Ocular Surface Disease Secondary to Vitamin A Deficiency in the Developed World: It Still Exists

Vitamin A deficiency remains a leading cause of preventable blindness worldwide but has only rarely been reported within the past 2 decades in the United States where nutritional deficiencies are not largely endemic. We describe 4 patients in the United States who had ocular surface disease as a result of vitamin A deficiency (Table).

Report of Cases. Case 1. A 79-year-old woman with a 15-year history of primary biliary cirrhosis and secondary Sjogren syndrome presented with a 1-year history of chronic conjunctivitis refractory to treatment with topical antibiotics. Three months prior, the patient underwent a tectonic penetrating keratoplasty in her right eye because of a perforated corneal ulcer. She had nyctalopia for 2 years. Her visual acuity was 20/200 OD and count-fingers at 3 ft OS. In addition to diffuse punctate epithelial erosions in both eyes, she had a peripheral corneal ulcer in the left eye, which was treated with topical antibiotics. Five days later, the ulcer had progressed to a small perforation. This was managed with cyanoacrylate glue and a bandage contact lens. Her vitamin A level was 20 µg/dL (to convert to micromoles per liter, multiply by 0.0349) (reference range, 38-98 µg/dL). After intramuscular vitamin A administration, the patient’s ocular condition stabilized, and she was discharged to follow up with her local ophthalmologist.

Case 2. A 54-year-old woman with a 10-year history of primary biliary cirrhosis was referred for severe dry eyes starting 6 months prior, which were unsuccessfully treated with cyclosporine A, 0.05%, and frequent lubrication. On examination, her visual acuity was 20/25 OD and 20/30 OS. Schirmer I test results were abnormal in both eyes. She had diffuse punctate epithelial erosions with filaments in both eyes and interpalpebral lissamine green staining. Her vitamin A level was 11 µg/dL, and she started treatment with vitamin A ointment, 0.01%, once daily at bedtime and oral vitamin A supplementation. Her symptoms and staining pattern improved significantly over 1 month.

Case 3. A 9-year-old autistic boy was referred for visual loss, in addition to red eyes and decreased night vision, over the past 4 months as noted by his mother. He had been diagnosed as having chronic conjunctivitis, which was unsuccessfully treated with a corticosteroid-antibiotic combination. On examination under anesthesia, he had chronic bilateral nonhealing epithelial defects, a relative afferent pupillary defect in the left eye, and profound optic atrophy in the left eye greater than in the right eye. His visual acuity was not attainable because of lack of cooperation. It was later discovered that his diet consisted exclusively of french fries. His vitamin A level was 3 µg/dL. His epithelial defects healed with frequent lubrication and remained healed with oral vitamin A supplementation.

Case 4. A 26-year-old homeless and severely depressed woman presented with recurrent corneal ulcers and corneal perforation necessitating penetrating keratoplasty in the right eye. Her ocular condition was thought to be secondary to severe atopic disease. On examina-

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Underlying Condition</th>
<th>Age at Presentation, y</th>
<th>Vitamin A Level, µg/dLα</th>
<th>Ocular Disease at Presentation</th>
<th>Nyctalopia</th>
<th>Route of Vitamin A Supplementation</th>
<th>Response to Treatment Time Course</th>
<th>Duration of Follow-up, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Primary biliary cirrhosis</td>
<td>79</td>
<td>20</td>
<td>Bilateral corneal perforations</td>
<td>+</td>
<td>Intramuscular</td>
<td>Stabilization (1 mo)</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>Primary biliary cirrhosis</td>
<td>54</td>
<td>11</td>
<td>Keratoconjunctivitis sicca</td>
<td>Unknown</td>
<td>Oral and topical</td>
<td>Improvement in symptoms and signs (1 mo)</td>
<td>10</td>
</tr>
<tr>
<td>3</td>
<td>Autism, malnutrition (diet of french fries only)</td>
<td>9</td>
<td>3</td>
<td>Bilateral nonhealing corneal epithelial defects</td>
<td>+</td>
<td>Oral</td>
<td>Healing of epithelial defects (healed with lubrication alone in 1 wk, remained stable only on vitamin A supplementation)</td>
<td>7</td>
</tr>
<tr>
<td>4</td>
<td>Depression, malnutrition</td>
<td>26</td>
<td>5</td>
<td>Bilateral corneal melt</td>
<td>+</td>
<td>Oral</td>
<td>Stabilization (2 mo)</td>
<td>2</td>
</tr>
</tbody>
</table>

