CASE REPORT

Xerophthalmia and vitamin A deficiency in an autistic child with a restricted diet

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SUMMARY

We report the ocular and systemic manifestations of vitamin A deficiency in a child with a complicated medical history including autism and a restricted diet, living in a developed country. This child had significant vitamin A deficiency despite being under long-term medical care, yet the diagnosis was not considered until he had an ophthalmology review for visual deterioration.

BACKGROUND

Vitamin A deficiency is the most common form of malnutrition leading to ocular disease, and the leading cause of childhood blindness worldwide; the WHO estimates that approximately 228 million children are affected. In developed countries, the diagnosis of malnutrition leading to eye disorders may be missed or delayed due to its rarity. Although rare, there have been cases of vitamin A deficiency in developed countries, secondary to poor diet, abnormal metabolism, gastrointestinal malabsorption and liver disease.^{1–9} Timely diagnosis and treatment of xerophthalmia (ocular disease secondary to vitamin A deficiency) is vital to prevent potentially avoidable blindness.

CASE PRESENTATION

A 12-year-old boy with a 2-month history of reduced visual acuity was referred to a corneal specialist by an ophthalmologist. He had a history of high functioning autism and iron deficiency. At age 9, he had developed right optic nerve neuropathy, which had reduced his right eye visual acuity to 6/60 and was attributed to an Epstein-Barr virus infection. There was no significant family history. Dietary history revealed a restricted diet, consisting only of hot chips and nuggets.

On presentation, the patient was short, extremely underweight and pale, with mild proximal muscle weakness. Visual examination showed only light perception in the right eye and 1/60 in the left eye. A relative afferent pupillary defect (RAPD) was noted in the right eye. Supratemporal field loss was noted in the left eye. Slit lamp examination revealed bilateral corneal and conjunctival keratinisation (figure 1), normal anterior and posterior chambers, and clear lenses. He had marked pallor of the right optic nerve disc and temporal pallor of the left disc.

INVESTIGATIONS

Systemic investigation revealed hypovitaminosis A ($<0.4 \mu\text{mol/L}$ (reference range $0.9\text{--}2.5 \mu\text{mol/L}$)); anaemia (haemoglobin= 109 g/L); low iron levels

Figure 1 Note the dull and irregular light reflex on the left cornea and conjunctiva, indicating ocular surface keratinisation.

despite iron supplementation; and low folate levels. Results for screening for haemolytic anaemia were unremarkable.

CT and MRI of the brain showed narrowing of the left optic canal and internal auditory canal secondary to bony medullary expansion (figure 2). Electrophysiology confirmed bilateral optic nerve dysfunction. There was mild to moderate bilateral sensorineural hearing loss above 4000 Hz. His bones and skull were found to be generally osteopenic on skeletal survey, with mild thinning of cortices in the long bones. He had normal electrophoresis, rendering thalassaemia unlikely; vitamin C, vitamin D and calcium levels were within normal limits.

Figure 2 CT of the skull: narrowing of optic nerve canal secondary to bony medullary expansions.

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TREATMENT

The patient was treated with topical retinoic acid and high-dose vitamin A supplementation as per WHO guidelines: 200 000 units of vitamin A initially as a single dose daily for two consecutive days, followed by another dose 2 weeks later. He was also started on a regular multivitamin regimen and given lubricating eye drops. To preserve the remaining vision in the left eye, surgical decompression of the left optic canal was performed.

OUTCOME

The patient's ocular surface keratinisation resolved. At 1 year, his visual acuity remained poor with 2/60 in the left eye and only light perception in the right eye, presumed due to optic atrophy.

DISCUSSION

We report a case of xerophthalmia associated with vitamin A deficiency in a child with autism, in a developed country. Our case was associated with very low levels of serum vitamin A. Vitamin A deficiency was not suspected due to its rarity in developed countries, resulting in delayed diagnosis. In developing countries, where vitamin A deficiency is common, suspicions of deficiency are raised much earlier, and diagnosis is often made based on clinical examination findings. Our patient had been under long-term medical care, yet the deficiency had not been diagnosed until presentation with severe eye disease, leaving the child with permanent visual deficits, even after treatment. Recognition of keratinisation of the ocular surface led to investigation for vitamin A deficiency. Our case highlights the existence of this rare disease in a developed country such as Australia, and the importance of prompt ophthalmology referral for further assessment and early treatment.

This case demonstrates the importance of dietary history and identification of risk factors for vitamin A deficiency in subgroups of the Australian paediatric population. There are five reported cases of vitamin A deficiency due to poor dietary habits in children with autism living in the developed world: four from the USA and one from Japan (see [table 1](#)). Autistic children are known to have increased rates of selective diets with decreased fruit, dairy, vegetables and protein intake.¹⁰ Children with selective diets, especially those with autism, should receive nutritional monitoring. Despite the relative rareness of vitamin A deficiency in the developed world, in these children with restricted diets, medical practitioners should consider serum testing of vitamin A levels, and referral to an ophthalmologist for eye examination and electrophysiology to

detect retinal dysfunction, especially in the presence of symptoms such as reduced vision and light sensitivity. Given that autistic behavioural disturbances can make eye examination difficult, extra effort should be devoted towards ensuring these patients receive thorough reviews.

