woman with the disease who had (along with her daughter) systemic symptoms characteristic of coxsackievirus infection preceding her visual symptoms. However, the acute and convalescent coxsackievirus antibody titers that were obtained in the woman were not abnormal. There have been several reports of coxsackievirus infection associated with chorioretinitis, and the lesions described bear some resemblance to UAIM.

Coxsackievirus A16 and less commonly coxsackie variants A2, A5, A7, A9, A10, B1, B2, B3, B4, B6, and enterovirus 71 are generally responsible for hand-foot-and-mouth disease. Clinical interpretation of complement fixation test results for coxsackievirus ideally requires comparison of a short-term serum sample with a convalescent serum sample. In our first patient, although only convalescent serum samples were obtained, the level of coxsackievirus A16 and B6 antibodies was elevated. The second case of hand-foot-and-mouth disease was diagnosed clinically based on the presence of the classic physical findings that defined the disease in the patient and his 2 children. The temporal relationship between the onset of hand-foot-and-mouth disease and the development of retinal findings consistent with UAIM suggests that they may be related. Heightened awareness of this possible relationship should prompt retinal specialists to obtain acute and convalescent coxsackievirus antibody titers so that we can determine whether UAIM should be renamed “coxsackievirus maculopathy.”

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Isolated Vitreoretinal Amyloidosis in the Absence of Transthyretin Mutations

Vitreoretinal amyloidosis is believed to be associated universally with mutations in the genes encoding transthyretin and found exclusively as part of the familial amyloidotic polyneuropathy (FAP) syndrome. We describe herein an unusual case of biopsy-proved vitreoretinal amyloidosis without systemic involvement and demonstrate that vitreoretinal amyloidosis can occur with intact wild-type transthyretin genes.

Report of a Case. A 70-year-old woman with a history of hypercholesterolemia, chronic obstructive pulmonary disease, a distant cerebrovascular accident, and bilateral cataract extractions was first seen by us with “black snow” clouding her vision in both eyes. Review of systems was otherwise unremarkable, and her family history was negative for amyloidosis. Her visual acuity was 20/50 OD and 20/60 OS and worsened with pinhole examination. There was no relative afferent pupillary defect, intraocular tensions were within normal limits, and
slitlamp examination disclosed quiet anterior segments and clear well-centered posterior chamber intraocular lens implants bilaterally. Dilated fundus examination showed multiple, white, refractile vitreous opacities dispersed in a syneretic vitreous in both eyes (Figure 1A). Yellow deposits were also seen deep to the retina in the periphery (Figure 1B). A therapeutic and diagnostic left vitrectomy was then performed.

Histopathologic analysis of the vitreous biopsy specimen showed eosinophilic lobules that stained positively with Congo red (Figure 2A) and demonstrated birefringence when examined under polarized light (Figure 2B). These findings were diagnostic of amyloidosis. Oil-red-O stain was negative for lipids and von Kossa stain was negative for calcium phosphate salts. Genomic DNA was then isolated from peripheral blood, and exons corresponding to the entire transthyretin protein were amplified by the polymerase chain reaction. Direct DNA sequence analysis of the amplified fragments revealed no mutations in the entire coding sequence, demonstrating that this patient was homozygous for wild-type transthyretin. Moreover, single-stranded conformational polymorphism and isoelectric focusing analyses did not show any abnormal patterns for transthyretin. The patient subsequently underwent vitrectomy of the right eye. With 7 years of clinical follow-up at this report, she has not developed any signs or symptoms of systemic amyloidosis, although there have been increases in the vitreous deposits in both eyes.

