

Xerophthalmia with secondary malabsorption syndrome in a young lady

Shama Irfan Khan¹, Arvind Kumar², Prasan Kumar Panda³, Neeti Gupta¹

Departments of ¹Ophthalmology, ²Pathology, and ³Medicine, All India Institute of Medical Sciences (AIIMS), Rishikesh, Uttarakhand, India

ABSTRACT

Delayed recognition and treatment of vitamin A deficiency (VAD) in adults leads to devastating complications. A 24-year-old woman presented with diarrhea, malaise, and shortness of breath. Her medical history included blunt abdominal trauma for which, she had bowel resection surgery and revision surgery within a year of the last surgery at the age of 8 years. She had difficulty in night vision and dry eyes. The best-corrected visual acuity was 6/18 in the BE. On slit-lamp examination in the both eyes (BE), the conjunctiva was thick, dry-looking with wrinkling, and the cornea had diffused superficial punctate keratitis and in the left eye, there was corneal xerosis of 1.5 × 1.5 mm. Tear film breakup time was 0-s in the BE. Schirmer's were 30 mm BE. The rest of the ocular examination was within normal limits. A clinical diagnosis of xerophthalmia secondary to malabsorption was made and treated with systemic vitamin A and intense lubrication. With time, ophthalmic conditions improved, but she died due to poor general wellbeing and repeated hospital-acquired infections. The infrequent presentation of VAD in adults and the unusual etiology in this patient make this case interesting, whereas its potentially devastating consequences highlight the importance of its early recognition, treatment, and regular follow up needed by both patient and physician in the community (general practitioner and ophthalmologists) for the prevention of VAD complications and poor prognosis.

Keywords: Bowel resection, delayed recognition, diarrhea, keratinization, retinol, vitamin A deficiency

Introduction

Xerophthalmia refers to the constellation of ocular signs and symptoms associated with vitamin A deficiency (VAD).^[1] It includes conjunctival xerosis, corneal xerosis, Bitot's spots, keratomalacia, nyctalopia, and retinopathy. VAD, not only causes blindness, but also affects growth, general morbidity, and mortality. In developing countries, xerophthalmia is one of the most common causes of ophthalmologic morbidity and mortality due to insufficient vitamin A intake. The affected population

mainly includes children and pregnant women. Xerophthalmia in an adult is rare and mainly seen in developed countries because of the large storage of vitamin A in the liver, and if present should be suspicion for secondary causes of VAD because of defects in metabolism and storage, and examples include biliary cirrhosis, chronic pancreatitis, cystic fibrosis, inflammatory intestinal diseases, bariatric surgery, and ample intestinal resections.^[2,3]

The diagnosis of xerophthalmia is mainly based on clinical signs and supplemented by a positive medical history. It is always important to take a thorough dietary history, social history, and history of alcohol intake, history of bowel resection in all cases of dry eyes unresponsive to conventional treatment. Serum vitamin A assays help to confirm the diagnosis of xerophthalmia. Serum retinol levels greater than 0.70 μM/L are considered to be normal.^[4] Dark adaptometry and night vision threshold tests help in the diagnosis of defective night vision. Impression cytology

Address for correspondence: Dr. Prasan Kumar Panda, Department of Medicine, Sixth Floor, College Block, All India Institute of Medical Sciences (AIIMS), Rishikesh - 249 203, Uttarakhand, India.
E-mail: motherprasanna@rediffmail.com

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and electroretinogram help as supplemental tests to aid the diagnosis. Delayed recognition and treatment of VAD in adults lead to devastating complications in the community.

Thereby, we report an adult case who presents with xerophthalmia with chronic malabsorption after 16 years of bowel resection surgery and died later on with complications.

Case Presentation

A 24-year-old woman reported to the Medicine Outdoor Department complaining of loose stools with an increase in frequency, lethargy, difficulty in breathing, weight loss (documented loss of 15 kg over 2 years) for 2 years. She had a history of multiple hospitalizations for diarrhea and significant malaise. Her medical history included primary hypothyroidism, amenorrhea, and hormonal therapy for 8 months. She had an abdominal trauma with intestinal perforation and surgical repair at the age of 8 years. She had graduated in mass communication and was working as a journalist without any significant family history. Social history included a mixed diet of 2 to 3 meals a day. She never took alcohol or any form of tobacco.

