

Grand Rounds

An 11-month-old girl with a retinal detachment

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History

An 11-month-old girl was referred to the London Retinoblastoma Unit with a 2-month history of a unilateral, dull red reflex, strabismus, and an intraocular mass suspicious for retinoblastoma. There was no family history of note, and she was otherwise a normal developing child.

Examination

On examination, the child objected to occlusion of the right eye and was not able to fix and follow consistently with the left eye. Pupils appeared to be normal, with no manifest strabismus. A relative afferent pupillary defect was not established. On indirect fundoscopy, a yellow pupillary reflex (xanthocoria) was seen in the left eye. The right eye appeared normal. On examination under general anesthesia, the anterior segment of each eye showed no abnormal neovascularization or tumor seeds, and the horizontal corneal diameters were within normal limits. Intraocular pressure was normal in both eyes. On posterior segment examination, a total retinal detachment was noted in the left eye (Figure 1); indirect ophthalmoscopy revealed yellow, subretinal exudation, and there were also anomalous retinal vessels. Fundus images were captured with the RetCam 3 (Clarity Medical Systems Inc, Pleasanton, CA).

Ancillary Testing

Fundus fluorescein angiography performed during the same examination under anesthesia highlighted aneurys-



Figure 1. Fundus photograph showing vascular abnormalities in the retina with a yellow, bullous retinal detachment.

mal dilatations (Figure 2A) and telangiectatic vessels (Figure 2B) along the detached retina. Adjacent to the vessel anomalies were moderate-to-large areas of capillary dropout. Video 1 shows the red blood cells traveling along the dilated retinal vessels and further emphasise of the abnormal retinal vasculature. A B-scan ultrasound (Figure 3) revealed an exudative retinal detachment, with no signs of calcification.

Treatment

The patient was treated with laser ablative therapy for the abnormal blood vessels. Long burns were aimed at

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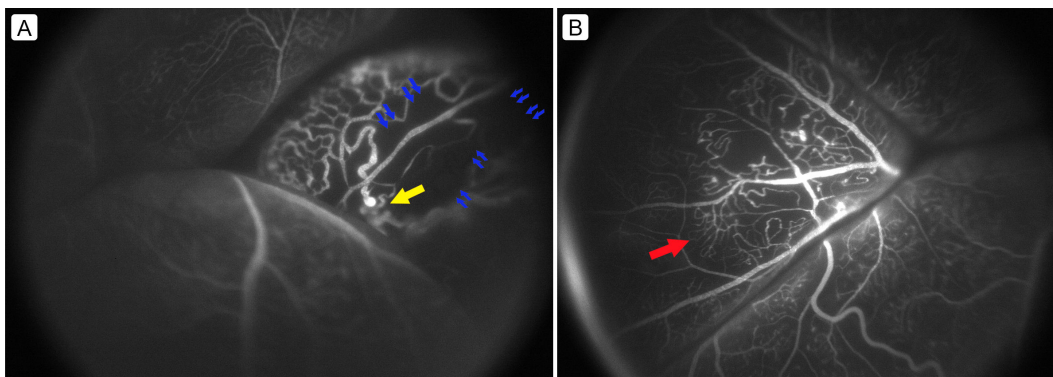


Figure 2. Fluorescein angiogram. A, Aneurysmal dilatations (yellow arrow) and capillary dropout (blue arrows). B, Telangiectatic vessels (red arrow).



Video 1. Sluggish dynamics of the red blood cells traveling along the dilated retinal vessels and further highlights of the anomalous retinal vasculature.

the abnormal blood vessels, using a 532 nm wavelength laser guided by the fundus fluorescein angiogram. In total, 1,361 shots (of 200–300 mW, with an average duration of 300 ms) were administered in areas of non-perfusion and over the abnormal blood vessels. She did not receive an intravitreal injection of anti-vascular endothelial growth factor (anti-VEGF).

A reduction in subretinal fluid was noted 3 months after laser treatment. At the final follow-up, 7 months after the procedure, the child could not fixate with this eye. A white cataract in the affected eye prevented visualization of the fundus. However, intraocular pressure remained normal, and there was no iris rubeosis. Current treatment for the affected eye is atropine 1% eye drops once a day for comfort. The right eye remains normal.

Differential Diagnosis

In this case, the asymmetry of the red reflexes between the eyes identified the presence of pathology, which warranted an urgent diagnosis. The findings in this



Figure 3. B-scan ultrasound showing an intraocular, hyperechoic mass representative of an exudative retinal detachment. Subretinal areas are hypoechoic (arrows), which goes against calcification, a feature associated with retinoblastoma and appearing as bright hyperechoic lesions.

patient suggested Coats disease (stage 3B) as the most likely diagnosis. However, other conditions that produce retinal detachment or an abnormal red reflex in children are important to consider as differential diagnoses.

Retinoblastoma is an important differential consideration for leukocoria with a mass, because it is the most common primary ocular tumor in children. Other pediatric ocular tumors, such as choroidal melanoma, choroidal hemangioma, and medulloepithelioma are also important diagnoses. Leukocoria is also commonly seen in congenital cataracts.

The etiologies for retinal detachment in children differ from those in adults. A large proportion of pediatric retinal detachments are congenital in nature and include rare hereditary vitreoretinal conditions, such as familial exudative vitreoretinopathy, incontinentia pigmenti, Stickler syndrome, X-linked retinoschisis, Marfan syndrome, and Norrie disease.

