

# Diagnostic and Therapeutic Challenges

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## Case Report

A 10-year-old Hispanic boy presented with painless vision loss in the right eye for 1 month. There was no significant medical or birth history except a hospitalization for pneumonia as an infant. The family moved from the Dominican Republic 4 months before presentation. Family history was unremarkable except for an 11-year-old cousin with an undiagnosed eye problem.

His best-corrected visual acuity was 20/150 in the right and 20/70 in the left eye. Intraocular pressure and pupillary examination were within normal limits. The anterior segment examination was normal, and there were no signs of inflammation in the vitreous.

Fundus examination of both eyes revealed peripapillary, subretinal fibrosis partially surrounding the nerves and extending toward the fovea (Figure 1, A and B). There was a distinct ring of geographic atrophy within the fovea of the right eye. Subretinal hemorrhage was present within the left macula and also adjacent to the disk nasally (Figure 1B). A cluster of telangiectasias, perivascular exudation, and abnormal vascularization was seen in the right superotemporal periphery (Figure 1C). A superotemporal chorioretinal scar was present in the periphery of the left eye.

Fluorescein angiography demonstrated bilateral, peripapillary hyperfluorescence consistent with staining (Figure 1, E and F); however, there was no evidence of macular leakage. Views of the right superotemporal periphery revealed capillary nonperfusion and "light bulb" hyperfluorescent lesions corresponding to telangiectasias. Optical coherence tomography revealed subretinal hyperreflectivity in both the right and left eyes (Figure 1, E and H) as well as intraretinal fluid in the left eye, suggesting active choroidal neovascularization (Figure 1H).

An extensive workup was performed to rule out known causes of posterior uveitis. Serologic testing was performed to rule out infectious etiologies such as tuberculosis, syphilis, Lyme, rubella, and herpes viruses. Inflammatory and infectious laboratory tests including HLA-B27, Toxoplasmosis, Lyme, Syphilis, Herpes Simplex Virus and Herpes Zoster Virus, were sent in addition to testing for other systemic conditions such as sickle-cell disease and sarcoidosis. A chest x-ray and magnetic resonance imaging of the brain and orbits were performed. All laboratory test results and

imaging were negative, with the exception of a mildly elevated herpes simplex virus (HSV)-1 immunoglobulin G.

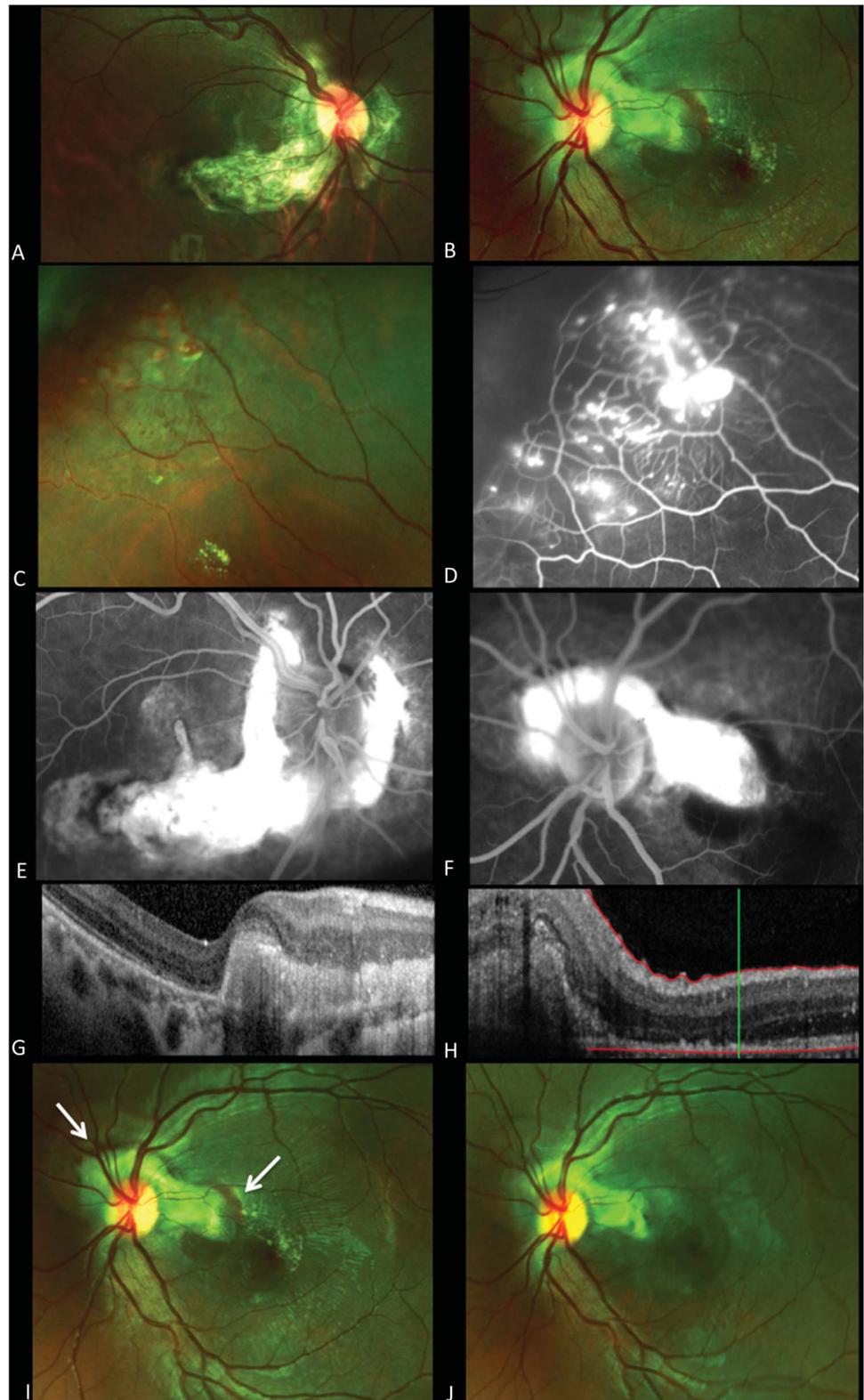
The patient subsequently underwent a dilated fundus examination under anesthesia. Laser photocoagulation was used to treat the telangiectasias and nonperfused retina present in the right eye. The left eye was treated with an intravitreal injection of 1.25 mg bevacizumab using a standard sterile ophthalmic technique.