Upon admission, she was cachexic and dehydrated. Her temperature was 36.6°C, blood pressure 98/65 mmHg, pulse 94 beats per min, and respiration 22 breaths per min. Her height and weight were 150 cm and 35 kg, respectively, with a body mass index of 15.5 kg/m². She had glossitis, severe subcutaneous fat depletion, generalized flaky skin, brittle hair and nails, and associated muscle wasting. Volume replenishment and empirical treatment with multivitamin supplementation were initiated till the availability of laboratory investigations.

The patient was evaluated, and numerous laboratory tests were ordered. The majority of laboratory parameters were normal except as in Table 1.

The primary diagnosis was malabsorption syndrome with secondary amenorrhea and hypothyroidism. Stool routine and microscopy were unremarkable except for visible parasites, most likely hookworms. As liver function tests and ultrasonography abdomen showed normal liver, liver-related pathologies as the cause of multiple deficiencies were ruled out. No pain in the abdomen, no history of steatorrhea, and normal pancreas on ultrasonography ruled out chronic pancreatitis as the cause for malabsorption. Abdominal evaluation and radiological examination excluded bowel obstruction. Work-up for tuberculosis and autoimmune pathology was unremarkable. The history of blunt abdominal trauma (at the age of 8 years) was explored further, we found documents of exploratory laparotomy for small bowel loop perforation, revision surgery, and adhesiolysis after a year of primary repair. So after excluding the possible pathologies, the diagnosis of malabsorption syndrome due to small bowel resection was made. Biochemistry showed multiple deficiencies, in particular of the fat-soluble vitamins and calcium. Endoscopy revealed chronic esophagitis

and dilated residual small bowel loops. Intestinal histopathology showed an inflammatory reaction.

Vitamin A deficiency was suspected because of dry eye, difficulty seeing at night (on leading questions), and foreign body sensation. An ophthalmic consultation was ordered to confirm xerophthalmia. Ophthalmological examination showed the best-corrected visual acuity was 6/18 in the both eyes (BE). On slit-lamp examination in BE, the conjunctiva was thick, dry-looking lusterless with wrinkling, and the cornea had diffuse superficial punctate keratitis with the uptake of fluorescein stain and in the left eye, there was the presence of corneal xerosis of 1.5 × 1.5 mm at 5 o'clock not involving the visual axis [Figure 1]. Tear film breakup time was 0 s in BE. Schirmer's were 30 mm BE. The rest of the ocular examination was within normal limits. Based on clinical signs, a diagnosis of xerophthalmia secondary to malabsorption syndrome was made. Laboratory workup confirmed low vitamin A levels and associated deficiencies. A 2x2 mm conjunctival biopsy was sent from the junction of keratinised and non keratinised conjunctiva that showed keratinization of the conjunctival epithelium [Figure 2].

Dietary supplementation, intensive ocular surface lubrication, oral Vitamin A administration of 2,00,000 IU on day 1, 2, and 14 along with treatment of associated deficiencies were administered. After a week of systemic vitamin A administration, the patient had improvement in ophthalmic manifestations, but the patient could not come out of general wellbeing. She developed hospital-acquired infections repeatedly and died after 1 month of hospitalization.

Discussion

Vitamin A deficiency is seen in patients with severe liver disease leading to storage and metabolic abnormalities. Bowel disease or

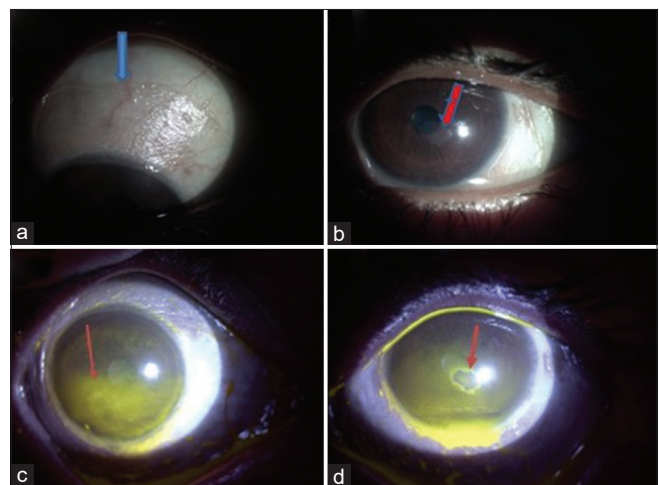


Figure 1: Slit-lamp images of both eyes (a) Showing dry looking upper bulbar conjunctiva with demarcation line (blue arrow) between keratinized and non-keratinized conjunctiva; (b) Showing corneal xerosis (arrow) of size 1.5 × 1.5 mm at 5 O'clock not involving the visual axis; (c and d) showing superficial punctate keratitis after staining with sodium fluorescein dye (arrow)

