You:** Project Administration, Supervision

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