Bilateral Serous Retinal Detachment Due to Protein-Losing Enteropathy

Protein-losing enteropathy (PLE) refers to a group of disorders causing hypoproteinemia and edema in the absence of proteinuria or defects in protein synthesis. It is characterized by increased protein loss in the gastrointestinal tract and is commonly suggested by the presence of peripheral edema and low serum albumin and globulin levels, in the absence of renal and hepatic disease. We describe an unusual patient with a corticosteroid-responsive PLE who developed bilateral serous retinal detachments (RDs) coincident with a flare of her enteropathy. With appropriate treatment of the enteropathy, there was resolution of the serous detachments.

Report of a Case. A 47-year-old woman was diagnosed as having idiopathic PLE 8 years before referral to the Retina Service of the Department of Ophthalmology and Visual Sciences, University of Wisconsin–Madison clinic. As her upper respiratory symptoms began to resolve, she sought care from a primary care physician because of complaints of increased abdominal girth, profound anorexia, diarrhea, and shortness of breath.

The medical workup revealed abnormal liver function test results, including a low serum albumin and elevated (9.94 µmol/L),2 and 24-hour serum analysis for α₁-antitrypsin clearance was 964 mL/24 h (normal, <27 mL/24 h).

Intestinal clearance of α₁-antitrypsin has been shown to be a reliable diagnostic test for PLE. Esophagogastroduodenoscopy and gastric biopsy revealed a congestive gastropathy. A diagnosis of PLE was made.

Given the patient’s history of responsiveness to corticosteroid administration, she was successfully treated with intravenous corticosteroids (methylprednisolone), intravenous furosemide, and albumin, with resolution of the anasarca. The PLE was subsequently well controlled with 10 mg of methylprednisolone (Medrol) every other day and 50 mg of mercaptopurine (Purinethol) daily for the subsequent 8 years.

The patient developed a systemic viral illness 4 weeks before being seen at the Department of Ophthalmology and Visual Sciences, University of Wisconsin–Madison clinic. As her upper respiratory symptoms began to resolve, she sought care from a primary care physician because of complaints of increased abdominal girth, profound anorexia, diarrhea, and shortness of breath.

The medical workup revealed abnormal liver function test results, including a low serum albumin...
min level of 2.3 g/dL and elevated alkaline phosphatase (750 U/L), aspartate aminotransferase (147 U/L), and alanine aminotransferase (201 U/L). An abdominal ultrasound revealed no structural pathologic condition of the hepatobiliary system.

She was diagnosed as having a systemic viral syndrome causing exacerbation of her underlying PLE, primarily by interfering with hepatic protein synthesis. Epstein-Barr virus, cytomegalovirus, and hepatitis A, B, and C titers were negative.

During the systemic evaluation, the patient also complained of a gradual, progressive loss of the bilateral superior visual fields. She reported that her central vision was blurry in the morning on waking and when lying in a supine position. She denied pain, floaters, or photopsias. Her local ophthalmologist diagnosed bilateral inferior RDs and referred the patient for further evaluation and treatment.

Visual acuity was 20/40 OU. Intraocular pressures were normal. Slitlamp examination revealed anterior chamber cells and flare and moderate anterior vitreous cells. Dilated funduscopic examination revealed bilateral inferior bullous RDs when the patient was in an upright posture (Figure 1 and Figure 2). There was a superior subretinal fluid shift, involving the macula, with supine positioning. Shallow peripheral choroidal detachments were noted. Diffuse choroidal thickening was confirmed by ultrasonography (Figure 3).

Fluorescein angiography revealed deep-speckled hyperfluorescence in the inferior macula and inferior periphery (Figure 4). Mild choroidal leakage was noted late in the angiogram. No retinal vascular leakage or vessel wall staining suggesting retinal vasculitis was present.

Following reevaluation by and discussion with the patient’s primary care physician, treatment of the PLE exacerbation was initiated with an increase of methylprednisolone...
to 30 mg/d. There was a rapid resolution of her systemic edema, with a weight loss of 12 kg, and resolution of the shortness of breath and diarrhea. The dosage was tapered during the following 3 to 4 weeks to her baseline level of 10 mg of methylprednisolone every other day. The serous RDs gradually resolved during 5 months of follow-up, with her visual acuity improving to 20/25 OU (Figures 1 and 2). There was persistent mild anterior chamber inflammation, with iris-lens synechiae formation. As the high-dose systemic corticosteroids were tapered, she required topical treatment with 1% prednisolone acetate. Anterior segment inflammation resolved during 5 months of follow-up.

