Bitot’s Spots following Bariatric Surgery: An Ocular Manifestation of a Systemic Disease

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Abstract
Background: To present a case of ocular complications from vitamin A deficiency following bariatric surgery. Case Report: A 41-year-old woman presented with symptoms of dryness and diminished night vision. Examination revealed corneal punctate staining, keratinization of the conjunctiva, and multiple mid-peripheral white lesions at the level of the retinal pigment epithelium. Given the patient’s history of bariatric surgery, anemia, and vitamin D deficiency, further investigation into micronutrient levels was performed and indicated a severe vitamin A deficiency. Oral vitamin A supplementation resulted in the complete resolution of her symptoms within two months. Conclusions: Nutritional deficiencies following bariatric surgery are common and can be disruptive to normal systemic health and visual function. Given that the number of patients pursuing bariatric surgery for weight loss management has increased over the past 50 years, eye care professionals should be aware of the ophthalmic manifestations associated with micronutrient deficiency.
Introduction

The risk of nutrient deficiency is low in developed countries; less than 10% of the population in the United States exhibits some level of nutritional deficiency [1]. In developed nations, certain populations are at risk for malnutrition, such as those with celiac disease, Crohn’s disease, end-stage liver failure, and pancreatic disease [1, 2]. This particular case reviews the effect of vitamin A deficiency on the eyes, outlines various supplementation recommendations for managing the deficiency, and raises awareness of the unintentional ophthalmic complications in a specific population at risk of malnutrition.

Case Report

A 41-year-old female presented to the Wilmer Eye Institute for a second opinion, as she had been experiencing dryness for several months. Her symptoms included tearing and burning, exacerbated by walking into a bright room. Over the past two months, she reported decreased vision at night and overall loss of contrast.

She was followed at Johns Hopkins Internal Medicine for approximately three years for pre-existing comorbidities that included anemia, vitamin D and B₁₂ deficiencies, as well as an increased BMI (37 kg/m²). Her surgical history was significant for several bariatric procedures including stomach stapling, gastric bypass, and subsequent revisions of the bypass. At presentation, she was taking 324 mg ferrous sulfate and 50,000 international units (IU) vitamin D. She reported that she was noncompliant with her quarterly B₁₂ injections and daily vitamin D supplementation. She had no family history of macular degeneration, glaucoma, or other hereditary retinal degenerations.

Table 1 summarizes the pertinent findings from each patient encounter. Visual acuity at initial presentation was 20/25+2 in each eye. Slit-lamp examination was significant for grade 3 corneal punctate staining, visible after application of fluorescein sodium strips. Dilated fundus examination revealed a normal optic nerve and macula, but dozens of round, yellow punctate, subretinal deposits were present throughout the arcades of each eye; there was no evidence of bone spicules.

The patient was instructed to increase the use of nonpreserved artificial tears from an as-needed basis to every hour and she was referred for a retina consultation. The retinal specialist agreed with the initial findings, and the primary differential diagnosis for the posterior segment findings was fundus albipunctatus. The patient was referred for an electroretinogram in hopes to assist in diagnosing a particular retinal disease process.

One month after the baseline visit, she indicated that her symptoms had improved with frequent use of lubricating drops. Visual acuity improved to 20/20 in each eye, but there were new areas of dense lissamine green staining on the bulbar conjunctiva as shown in Figure 1. The patient was instructed to switch to a more viscous lubricating drop and asked to return for a consultation with the cornea service.

On examination by a corneal specialist, the conjunctival lesions were diagnosed as Bitot’s spots. These findings were highly suggestive of vitamin A deficiency, supported by the presence of severe ocular surface dryness, night blindness, and history of bariatric surgery and subsequent nutritional deficiencies. Lab work was obtained. Vitamin A levels were in-
deed low at 3 μg/dL (reference range: 38–98 μg/dL), and her primary care physician initiated 8,000 international units (IU) of oral vitamin A supplementation daily.

The patient reported for a follow-up three weeks after starting supplementation. She had complete resolution of all her symptoms of dryness and night blindness. Although she still had evidence of conjunctival punctate staining with lissamine green, her Bitot’s spots and corneal staining had resolved as shown in Figure 2. Despite encouragement, the patient did not return for additional retinal photo documentation and electroretinogram testing since her symptoms had improved.

**Discussion**

More than 95% of the US population has adequate levels of vitamin A, defined as serum retinol ≥20 μg/dL or ≥70 μmol/L [1]. Vision loss associated with vitamin A deficiency is relatively common in developing countries and a primary cause of preventable blindness in the world. Globally, 190 million preschool-age children and 19.1 million pregnant women are impacted by low serum retinol, according to estimates by the World Health Organization (WHO) [3]. In developed countries, vision loss as a result of vitamin A deficiency generally corresponds with liver failure and poor diet [2, 4]. Similar to systemic disease, bariatric procedures have demonstrated a high incidence of elemental and micronutrient deficiencies, including vitamin A [5]. An estimated 69% of patients following bariatric surgery demonstrate vitamin A deficiency with approximately 10% manifesting clinical signs [6].

