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.3-5

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.6 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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The authors have no relevant financial interest in this article.

This study was supported in part by an unrestricted grant from Research to Prevent Blindness Inc, New York, NY, to Northwestern University, Chicago.

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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.1 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

Figure 4. Case 2. A, Lesion has rapidly evolved to a bull’s-eye lesion. B, Fluorescein angiogram shows a variably pigmented lesion with alternating hyperfluorescent and hypofluorescent rings.
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

![Figure 1. A, Preoperative fundus photograph demonstrating white vitreous deposits. B, Postoperative fundus photograph of the peripheral retina demonstrating yellow deposits under the retina.](image1)

![Figure 2. Histopathologic analysis of the vitreous biopsy specimen. A, Positive staining for eosinophilic lobules with Congo red is evident (original magnification ×250). B, Birefringence is seen when the specimen is examined under polarized light (original magnification ×250).](image2)
amyloid deposits, including wild- 
type transthyretin\(^2\) as well as other 
 fibrillar proteins.\(^4\)

To our knowledge, this is the 
 first case report of vitreoretinal amyl- 
loidosis in the absence of transthyre- 
tin mutations. In addition, no signs 
of systemic amyloidosis suggestive of 
FAP were evident 7 years after the pa-
tient’s initial presentation, although 
we cannot exclude the possibility of 
a subclinical level of amyloid depo-
sition in other tissues.\(^5,6\) These find-
ings raise the possibility that iso-
lated vitreoretinal amyloidosis may 
represent a disorder separate from 
FAP. We conclude that vitreoretinal 
amyloidosis encompasses a more het-
erogeneous group of disorders than 
has been previously described.

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1. Bhistitkul RB, Mukai S. Vitreous amyloidosis. In: 
Albert DM, Jakobiec FA, eds. Principles and Prac-
tice of Ophthalmology. 2nd ed. Philadelphia, Pa: 

2. Kantarian AD, De Jong RN. Familial primary 
amyloidosis with nervous system involvement. 

3. Westermark P, Sletten K, Johansson B, Corn-
well GG III. Fibril in senile systemic amyloidosis 
is derived from normal transthyretin. Proc Natl 
Acad Sci U S A. 1990;87:2843-2845.

4. Lachmann HJ, Booth DR, Booth SE, et al. Mis-
diagnosis of hereditary amyloidosis as AL (pri-
mary) amyloidosis. N Engl J Med. 2002;346: 
1786-1791.

5. Sandgren O. Ocular amyloidosis, with special re-
ference to the hereditary forms of vitreous in-

6. Schwartz MF, Green WR, Michels RM, Kincard 
MC, Fogel J. An unusual case of ocular involve-
ment in primary systemic nonfamilial amyloi-

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

Optic nerve aplasia is a rare deve-
lopmental anomaly characterized by 
the congenital absence of the optic 
nerve, retinal blood vessels, and reti-
ganglion cells.\(^3,4\) Optic nerve apla-
\(sia seems to fall within a malforma-
tion complex that is fundamentally 
distinct from optic nerve hypopla-
sia, as evidenced by its tendency to 
occur unilaterally and its frequent as-
\ociation with microphthalmos and 
other malformations that are con-
fined to the involved eye.\(^3,4\) Unilat-
eral optic nerve aplasia is generally 
associated with otherwise normal 
brain development, while bilateral 
optic nerve aplasia is usually accom-
p\(\)\(\(\)panied by other central nervous sys-
\(\(\(\)tem derangement.\(^4\) To our knowl-
edge, optic nerve aplasia has not been 
associated with endocrinologic defi-
cence. This report describes con-
genital hypopituitarism and poste-
rior 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 fam-
ily history of microphthalmos or colo-
boma. The mother had a history of 
hyperthyroidism, which was treated 
in late pregnancy with propothiora-
cil. Both of the child’s eyes were noted 
to be small at birth, but no other sys-
temic anomalies were observed. The 
newborn screen showed a total thy-
roxine level of 4.1 µg/dL (53.0 
nmol/L) (normal range, 11-23 µg/dL 
[142-296 nmol/L]) and an initial se-
\(rumin level of 28 mg/dL (1.6 
\(\)nmol/L). The patient required intra-
\(\)venous dextrose to maintain a nor-
mal serum glucose level. At 4 days of 
age, magnetic resonance images of the 
brain disclosed posterior pituitary ecto-
pia with absence of the optic nerves, 

ti, and posterior pituitary infundibulum 
(Figure 1). Endocrinologic testing 
at 1 week of age showed a free thy-
oxine 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 se-
\(rumin cortisol level of 3 µg/dL (77 
nmol/L) (normal range, 4-11 µg/dL 
[110-304 nmol/L]), and a random 
\(\)rowth hormone level of 4 ng/mL 
(185 pmol/L) (normal level > 10 
\(\)ng/mL [> 240 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 hypo-
glycemia, low anterior pituitary hor-
\(\)mone levels, and posterior pituitary 
ectopia, supplementation with growth 
hormone, thyroxine, and hydrocor-
tisone was initiated.

The patient had no behavioral 
response to light shined into either 
eye during an ophthalmologic ex-
\(\)amination at 2 months of age. Both 
\(\)alpebral 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 
\(\)etina of the right eye could not be 
visualized. The left eye showed ab-
sence of the left optic nerve and cen-