Table 1: Abnormal laboratory details of the patient

Parameters	Result	Reference range
Alkaline phosphate	417	30-120 IU/L
Albumin	3	3.5-5 g/dl
Prealbumin	2.2	19-38 mg/dl
Hemoglobin	7.256	11.6-15 g/dL
WBC	11.81	3.4-9.6 thou/mm ³
DC (N/L/M/E/B)	63/32/4.5/0.045/0.43	(N) 55%-75%, (L) 20%-40%, (M) 2%-8%, (E) 1%-4% and (B) 0.5%-1%
Reticulocyte count	4.5	0.5%-2%
Serum Calcium	6.8	8-10 mg/dL
Serum vitamin B12	170	190-950 pg/mL
Serum iron	67.0	60-180 µg/dL
Serum ferritin	359.50	12-300 ng/mL
Total Cholesterol	122	< 200 mg/dL
Triglycerides	34	< 150 mg/dL
LDL	101	70 to 130 mg/dL
HDL	54	40 TO 60 mg/dL
Anti-Mullerian Hormone	0.81	>1.0 ng/mL
Vitamin-D	4.5	25-80 ng/mL
Vitamin-A	Extremely low (undetectable)	20-60 mcg/dL
Urine microscopy	6 to 8 (cells/HPF)	
Stool routine	Mucus present	
Stool microscopy	Occasional <i>Entamoeba histolytica</i> cysts present	
ESR	95	0-20 mm/h
X-ray abdomen	Dilated pelvic bowel loops?	
Ultrasonography (abdomen)	Left kidney - Grade 1 hydronephrosis, echogenic focus in the upper part of left ureter	
Upper GI Endoscopy	Esophagitis, duodenal mucosal edema	
Histopathology -	Inflammatory cells present	
Small bowel	Keratinization of conjunctival epithelium	
Conjunctiva - Impression cytology		

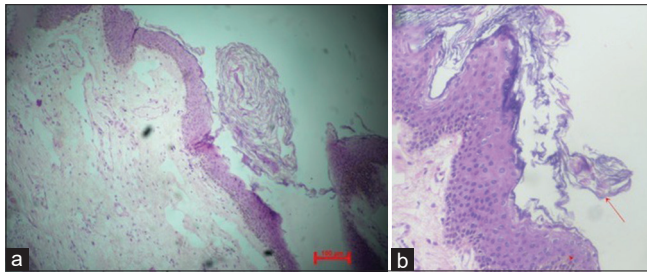


Figure 2: Histopathology images of multi-layered conjunctival epithelium (a) showing 10x keratinized conjunctival epithelium with keratin pearl; (b) 100x magnified view of keratinized epithelium (arrow ahead) and keratin pearl (arrow)

surgical shortening can cause inadequate absorption resulting in multiple nutrient deficiencies including VAD as in our patient. The amount and site of bowel resection determine how much tolerance and adaptation can take place. Multiple chronic nutritional deficiencies, liver disease, and bacterial overgrowth are common complications of large bowel resection.^[5] The manifestations of hypovitaminosis A appear after prolonged years of vitamin A depletion and a significant time lag between the causative event and presentation.^[6,7] This may be the reason for delayed recognition by health care providers and the patient population.