The first 70 cm of the small intestine is responsible for 75% of sugar, protein, and lipid absorption [5]. Micronutrients, vitamins, and trace elements are absorbed throughout the length of the small intestine; however, zinc, iron, selenium, and calcium are absorbed by means of the duodenum and jejunum and often require acidic environments for optimal absorption [5]. Fat-soluble vitamins require bile and lipase secreted by the gall bladder and pancreas into the duodenum. Given that surgical intervention influences absorption by means of bypassing a portion of the intestinal tract, manipulating the length and location of the bypass achieves a greater therapeutic effect of weight loss.

In this case, the patient underwent three separate bariatric procedures, the most recent surgery dating back 10 years. Her primary care physician monitored her vitamin D, B₁₂, and iron deficiencies. Upon presentation to her eye exam, the patient was suffering from night vision changes and dry eye, which later progressed to conjunctival xerosis and keratinization. Vitamin A deficiencies reported following bariatric surgery rarely discuss the visual disturbances associated with reduced serum retinol in this population of patients.

Sommer [7] reviewed the ophthalmologic findings associated with vitamin A deficiency. In early stages, patients generally suffer from varying degrees of ocular surface dryness. Severe ocular dryness can lead to corneal melting, which negatively impacts visual prognosis and ultimately yields permanent blindness. In the early stages of corneal ulceration, the eyes will respond positively to vitamin A supplementation. Vitamin A acts to slow the damaging effects of xerophthalmia once the cornea becomes necrotic; however, there is little evidence of reversal. Patients with vitamin A deficiency commonly report nyctalopia, or night blindness. The mechanism is secondary to the degeneration of both rods and cones [7]. The patient evaluated at the Wilmer Eye Institute presented with retinal findings and dry eye
symptoms, but lacked obvious xerophthalmia making the systemic vitamin A deficiency difficult to diagnose. Once the patient returned for a follow-up, she progressed to a level of conjunctival keratinization, making the possibility of vitamin A deficiency more evident.

The recommended daily intake of vitamin A is 900 µg/day for men and 700 µg/day for women [1]. The WHO recommends high-dose (200,000 IU) oil-based vitamin A supplementation for vitamin A deficiency [3]. There are no standardized reports for supplementation to prevent or manage clinically significant vitamin A deficiency in patients who have undergone bariatric surgery [2, 4, 8, 9]. A number of cases reported in the literature illustrate the wide array of clinical presentations and treatment regimens for vitamin A deficiency (summarized in Table 2). Clinical presentation is widely variable, making the diagnosis hard to determine. This particular case highlights the importance of taking a thorough medical history when evaluating patients for ocular complaints. This particular diagnosis did not require additional electrophysiology testing; specialized equipment like ERG is not always readily available or convenient. The case also highlights the value in understanding the influence of nutrition on a patient’s ocular and systemic health.

**Conclusion**

Currently, the presence of vitamin A deficiency remains low in the United States. Presently, about 35% of Americans are considered obese [10]. Approximately 160,000 surgical procedures are performed each year [5]. As this form of weight loss management becomes more widely acceptable, medical professionals may begin to see a spike in micronutrient deficiencies. While ophthalmic complications of nutrient deficiency are uncommon in developed nations, the index of suspicion should be heightened in patients with risk of malabsorption as seen in liver failure, poor diet, obesity, and bariatric surgery. Thus, it is important to consider micronutrient deficiencies in patients with dry eye and night blindness.

**Statement of Ethics**

The authors have no ethical conflicts to disclose.

**Disclosure Statement**

No conflicting relationships exist for the authors.
References

1. Second national report on biochemical indicators of diet and nutrition in the U.S. population [Internet]. 2012. Available from https://www.cdc.gov/nutritionreport/pdf/exesummary_web_032612.pdf (accessed April 28, 2017).

2. Abbott-Johnson W, Kerlin P, Abiad G, Clague AE, Cuneo RC: Dark adaptation in vitamin A-deficient adults awaiting liver transplantation: improvement with intramuscular vitamin A treatment. Br J Ophthalmol 2011;95:544.

3. Vitamin A supplements: a guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia [Internet]. Available from: http://apps.who.int/iris/bitstream/10665/41947/1/9241545062.pdf (accessed April 29, 2017).

4. Duignan E, Kenna P, Watson R, Fitzsimon S, Brosnahan D: Ophthalmic manifestations of vitamin A and D deficiency in two autistic teenagers: case reports and a review of the literature. Case Rep Ophthalmol 2015;6:24–29.