Abbreviation: +, present.
SI conversion factor: To convert vitamin A to micromoles per liter, multiply by 0.0349
αReference range, 38-98 µg/dL.
tion, she had hand motions vision OU, a failed corneal graft with corneal thinning and an epithelial de- fect in the right eye, and severe corneal thinning with a corneal perforation in the left eye. The corneal perforation in the left eye was managed with cyanoacrylate glue and a bandage contact lens. The patient was malnourished because of her socio- situation and psychiatric deters- riation, with a vitamin A level of 5 µg/dL. After improving nutritional intake, both eyes improved, with resolution of the epithelial de- fect in the right eye and stabilization of the perforation in the left eye. She was discharged with recommenda- tions to continue oral vitamin A supplementation.

Comment. The World Health Or- ganization lists vitamin A defi- ciency as one of the most impor- tant causes of preventable childhood blindness.1 Dysfunction of corneal and conjunctival epithelial cell differ- entiation governed by vitamin A results in graded abnormalities in the ocular surface ranging from punctate epithelial erosions to corneal perforation.2,3 It can be initially misdiagnosed since the signs are easily mistaken for epithelial erosions seen in keratoconjunctivitis sicca or exposure keratopathy. Without treating the underlying vitamin A de- ficiency, these ocular surface condi- tions are progressive and refrac- tory to lubricating therapy or even surgical intervention.

In the developed world where vita- min A deficiency is thought to be nearly eradicated, severe ocular sur- face disease due to vitamin A defi- ciency has been isolated to cases of malnutrition in patients with psychi- atric conditions or malabsorp- tion syndromes due to chronic liver or gastrointestinal disease.2,4 Cooney and associates4 described a malnour- ished psychiatric patient who, like case 4, had bilateral corneal perfor- rations secondary to vitamin A de- ficiency before she was diagnosed and treated with the appropriate supplementa- tion. Lewis and col- leagues,5 similar to case 3, de- scribed an autistic child with a diet restricted mainly to carbohydrates who developed xerophthalmia due to profound vitamin A deficiency that improved only with vitamin A supplementation. The association between xerophthalmia and iatro- genically induced malabsorption syndromes in obese patients who have undergone bariatric surgery is also noteworthy given the increasing rate of obesity in the United States.6

Primary biliary cirrhosis is an au- toimmune condition characterized by the progressive destruction of intrahepatic biliary canaliculi, ultimately resulting in malabsorption of fat-soluble vitamins. A significant proportion of patients with pri- mary biliary cirrhosis also have sec- ondary Sjogren syndrome. In the pa- tients who have developed vitamin A deficiency, mucin deficiency oc- curs as a result of abnormal terminal differentiation of the conjunct- ival goblet cells in which vitamin A plays a crucial role, and aqueous tear deficiency from secondary Sjogren syndrome compounds the effect of mucin deficiency on corneal health. In cases 2 and 3, although anti-Ro and anti-La antibody tests were not performed, given that clinical improve- ment was only seen after initia- tion of vitamin A therapy, we be- lieve that the vitamin A deficiency played a more significant role than the secondary Sjogren syndrome in the development of the clinical findings.

In all 4 cases, the underlying vi- tamin A deficiency was not recog- nized until severe ocular surface disease was seen, in many cases re- quiring surgical intervention. This may be because of the perception that vitamin A deficiency does not occur in developed nations. How- ever, our cases remind us that in re- fractory cases of ocular surface dis- ease not amenable to standard treatments, especially in the setting of psychiatric conditions, autistic children, and malabsorption syn- dromes, one should consider vita- min A deficiency. Complications of this condition are preventable with vitamin A supplementation by the appropriate route.

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Retinal Dystrophy
in 2 Brothers
With α-Mannosidosis

α-Mannosidosis is a rare, auto- somal, recessive, lysosomal storage dis- ease that arises from a deficiency in lysosomal α-mannosidase. It oc- curs in approximately 1 in 500 000 births and can be caused by 40 dif- ferent mutations in the gene, MAN2B1, which is located on chro- mosome 19. Clinical characteristics include cognitive, motor, and hearing impairment, facial and skel-