Vitamin A is a fat-soluble vitamin that is important for retinal photoreceptor function, epithelial proliferation and keratinization, skeletal tissue maintenance, spermatogenesis, placenta generation, and maintenance.^[8] Vitamin A is absorbed in the small intestine in the form of retinol.^[9] Retinol is crucial in maintaining conjunctival and corneal epithelial integrity, whereas in the retina it plays a major role in phototransduction in rod and cone cells. Anything compromising absorption in the small intestine will, therefore, affect vitamin A absorption. The ocular symptoms and signs are variable but most commonly present with xerophthalmia and range from simple dryness of the conjunctiva and the cornea to its xerosis, keratomalacia, scarring, and perforation of the cornea.^[10] Night blindness is the earliest and reversible symptom of VAD.^[11] Whereas the diagnosis of VAD is mainly clinical, serum vitamin A levels can be requested to confirm the diagnosis, but should not delay the treatment and is usually not available in community settings.

The World Health Organization (WHO) advises that treatment is a single oral dose of 200000 IU vitamin A, followed by a further dose the following day and a final dose 2 weeks later.^[4] Typically, in cases of malabsorption such as this, the WHO recommends treatment of VAD via the intramuscular route rather than the oral route.

In our case, the patient had a clinical diagnosis of xerophthalmia which was confirmed with a blood test. The cause was chronic diarrhea with signs of malabsorption due to short bowel syndrome because of post-traumatic bowel perforation for which she had undergone surgery. However, due to the presence of considerable liver stores of vitamin A, the development of deficiency-related symptoms can occur many years after surgery.^[12] We treated our patients with oral vitamin A, topical treatment with preservative-free eye drops, and dietary consultation. The patient improved clinically and symptomatically and partial restoration of the corneal and conjunctival xerosis was observed before the patient's death due to compromised general condition. The direct cause of death is not due to VAD, but indirectly this leads to immune deficiency and superadded infection that may be the cause of death in the present case.^[13] Hence, community education is the need of the hour to prevent VAD early.

In summary, the article aims at drawing the attention of general physicians and ophthalmologists to the importance of a history of previous bowel resection and the presence of ocular surface abnormalities to diagnose and treat the VAD-associated morbidity and mortality. The infrequent presentation of VAD in adults and the unusual etiology in this patient highlight the importance of its early recognition, treatment, and regular follow-up needed by both patient and physician for prevention of VAD complications and associated morbidity and mortality.

Research quality and ethics statement

The authors of this manuscript declare that this scientific work complies with reporting quality, formatting, and reproducibility guidelines set forth by the Enhancing the Quality and Transparency Of Health Research (EQUATOR) Network (CARE guideline). The authors also attest that this clinical investigation was determined to not require Institutional Review Board/Ethics Committee review but have taken patient consent from deceased relatives.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other

clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. McLaren DS, Kraemer K. Xerophthalmia. *World Rev Nutr Diet* 2012;103:65-75.
2. Lee WB, Hamilton SM, Harris JP. Ocular complications of hypovitaminosis after bariatric surgery. *Ophthalmology* 2005;112:1031-4.
3. Chae T, Foroozan R. Vitamin A deficiency in patients with a remote history of intestinal surgery. *Br J Ophthalmol* 2006;90:955-6.
4. Feroze KB, Kaufman EJ. Xerophthalmia. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
5. Vanderhoof J, Langnas A. Short-bowel syndrome in children and adults. *Gastroenterology* 1997;113:1767-78.
6. Ettl A, Daxecker F. Xerophthalmia in liver cirrhosis. Correct diagnosis after 15 years. *Ophthalmologica* 1992;204:63-6.
7. Perlman I, Barzilai D, Haim T, Schramek A. Night vision in a case of vitamin A deficiency due to malabsorption. *Br J Ophthalmol* 1983;67:37-42.
8. Edem DO. Vitamin A: A review. *Asian J Clin Nutr* 2009;1:65-82.
9. Borel P. Factors affecting intestinal absorption of highly lipophilic food microconstituents (fat soluble vitamins, carotenoids and phytosterols). *Clin Chem Lab Med* 2003;41:979-94.
10. Gilbert C. The eye signs of vitamin A deficiency. *Community Eye Health* 2013;26:66-7.
11. Ross DA. Recommendations for vitamin A supplementation. *J Nutr* 2002;132(Suppl 9):2902S-6.
12. Spits Y, De Laey JJ, Leroy BP. Rapid recovery of night blindness due to obesity surgery after vitamin A repletion therapy. *Br J Ophthalmol* 2003;88:583-5.
13. Hodge C, Taylor C. Vitamin A Deficiency. [Updated 2021 May 09]. In: *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2021.