One month postoperatively, the patient's vision on the left improved to 20/50 from 20/70 and remained stable on the right at 20/150. Fundus examination revealed a complete resolution of subretinal hemorrhage within the left macula (Figure 1, I and J). Optical coherence tomography revealed a decrease in central subfoveal thickness from 248  $\mu\text{m}$  to 130  $\mu\text{m}$ . At the 3-month follow-up, the vision remains stable and the choroidal neovascularization (CNV) seems controlled.

This case is presented for discussion of diagnosis and management.

## Dr. Lucia Sobrin (Boston, Massachusetts):

Drs. Wang and Johnson present a challenging case of peripapillary subretinal fibrosis accompanied by choroidal neovascularization and signs of Coats disease. This constellation of findings is unique. The first thing to consider is whether the peripapillary subretinal fibrosis is due solely to choroidal neovascularization that has scarred adjacent to the nerve but is still active at the outer border or due to inflammatory cell infiltration with secondary adjacent choroidal neovascularization. The subretinal fibrosis and uveitis syndrome is a rare idiopathic posterior uveitis characterized in the early stages by a multifocal choroiditis, followed by progressive subretinal fibrosis.<sup>1</sup> It usually is seen in otherwise healthy, young myopic women with no systemic disease. Examination reveals transient, multiple, small, whitish-yellow retinal pigment epithelial or choroidal lesions in the posterior pole and midperiphery. These lesions can fade or enlarge and coalesce to create areas of white subretinal fibrosis, a progression that occurs over weeks to months. In the current patient's case, there were no new independent choroidal lesions



**Fig. 1.** Fundus photograph of the right (A) and left (B) eye, revealing bilateral, peripapillary subretinal fibrosis, and choroidal neovascularization with macular exudation (B). Fundus photograph of telangiectatic vessels and yellow exudate in the right superotemporal periphery (C). Fluorescein angiography of the right (D and E) and left (F) eye showing light-bulb telangiectasias and peripapillary hyperfluorescence. Optical coherence tomography through the right (G) and left (H) macula, revealing subretinal hyperreflectivity in both eyes and intraretinal fluid in the left eye (H). Fundus photograph of the left eye before (I) and after (J) intravitreal bevacizumab. Arrows in panel “I” demarcate the subretinal hemorrhage that was subsequently resolved in panel “J” after intravitreal bevacizumab injection.

documented and there was no anterior chamber or vitreous inflammation. The solely peripapillary location of these lesions is also atypical for this entity. Subretinal

fibrosis and uveitis syndrome is very uncommon, and there are no clear reports of its association with choroidal neovascularization. An inflammatory etiology of the

subretinal fibrosis would be bolstered if the patient were to develop new choroidal infiltrates that evolved into subretinal fibrosis with additional follow-up. In the absence of such findings, it is still possible that the fibrosis is secondary to choroidal neovascularization alone.

