CASE REPORT

Vitamin A deficiency due to chronic malabsorption: an ophthalmic manifestation of a systemic condition

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Accepted 25 April 2017

SUMMARY

A 47-year-old woman presented with a 4-week history of progressive loss of vision, first manifesting as night blindness. Additionally, the patient reported frequent severe episodes of diarrhoea over the past month. Her medical history included end-stage renal failure for which she was currently on haemodialysis after a failed renal transplant, chronic pancreatitis and autonomic diabetes mellitus. Ophthalmological examination revealed severe bilateral corneal xerosis, bilateral Bitot's spots and inferior ulceration of the right cornea. A diagnosis of xerophthalmia due to vitamin A deficiency was made, most likely due to the presence of small intestinal bacterial overgrowth and the patient's chronic malabsorptive state. Standard management using oral vitamin A tablets was ineffective, resulting in the patient requiring intravenous supplementation. The extent of visual deterioration on presentation and the difficulties encountered managing the patient resulted in the patient's vision failing to improve.

itchy with frequent sticky discharge. There was no history of trauma to the eyes. In addition to her visual symptoms, the patient reported frequent severe episodes of diarrhoea over the past month. Her medical history included end-stage renal failure for which she was currently on haemodialysis after a failed renal transplant, chronic pancreatitis and autonomic diabetes mellitus.

On examination, the patient was severely cachectic (34 kg, body mass index 13.3). Ophthalmological examination revealed an inflamed right conjunctiva and bilateral Bitot's spots with evidence of bilateral conjunctival and corneal xerosis. Right inferior corneal ulceration was evident ([figure 1](#)). Both pupils were reactive to light, with unrestricted eye movements, and the colour vision was normal. Application of fluorescein eye-drops better demonstrated the right inferior corneal ulceration ([figure 2](#)). Based on the history and clinical findings, a diagnosis of xerophthalmia due to VAD was made.

BACKGROUND

Vitamin A deficiency (VAD) is a leading cause of preventable blindness in the low-income/middle-income countries,¹ which if left untreated can lead to blindness. While uncommon in developed countries, it has been reported in severely malnourished patients² and has been previously reported following bariatric surgery^{3–5} and in patients with previous extensive bowel resection.^{6,7} Prompt diagnosis and vitamin supplementation can prevent further deterioration, and depending on the extent of damage may even reverse any visual loss.⁵

While the management of VAD is usually straightforward with oral vitamin supplementation, the patient's comorbidities and chronic malabsorptive state made management somewhat trickier. The infrequent presentation of VAD in the developed world and the unusual aetiology in this patient make this case interesting, while its potentially devastating consequences highlight the importance of its early recognition and treatment.

INVESTIGATIONS

Abnormal tear production during Schirmer's test of 5 mm and 8 mm in the left and right eye, respectively (normal >10 mm) confirmed the diagnosis of xerophthalmia, while a serum vitamin A level of 0.15 µmol/L (normal 0.99–3.35 µmol/L) confirmed VAD as the cause. A corneal scrape isolated *Staphylococcus aureus* on culture. Breath testing revealed small intestinal bacterial overgrowth (SIBO).

DIFFERENTIAL DIAGNOSIS

A diagnosis of xerophthalmia due to VAD can usually be made clinically. A history of night blindness and the presence of Bitot's spots and corneal ulceration are pathognomonic of VAD.

Xerophthalmia, the pathological drying of the conjunctiva and cornea, can also occur in autoimmune conditions such as rheumatoid arthritis, scleroderma and systemic lupus erythematosus, and so could be considered in the list of differentials; however, none were relevant here.

TREATMENT

Initial oral vitamin A supplementation with 200 000 IU failed to correct either the patient's serum vitamin A levels or her symptoms, so the patient was switched to intravenous supplementation. The volume of intravenous vitamin A required meant that the patient had to receive daily dialysis as an inpatient, instead of her usual

CASE PRESENTATION

A 47-year-old woman presented with a 4-week history of progressive loss of vision in her right eye and a 1-week history of progressive loss of vision in the left, first manifesting as night blindness. Gradually daylight vision became affected, with the patient reporting blurred vision and photophobia. The patient stated that both eyes felt gritty and

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To cite: Cheshire J, Kolli S. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-220024

Figure 1 Unstained image illustrating the patient's right conjunctival inflammation, inferior corneal ulceration and Bitot's spots.

three times weekly regimen, in order to remove the additional volume of fluid.

The patient was started on an intense lubrication regimen using Celluvisc 1% eye-drops two hourly and was given chloramphenicol 0.5% four times a day, following the positive bacterial culture on corneal scrape. Punctal plugs were inserted bilaterally to prevent tear duct drainage in the hope of keeping the cornea moist.

Breath testing revealed SIBO as the cause of the patient's diarrhoea, for which she received a month's cycle of oral ciprofloxacin. The patient was also given lanreotide, a somatostatin analogue, to improve her gastrointestinal dysmotility.

OUTCOME AND FOLLOW-UP

A month after diagnosis, serum vitamin A levels had returned to within normal limits ($1.9\mu\text{mol/L}$). However, despite vitamin supplementation, intense lubrication and the insertion of punctal plugs, the epithelial defects failed to heal. Temporary tarsorrhaphy was performed, which enabled complete epithelial healing. Despite this the patient's sight did not improve due to corneal scarring and cataract. Due to the patient's deteriorating health and extremely frail state, she was deemed unsuitable for cataract surgery, being registered as severely sight-impaired.

DISCUSSION

Vitamin A is a fat-soluble vitamin absorbed in the small intestine in the form of retinol. Retinol is crucial in maintaining conjunctival and corneal epithelial integrity, while 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.