Comment. Amyloidosis is a heterogeneous group of disorders involving the deposition of insoluble fibrillar hyaline aggregates in peripheral tissues. Amyloidosis affecting the vitreous was first reported in 1953 in individuals with FAP, an autosomal dominant disorder that includes vitreopathy, cardiomyopathy, and peripheral neuropathy. In fact, vitreoretinal amyloidosis is thought to be found exclusively in individuals with FAP and associated universally with mutations in the transthyretin gene. To date, more than 80 such transthyretin mutations have been described. In contrast, systemic amyloidosis can result from a number of distinct
amylloid deposits, including wild-type transthyretin as well as other fibrillar proteins. To our knowledge, this is the first case report of vitreoretinal amyloidosis in the absence of transthyretin mutations. In addition, no signs of systemic amyloidosis suggestive of FAP were evident 7 years after the patient’s initial presentation, although we cannot exclude the possibility of a subclinical level of amyloid deposition in other tissues. These findings raise the possibility that isolated vitreoretinal amyloidosis may represent a disorder separate from FAP. We conclude that vitreoretinal amyloidosis encompasses a more heterogeneous group of disorders than has been previously described.

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Figure 1. T1-weighted sagittal magnetic resonance image showing ectopic posterior pituitary gland (solid arrow) and absence of the pituitary infundibulum (open arrow denotes normal position of infundibulum).

Optic Nerve Aplasia in an Infant With Congenital Hypopituitarism and Posterior Pituitary Ectopia

Optic nerve aplasia is a rare developmental anomaly characterized by the congenital absence of the optic nerve, retinal blood vessels, and retinal ganglion cells. Optic nerve aplasia seems to fall within a malformation complex that is fundamentally distinct from optic nerve hypoplasia, as evidenced by its tendency to occur unilaterally and its frequent association with microphthalmos and other malformations that are confined to the involved eye. Unilateral optic nerve aplasia is generally associated with otherwise normal brain development, while bilateral optic nerve aplasia is usually accompanied by other central nervous system derangement. To our knowledge, optic nerve aplasia has not been associated with endocrinologic deficiency. This report describes congenital hypopituitarism and posterior pituitary ectopia in an infant with bilateral optic nerve aplasia.

Report of a Case. A male infant was born to nonconsanguineous parents at 38 weeks’ gestation with a birth weight of 2750 g. There was no family history of microphthalmos or coloboma. The mother had a history of hyperthyroidism, which was treated in late pregnancy with propylthiouracil. Both of the child’s eyes were noted to be small at birth, but no other systemic anomalies were observed. The newborn screen showed a total thyroxine level of 4.1 µg/dL (53.0 nmol/L) (normal range, 11-23 µg/dL [142-296 nmol/L]) and an initial serum glucose level of 28 mg/dL (1.6 mmol/L). The patient required intravenous dextrose to maintain a normal serum glucose level. At 4 days of age, magnetic resonance images of the brain disclosed posterior pituitary ectopia with absence of the optic nerves, chiasm, and pituitary infundibulum (Figure 1). Endocrinologic testing at 1 week of age showed a free thyroxine level of 0.7 ng/dL (9.0 pmol/L) (normal range, 0.7-1.9 ng/dL [9.0-24.0 pmol/L]), a late afternoon serum cortisol level of 3 µg/dL (77 nmol/L) (normal range, 4-11 µg/dL [110-304 nmol/L]), and a random growth hormone level of 4 ng/mL (185 pmol/L) (normal level > 10 ng/mL [>440 pmol/L]). An insulin-like growth factor I/somatotropin C level obtained 2 months later was 14 ng/mL (normal range, 17-248 ng/mL). Based on the severe hypoglycemia, low anterior pituitary hormone levels, and posterior pituitary ectopia, supplementation with growth hormone, thyroxine, and hydrocortisone was initiated.

The patient had no behavioral response to light shined into either eye during an ophthalmologic examination at 2 months of age. Both palpebral fissures were small, and there was bilateral microphthalmos. The corneas were clear, with a corneal diameter of 4 mm OD and 9 mm OS. The pupils were fixed, round, and nonreactive to light. The retina of the right eye could not be visualized. The left eye showed absence of the left optic nerve and cen-