Comment. There are multiple known causes of serous (exudative) RD, including inflammatory etiologies such as scleritis, vascular tumors (eg, diffuse choroidal hemangioma), neoplastic disease, or autoimmune pathologic conditions (eg, Vogt-Koyanagi-Harada syndrome [VKH]). To our knowledge, this is the first case reported of bilateral serous RD secondary to a PLE. The neurosensory retina maintains attachment to the retinal pigment epithelium largely through dynamics of retinal fluid flow. Although no study has shown that lower intravascular oncotic pressure leads directly to serous RD, Negi and Marmor demonstrated the importance of oncotic pressure in maintaining the necessary fluid dynamics for intact retinal attachment. They showed that nonrhegmatogenous RDs induced by subretinal injection of fluids of higher osmolality took longer to resolve spontaneously than those induced by fluids of lower osmolality. Sustained reduced oncotic pressure in the choriocapillaris due to severe hypoalbuminemia could have led to a decreased vitreoretinal to choroidal fluid outflow in this patient, thereby causing bilateral serous RDs. This was exacerbated by the outflow of serous fluid from the vascular space as the oncotic pressure of the choroid fell due to wasting of intravascular protein.

Because the patient's medical systemic disease was appropriately treated with systemic corticosteroids, the hypoalbuminemia was reversed and normal pump function of the retinal pigment epithelium was able to remove the serous fluid from the subretinal space. This was coincident with a reversal of her systemic edema and a loss of more than 12 kg of fluid overload.

Protein-losing enteropathy is an unusual systemic disorder. Nevertheless, it must be considered in the differential diagnosis of causes of serous RD.

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Phenotypic Variation in Ophthalmic Manifestations of MIDAS Syndrome (Microphthalmia, Dermal Aplasia, and Sclerocornea)

The term MIDAS syndrome was coined by Happle et al in 1993 to describe the predominant features of a genetic disorder with microphthalmia, dermal aplasia, and sclerocornea. This syndrome has also been called the “MLS syndrome,” which stands for “microphthalmia with linear skin defects.” The dermal aplasia in MIDAS syndrome consists of linear erythematous skin defects that typically involve the face, scalp, neck, and upper part of the thorax. In addition to the ocular and skin findings, there are multiple nonocular abnormalities commonly reported to be associated with MIDAS syndrome. Some of these include congenital heart defects, hypospadias, developmental delay, absence of the corpus callosum, nail dystrophy, and hydrocephalus.

The underlying defect in MIDAS syndrome is due to a deletion at Xp22.3. The disease is believed to be transmitted as an X-linked dominant trait that is lethal in the male hemizygous state. This theory has been supported by the fact that there have been no reported cases of XY males with this syndrome. The few reported cases of males with MIDAS syndrome have 46.XX karyotypes with a deletion of the Xp22.3 region due to an X/Y translocation. Although these patients are genotypically female, they are phenotypically male.

Recently we examined twin boys and 2 single-birth girls with genetically proven deletion of chromosome Xp22.3. Examination with the patient under anesthesia, including biometry and ultrasonography, was performed to detail the ocular findings associated with this syndrome. Other nonocular abnormalities were also noted.

Report of Cases. Cases 1 and 2. The twin males were born to a gravida 1, para 0, healthy 20-year-old single mother. The father was unrelated, and family history was unremarkable. Complications during the pregnancy included a positive maternal culture for group B streptococcus treated with amoxicillin and supraventricular tachycardia (SVT) of both fetuses treated with digoxin. The twins were born via an uncomplicated vaginal delivery. Estimated gestation was 35 weeks 4 days. Twin 1’s birth weight was 2.324 kg and twin 2’s birth weight was 2.350 kg.

In twin 1, external examination of the eyelids at birth was normal in both eyes. Intraocular pressure (IOP) obtained with a pneumotonometer was 36 and 33 mm Hg in the right and left eyes, respectively. Horizontal corneal diameter was 7.5 mm in each eye. Sclerocornea was noted in both eyes. The right and left corneas had central areas of less scleralized cornea measuring 4 and 5 mm, respectively (Figure 1). The fundus could not be visualized in the right eye, but funduscopic examination of the left eye showed a flat retina with a grossly normal optic disc and macula. Axial length was 15.17 mm in the right eye and 15.44 mm in the left eye. B-scan ultrasonography findings were normal in both eyes. A computed tomographic scan and mag-