In infants, developmental pathologies, such as persistent fetal vasculature and colobomas may be associated with retinal detachment, and retinopathy of prematurity is an important cause of retinal detachment in premature babies.

Retinal detachment may also occur because of trauma, inflammation, and infection; however, these usually present with more clues in the presenting history and have other signs of systemic involvement.

Diagnosis and Discussion

The fundus fluorescein angiogram (Figure 2) highlights the telangiectatic and aneurysmal dilatations classically seen in Coats disease. This finding is not usually associated with detachments secondary to retinoblastoma. Furthermore, the B-scan ultrasound (Figure 3) showed the absence of calcification, which is often found in retinoblastoma. Together, these findings confirmed the diagnosis of stage 3B Coats disease.¹

Coats disease is an ophthalmic condition classically presenting with reduced visual acuity, strabismus, or leukocoria.² It is a nonhereditary condition that manifests as an exudative process characterized by abnormal changes in retinal vasculature. The disease process involves intra- and subretinal exudation of fluids, which in later stages can lead to retinal detachment. The fundus is typically observed with telangiectasia, “light bulb” aneurysms, and intra- and subretinal exudates.^{3,4} There appears to be no reported racial or ethnic predilection.⁵ Additionally, it is unilateral in 80%–95% of cases.

The most widely used classification system for Coats’ disease was proposed by Shields et al in 2001.¹ Stage 1 refers to eyes that only have telangiectasia; stage 2, to eyes with exudation in the extrafoveal (2A) or subfoveal

(2B) locations. In stage 3 eyes there is partial (3A) or total (3B) exudative detachment; if this is accompanied by glaucoma, it is classified as stage 4. Finally, stage 5 is observed with a complete detachment of the retina, which commonly presents with cataract and phthisis, and this can lead to complete blindness.¹

Treatment of Coats disease is based on disease severity. Mild cases are managed conservatively. More advanced stages involving exudates and retinal or subretinal fluid are managed with laser photocoagulation or cryotherapy to abnormal vascular regions. The combination of these treatments is effective in preventing progression to neovascular glaucoma or phthisis in most patients, thus preserving the globe. In stage 3B Coats disease the aim of treatment is to prevent rubeosis through partial reattachment; thus, unrecordable visual acuity after treatment does not imply an unsuccessful outcome. There is also a role for anti-VEGF agents such as bevacizumab in early-stage macula-involving Coats disease; however, the safety profile in children is unclear.

The majority of patients presenting with Coats disease are male (75%) and usually present in the first decade of life, with the mean age of diagnosis at 5 years.⁵ The mean age of diagnosis of retinoblastoma in children is 15–24 months, with no sex predilection.⁶ Hence, while the diagnostic findings for Coats disease are typical with this case, the age and sex of the patient are atypical.

Retinoblastoma and Coats disease commonly mimic each other. Shields et al appraised 150 cases of Coats disease and established that the diagnosis was correct in only 64 cases (41%). The mistaken diagnoses included retinoblastoma in 43 cases (27%), retinal detachment in 12 (8%) and retinal hemorrhage in 7 (4%).⁵ Conversely, when the same authors analyzed 604 cases with lesions simulating retinoblastoma, they found that Coats disease was the most common cause of pseudoretinoblastoma (40%).⁷

In earlier stages of Coats disease, fundus examination alone is enough to differentiate Coats disease from retinoblastoma: typically the lesion in Coats disease has a yellow-colored appearance, whereas in retinoblastoma it has a chalky whitish-gray appearance (see Shields J and Shields C. J AAPOS 2011;15:e7: Abstract 026). However, when retinal detachment with subretinal exudation and dilated retinal vessels coexist, even an expert may have difficulty differentiating Coats disease from retinoblastoma by ophthalmoscopy.

Over the last three decades, there has been a significant improvement in the detection of Coats disease. Fluores-

cein angiography is critical in documenting classic findings to establish the diagnosis, because it highlights anomalies in the retinal vasculature. Computed tomography (CT) and magnetic resonance imaging have also proved to be extremely helpful in aiding the diagnosis of Coats disease.⁸ However, they cannot always be relied on for differentiating Coats from retinoblastoma. Sherman et al⁹ reported that CT imaging was unable to differentiate between unilateral noncalcifying retinoblastoma in 2 children with advanced Coats' disease. This limitation was emphasized by Haik et al's report¹⁰ of similar findings in 14 patients with Coats disease. However, it should be noted that any form of imaging involving radiation is contraindicated in children where retinoblastoma remains a suspicion, because they could carry a germline mutation in all their cells, predisposing them to secondary tumors.

Retinoblastoma can be treated with a combination of chemotherapy, transpupillary thermotherapy, cryotherapy, and brachytherapy; in severe cases, enucleation may be necessary. Although extraocular invasion and systemic spread are now rare in developed countries, this cancer can still lead to significant morbidity and mortality.

In the past, in cases where retinoblastoma could not be definitively excluded, ophthalmologists opted to enucleate an eye associated with a poor prognosis. This is vital to prevent a delay in diagnosis and definitive treatment of a potentially lethal condition. Inevitably, this

approach also involved enucleating eyes with advanced Coats disease.¹ Thus, establishing a correct diagnosis early is essential for proper treatment.

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