The second factor to consider in the differential diagnosis is the link between the posterior pole pathology and the peripheral vascular changes in the right eye that are quite consistent with Coats disease or a Coatslike response. Coats disease is characterized by congenital telangiectatic retinal vessels accompanied by yellow subretinal exudates. A fundus appearance similar to that of Coats disease, termed Coatslike response, has been reported in the setting of other ocular diseases, including uveitic entities such as pars planitis<sup>2</sup> and Fuch's heterochromic iridocyclitis.<sup>3</sup> If the posterior pole pathology is indeed secondary to an underlying autoimmune posterior uveitis, the Coatslike response could theoretically be due to ongoing damage to the retinal vasculature secondary to chronic inflammation. Secondary vascular changes are more likely when there is intraocular inflammation, which this patient did not demonstrate during the time he was being followed-up by the authors. It would be more difficult to make a connection between isolated posterior pole choroidal neovascularization and a Coatslike response. Coats disease can directly cause subretinal exudation in the posterior pole that leads to subretinal fibrosis, but the exudates typically collect in the macula. The peripapillary configuration of the fibrosis and the absence of any peripheral vascular changes in the left eye make this scenario unlikely. Two coexisting but unrelated diseases in the right eye—congenital Coats disease and peripapillary subretinal fibrosis—are possible, but this is less likely.

The authors performed a comprehensive laboratory and radiologic investigation for systemic diseases that could be associated with choroiditis and did not find evidence for the diseases that we would be most keen to exclude—sarcoidosis, syphilis, and tuberculosis. If the patient had a history of recent exposure to kittens or cats, I would have obtained *Bartonella* titers, although the fundus findings are not typical for that disease. Although the Caribbean origin of the patient and the peripheral chorioretinal scar in the left eye might suggest *Toxoplasmosis gondii* as a possible etiology, the optical coherence tomography findings in toxoplasmic chorioretinitis, with full-thickness disruption of the retinal architecture, are not seen in the peripapillary pathology in this case.

For idiopathic or inflammatory etiologies of choroidal neovascularization, I favor an as-needed treatment

protocol with anti-vascular endothelial growth factor agents. As with this patient's course so far, one injection may be sufficient to control the disease indefinitely. There are patients with choroiditis, however, who will require injections at regular intervals. To distinguish between those that will need regular injections and those that may not, I follow these patients monthly after the first injection, treating as needed and slowly spacing out the interval between monitoring examinations over time. For patients with recurrent choroidal neovascularization secondary to choroiditis, I consider long-term immunosuppressive therapy to address the inflammatory stimulus of the new vessels. For the current patient, I would not recommend immunosuppressive treatment at this point. I would consider such therapy if the choroidal neovascularization recurs or new choroidal inflammatory lesions appear. In these scenarios, either methotrexate or mycophenolate would be my choice for a first-line agent.

In summary, this case represents an unusual grouping of fundus findings—peripapillary subretinal fibrosis, choroidal neovascularization, and a Coatslike peripheral pathology. The posterior pole pathology has already robbed this child of a substantial amount of vision and close monitoring of his disease will be key to helping to preserve the vision he has.

#### Editor's Note:

Drs. Wang and Johnson have presented a 10-year-old boy with unilateral decreased vision of 1 month's duration. The predominant findings included posterior subretinal fibrosis. Telangiectasis was noted in one eye and a peripheral chorioretinal scar in the other.

Dr. Lucia Sobrin has consulted on this case. The differential diagnosis considered by the presenters, in addition to Dr. Sobrin, included:

- I. Inflammatory
  - A. Multifocal choroiditis
    1. Subretinal fibrosis and uveitis syndrome
  - B. Sarcoid
  - C. Pars planitis
  - D. Fuch's heterochromic iridocyclitis
  - E. Autoimmune posterior uveitis
    1. Coatslike response
- II. Infectious
  - A. Tuberculosis
  - B. Syphilis
  - C. Bartonella
  - D. Lyme disease
  - E. Herpes viruses
  - F. Rubella
  - G. Toxoplasmosis

Dr. Sobrin focuses on the subretinal fibrosis and uveitis syndrome, noting that this rare uveitis appears initially as a multifocal choroiditis, followed by progressive uveitis. These areas may coalesce and create white areas of subretinal fibrosis over weeks to months. These changes are noted predominantly in the peripapillary area, as in this patient.

She states that the Coatslike findings may be seen in a variety of inflammatory conditions and postulates that in this patient, the Coatslike response could be due to ongoing damage to the retinal vasculature secondary to chronic inflammation. However, she notes that there was no intraocular inflammation observed in this young patient, which brings up the possibility that the posterior changes are all secondary to Coats disease, or that the patient might have two unrelated diseases.

Dr. Sobrin recommends anti-vascular endothelial growth factor if necessary for active choroidal neovascularization. She would not recommend immunosuppressives at this point, but would consider such therapy if choroidal neovascularization recurred or if new choroidal lesions appeared.

We thank Drs. Wang and Johnson for their case and Dr. Lucia Sobrin for her consultation.

### References

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