Vitamin A has two roles in ocular metabolism. It allows conversion of light received at photoreceptor outer segments into electrochemical energy in the retina and is needed for differentiation of the stratified squamous epithelium of the ocular surface. The spectrum of ocular disease arising from vitamin A deficiency is known as xerophthalmia. It begins with night blindness (nyctalopia) secondary to rod photoreceptor dysfunction. As the disease progresses, there is atrophy of the normal mucosal surface with appearance of glistening white plaques of desquamated epithelium (Bitot's spots) followed by wrinkling of the conjunctiva and loss of goblet cells, known as conjunctival xerosis.¹¹ Keratinisation of the cornea is known as corneal xerosis; this keratinised layer may detach leaving corneal ulceration. In severe vitamin A deficiency, especially if concurrent with protein malnutrition, the stroma of the cornea can liquefy (keratomalacia), leading to corneal thinning or even perforation.¹² Uncommonly, vitamin A deficiency causes visual field scotoma due to focal retinal pigment epithelium defects (xerophthalmic fundus), which appear as yellow and white spots in the retinal periphery.¹¹

Vitamin A deficiency has systemic implications; it is important in maintaining the integrity of mucosal tissues, haematopoiesis, preservation of immune competence and bone growth.¹³ Vitamin A deficiency may cause anaemia both directly via the reduction of haematopoiesis and indirectly by the modulation of immunity to infectious disease, which may cause anaemia of infection as well as modulation of iron metabolism.¹⁴ Vitamin A deficiency was likely one of the factors contributing to anaemia in our case. Vitamin A is also involved in innate and adaptive immunity;^{15 16} mucosal integrity and T helper cell 2-mediated responses are compromised in vitamin A deficiency.¹⁷ Vitamin A deficiency is associated with an increased risk of some infections associated with the loss of mucosal surface integrity, such as diarrhoea and respiratory tract infections. Vitamin A deficiency causes altered bone growth and bony overgrowth.¹⁸ It has been postulated that pseudomotor cerebri in vitamin A-deficient children is due to bony skull overgrowth.¹⁹ This theory is supported by various animal studies; skull hypertrophy has been observed in vitamin A-deficient animals.^{20–22} Increased osteoblastic activity as evidenced by abundant osteoid present with resultant alterations to the bones surrounding optic canals of vitamin A-deficient calves have been observed, causing severe

Table 1 Reported cases of xerophthalmia in autistic children from developed countries

Authors	Age	Diet	Vitamin A level	Eye signs	Country
Clark <i>et al</i> ²³	8	French fries, water	<0.35 µmol/L	Mild xerosis with punctuate epithelial erosions bilaterally and small corneal scar on the right eye	USA
Steinemann and Christiansen ²⁴	5	Bacon and muffins	0.2 µmol/L (1.3–4.2 µmol/L)	Right eye: dry eye, corneal ulcer Left eye: Bitot's spots, keratinised conjunctival epithelium Xerophthalmic fundus lesion bilaterally: numerous yellow flecks in peripheral retina	USA
McAbee <i>et al</i> ²⁵	17	Potato chips, pretzels, snack mix, cookies and seltzer water	<0.02 µmol/L (0.9–2.5 µmol/L)	Bilateral dry, wrinkled conjunctiva, Bitot's spots, oedema of corneal limbus and diffuse corneal haze	USA
Tanoue <i>et al</i> ²⁶	5	Fried potato, rice balls	<0.5 µmol/L (7.0–21 µmol/L)	Keratinised conjunctiva, bilateral corneal ulceration and scarring	Japan
Lin <i>et al</i> ³	9 years	French fries only	0.1 µmol/L	Night blindness, bilateral non-healing epithelial defect, RAPD and optic atrophy of the left eye	USA

constriction and ischaemic necrosis of the optic nerve.^{21 22} Investigations to determine the cause of these bone changes in our case were inconclusive; vitamin A deficiency leading to optic canal bony expansion causing optic nerve atrophy should be considered.

Vitamin A deficiency, a common cause of blindness in the developing world, can also occur in developed countries. At risk children, including those with restricted diets and autism, should be referred for prompt ophthalmological review due to the risk of permanent visual loss. Vitamin A supplementation should be given according to the WHO protocols for xerophthalmia, to prevent visual loss.

Learning points

- ▶ Xerophthalmia is the most common cause of childhood blindness worldwide; although most cases occur in developing countries, more rarely, cases also occur in developed countries.
- ▶ Vitamin A deficiency should be considered in at-risk patients including autistic children with restricted diets and referred promptly for ophthalmology review.
- ▶ In addition to ocular manifestations, vitamin A deficiency has systemic effects, including anaemia, altered bone growth, reduced immunity and increased mortality.
- ▶ Children with restricted diets should be started on multivitamins and referred to dieticians for recommendation of a diet inclusive of all essential elements and vitamins.
- ▶ Advice to raise awareness should be provided to parents of children with restrictive diets as a preventive strategy.

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Competing interests None declared.

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