While one of the leading causes of preventable blindness in the low-income/middle-income countries,¹ VAD is uncommon in developed countries. It has however been reported in severely

malnourished patients² and following intestinal or bariatric surgery^{3–5} due to the resultant malabsorption.^{6,7}

VAD can lead to significant dysfunction of the ocular epithelial lining, resulting in a range of ocular manifestations, from xerosis (dry eye) to corneal ulceration and keratomalacia (necrosis and softening of the cornea leading to its perforation), and if left untreated, blindness. Due to retinol's role in phototransduction, night blindness is classically an early symptom of xerophthalmia. Cone function appears to be preserved in the early stages.⁸ Clinical findings suggestive of VAD include conjunctival and corneal xerosis and the presence of Bitot's spots. Bitot's spots are non-specific white plaques that develop on the conjunctiva due to collection of corneal substances. The clinical features of xerophthalmia have been classified by the WHO⁹ as follows: XN, night blindness; X1A, conjunctival xerosis; X1B, Bitot's spots; X2, corneal xerosis; X3A, corneal ulceration/keratomalacia $<1/3$ corneal surface; X3B, corneal ulceration/keratomalacia $\geq 1/3$ corneal surface; XS, corneal scar; and XF, xerophthalmic fundus.

While the diagnosis of VAD is mainly clinical, serum vitamin A levels can be requested to confirm the diagnosis, but should not delay treatment.

The WHO recommends an oral dose of 200 000 IU of vitamin A for 2 days followed by another dose 1–4 weeks later.^{10,11} Typically, in cases of malabsorption such as this, the WHO recommends treatment of VAD via the intramuscular route rather than the oral route. After failure to correct this patient's serum vitamin A level orally, the intravenous route was chosen. The decision not to use the intramuscular route in this patient was taken by the medical team in view of the patient's extremely low muscle mass.

There were two important factors that were likely to have hindered the absorption of vitamin A in this patient: first, her chronic malabsorptive state, a well-recognised consequence of chronic pancreatitis due to exocrine insufficiency¹²; and second the presence of SIBO.

SIBO is characterised by an increased number and/or abnormal type of bacteria in the small bowel.¹³ Its presence has been implicated as a cause of chronic diarrhoea and malabsorption particularly of fat-soluble vitamins (A, D, E, K). Patients typically present with irritable bowel-like symptoms, those of bloating, flatulence, diarrhoea and later with signs of malabsorption. There are several endogenous mechanisms in place to prevent SIBO from occurring, namely gastric acid secretion, intestinal motility, an intact ileocaecal valve and the bacteriostatic properties of pancreatic and biliary secretions.¹⁴ Chronic pancreatitis is complicated by SIBO in 30%–40% of cases due to diminished bacteriostatic properties of pancreatic secretions.¹⁴ Furthermore, the patient's background of autonomic diabetes mellitus is likely to have hindered intestinal motility.¹⁵ Treatment of SIBO usually consists of the eradication of bacterial overgrowth with a prolonged course of an antimicrobial, correction of the associated nutritional deficiencies and when possible correction of the underlying cause.¹³ For patients with underlying gastroparesis as the cause of their SIBO, the use of somatostatin analogues has been suggested to improve intestinal motility.^{16,17}

While the patient's sight did not improve, similar cases of patients with SIBO have reported resolution of symptoms on vitamin supplementation and correction of their bacterial overgrowth.¹⁸ The delay in this patient's presentation and the difficulties encountered in normalising her vitamin A levels are likely to have contributed to the failure of her vision to improve. An additional point of note and one with the benefit of hindsight is the role that the patient's treating physicians might have played. Given the patient's chronic malabsorptive state, early prophylactic

Figure 2 Image illustrating the patient's right inferior corneal ulceration following the application of fluorescein eye-drops.

vitamin supplementation might have prevented the poor visual outcome had the possibility of vitamin deficiency been anticipated. Similarly, earlier recognition of the patient's ocular manifestations might have ameliorated the eventual visual outcome.

This case report briefly touches on the difficulties of managing a severely unwell patient whose numerous comorbidities prevented effective treatment and complete resolution of her vision.

Learning points

- ▶ While vitamin A deficiency (VAD) is rare in developed countries, cases have been reported in severely malnourished patients and following intestinal and bariatric surgery.
- ▶ Diagnosis is primarily based on the patient's history and on clinical findings; night blindness, corneal ulcers and Bitot's spots are all pathognomonic of VAD.
- ▶ Corneal lesions are a medical emergency. Prompt treatment on the same day of diagnosis with oral vitamin supplementation can prevent further deterioration in vision and the resolution of epithelial defects. In patients with poor absorptive states, intramuscular or intravenous vitamin A supplements may be necessary.
- ▶ Small intestinal bacterial overgrowth is characterised by an abnormally high number of bacteria in the small bowel. It can manifest when any of the endogenous protective mechanisms are compromised: gastric acid secretion, intestinal motility, intact ileocaecal valve and the bacteriostatic properties of pancreatic and biliary secretions.
- ▶ In patients presenting with night blindness with a background of previous bariatric/bowel surgery or chronic malabsorption, a differential diagnosis of VAD must be considered.
- ▶ Poor visual outcome might have been reduced or even prevented had the possibility of vitamin deficiency been anticipated, given the patient's comorbidities, with earlier measures taken to supplement before ocular manifestations had occurred.

Contributors JC and SK contributed equally to the design of the work and acquisition of the data. Both JC and SK contributed equally to the drafting of the work, and both approved the final version of the manuscript.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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