5. Gletsu-Miller N, Wright BN: Mineral malnutrition following bariatric surgery. Adv Nutr 2013;4:506–517.

6. Zalesin KC, Miller WM, Franklin B, Mudugal D, Rao Buragadda A, Boura J, et al: Vitamin A deficiency after gastric bypass surgery: an underreported postoperative complication. J Obes 2011;2011.

7. Sommer A: Xerophthalmia and vitamin A status. Prog Retin Eye Res 1998;17:9–31.

8. Genead MA, Fishman GA, Lindeman M: Fundus white spots and acquired night blindness due to vitamin A deficiency. Doc Ophthalmol 2009;119:229–233.

9. Hatizifotis M, Dolan K, Newbury L, Fielding G: Symptomatic vitamin A deficiency following biliopancreatic diversion. Obes Surg 2003;13:655–657.

10. Ogden CL, Carroll MD, Kit BK, Flegal KM: Prevalence of childhood and adult obesity in the United States, 2011–2012. JAMA 2014;311:806–814.
Fig. 1. Bitot's spots, temporal bulbar conjunctiva, right eye. Before treatment.
Fig. 2. Resolution of Bitot’s spots, temporal bulbar conjunctiva, right eye. Following vitamin A supplementation.
### Table 1. Summary of the patient's visits

|                          | Visit 1 | Visit 2 (1 week later) | Visit 3 (1 month later) | Visit 4 (1 month later) | Visit 5 (1 month later) |
|--------------------------|---------|------------------------|-------------------------|-------------------------|-------------------------|
| **Visual acuity**        | 20/25+ OD | 20/20– OD              | 20/20 OD                | 20/20 OD                | 20/20 OD                |
|                          | 20/25+ OS | 20/20– OS              | 20/20 OS                | 20/20 OS                | 20/20 OS                |
| ** Conjunctiva**         | White and quiet OU | White and quiet OU | Bitot's spots OU | Bitot's spots OU | Punctate lissamine stain OU |
| **Cornea stain**         | G3+ diffuse punctate OU | G3+ diffuse punctate OU | G1+ OD G3+ OS | G1 OD G3 OS | Trace-G1 OU |
| **Periphery**            | Extensive subretinal, round deposits OU | Extensive subretinal, round deposits OU | – | – | – |
| **Intraocular pressure** | 23 OD 20 OS | 24 OD 23 OS | 19 OD 18 OS | 17 OD 17 OS | 16 OD 17 OS |
| **Vitamin A levels**     | – | – | – | 3 µg/dL | 14 µg/dL |
| (Ref.: 38–98 µg/dL)      |         |                        |                         |                        |                         |
| **Vitamin B12**          |         |                        |                         |                         |                         |
| (Ref.: 211–946 pg/mL)    |         |                        |                         |                         |                         |
| **25-hydroxyvitamin D**  |         |                        |                         |                         |                         |
| (Ref: 30–100 ng/mL)      |         |                        |                         |                         |                         |
| **Serum ferritin**       |         |                        |                         |                         |                         |
| (Ref: 15–150 ng/mL)      |         |                        |                         |                         |                         |

1 Pupils, ocular motility, confrontations were assessed and found to be normal at all visits. 2 Lids were normal, no evidence of blepharitis, anterior chamber was deep and quiet, irides were flat, and lenses were clear at each visit. 3 Vitreous was clear, disc was pink and flat, cup-to-disc ratio was 0.25, macula was flat, with bright reflexes and vessels were normal course and caliber assessed at visits 1 and 2. 4 One month after initiation of 8,000 IU vitamin A supplementation.
Table 2. Literature review of cases demonstrating ophthalmic manifestations of nutritional deficiency

| Authors [Ref.] | Etiology               | Deficiency          | Symptoms/signs reported                                | Supplementation                                           |
|----------------|------------------------|---------------------|-------------------------------------------------------|----------------------------------------------------------|
| This study     | Gastric bypass         | Vitamin A, D, iron  | Night blindness, dry eye; fundus deposits, Bitot’s spots | 8,000 IU oral (vitamin A) + 50,000 IU (vitamin D) + 324 mg ferrous sulfate |
| Hatizifotis et al. [9] | Laparoscopic band | Vitamin A, D, E, K, zinc, selenium | Night blindness                                        | 100,000 IU oral (vitamin A) + vitamin K, thiamine, zinc, pyridoxine, Caltrate, ferrous sulfate, and vitamin C |
| Genead et al. [8] | Gastric bypass         | Vitamin A, E, C     | Night blindness, fundus deposits                       | Intramuscular after 50,000 IU oral did not resolve symptoms |
| Abbott-Johnson et al. [2] | End-stage liver failure | Vitamin A          | Night blindness                                        | 50,000 IU oral                                           |
| Duignan et al. [4] | Autism, poor diet      | Vitamin A, D        | Bitot’s spots, bilateral optic disk swelling           | 25,000 IU                                                |