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Case report

Neurofibromatosis type 1 presenting with retinal detachment and laryngeal plexiform neurofibroma in a toddler

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ABSTRACT

Purpose: To present a 22-month-old girl with a complete retinal detachment who was found to have systemic exam findings consistent with neurofibromatosis type 1 during the course of multi-specialty exam under anesthesia.

Observations: During examination under anesthesia, ophthalmic exam findings demonstrated retinal detachment with cyst formation, as well as peripheral non-perfusion of the retina in the left eye. Non-ophthalmic findings discovered on difficulty with intubation included a laryngeal plexiform neurofibroma and café-au-lait spots.

Conclusions: Pediatric retinal detachments are uncommon compared to those in adults. Pediatric patients with neurofibromatosis type 1 can present with vision loss as the presenting symptom. Systemic signs and symptoms should be carefully screen and monitored.

1. Introduction

Neurofibromatosis type 1 (NF1) is an autosomal dominant neurocutaneous syndrome that impacts several organ systems, including the eye. Ocular manifestations of NF1 include iris Lisch nodules, optic pathway gliomas, eyelid or orbit plexiform neurofibroma, glaucoma, and, rarely, retinal hamartomas. Here, we present a 22-month-old girl who was referred for possible *Toxocara canis* retinal detachment (RD) of the right eye and noted to have a laryngeal mass and peripheral nonperfusion of the left eye.

2. Case report

A 22-month-old girl presented from Puerto Rico for evaluation of one month of leukocoria in the right eye with pain, inflammation, vision changes and exotropia. She was diagnosed with a possible *Toxocara canis* retinal detachment with negative Toxocara IgM and IgG. The patient was born at full term and had no other past medical history. She had no relevant family history of ophthalmic or inherited disorders.

On ophthalmic examination, she had a poor reaction to light in the right eye and was able to fix and follow in the left eye. Her pupil was fixed with posterior synechia in the right eye and 2.5 mm in the left eye. Her right eye demonstrated exotropia. There were no iris Lisch nodules present bilaterally.

During exam under anesthesia (EUA), her intraocular pressure was 37 mmHg in the right eye and 12 mmHg in the left eye. The right eye showed injected conjunctiva with a deep anterior chamber and a retrolental membrane of vascular tissue consistent with apposition of the retina to the posterior lens (Fig. 1a). B-scan echography of the right eye demonstrated a small globe with a total funnel retinal detachment, cyst formation with no evidence of retinoblastoma. Ultrasonography and fundus photography of the left eye was otherwise unremarkable. There were otherwise no issues with her initial EUA.

Fluorescein angiography (FA) showed a lack of patent vasculature in the right eye with abnormal vasculature in the posterior retrolental space consistent with a total retinal detachment. FA of the left eye was normal posteriorly with abnormal tortuosity and vasculature temporally (Fig. 1b) and peripheral nonperfusion noted temporally,

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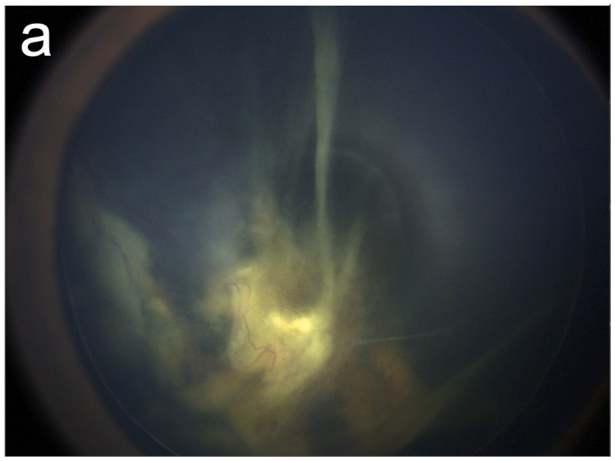

Fig. 1a. External photograph of the right eye, demonstrating injected conjunctiva with a deep anterior chamber and a retrolental membrane of vascular tissue consistent with apposition of the retina to the posterior lens.

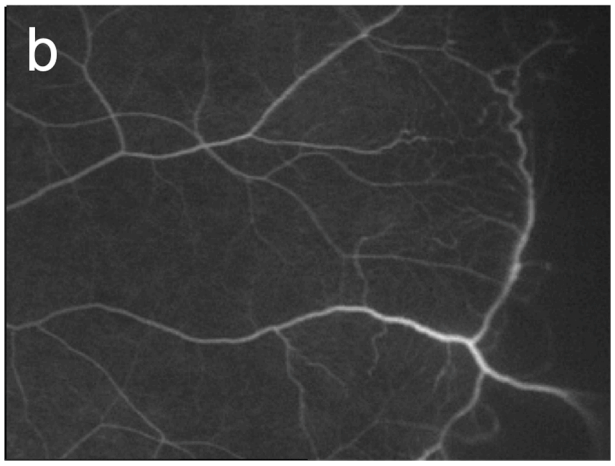

Fig. 1b. Fluorescein angiography of the left eye at 4 minutes, 28 seconds, with peripheral nonperfusion noted here temporally with abnormal tortuosity of retinal vasculature.

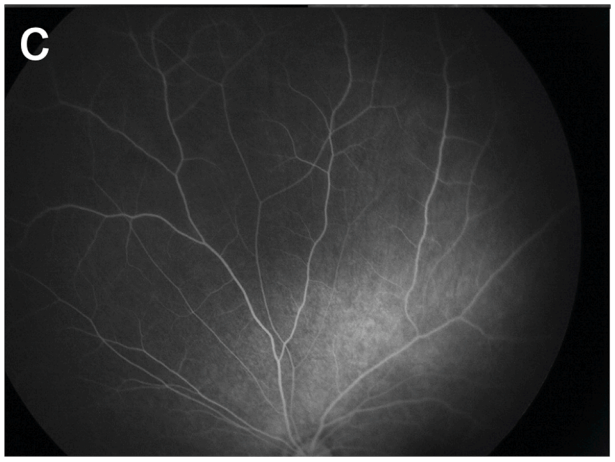

Fig. 1c. Fluorescein angiography of the left eye at 4 minutes, 45 seconds, with peripheral nonperfusion noted superotemporally.

superotemporally (Fig. 1c), and inferotemporally. The retinal detachment was determined to be inoperable and an injection of sub-Tenon's Kenalog was given to the right eye. The child was treated with topical prednisolone and glaucoma medications.

On repeat EUA four months later, the patient had a stable ocular exam with decreased IOP to 12 mmHG in the affected eye. It was noted that the patient had more than 6 cafe-au-lait spots larger than 5mm diameter present on her trunk and legs. During intubation, a large cystic mass was noted in the airway (Fig. 2a). Pediatric otolaryngology was then consulted, resulting in a hospital admission for direct laryngoscopy, imaging, and possible biopsy. The family stated they had noted problems breathing at night that had been diagnosed as enlarged adenoids in Puerto Rico.

Direct laryngoscopy revealed a large left supraglottic, submucosal posterior laryngeal lesion. The mass was debulked, with multiple biopsies taken. Pathology showed that the mass was a plexiform neurofibroma. MRI revealed a lobulated mass with enhancement (Fig. 2b) in the posterior left lateral aspect of the hypopharynx. Orbital MRI showed the presence of the retinal detachment in the right eye. Brain MRI showed areas representing dysplastic myelin gliomatosis cerebri, both of which are seen in patients with neurofibromatosis type 1 (Fig. 2c).

Based on oculocutaneous and laryngeal findings, this patient was diagnosed with neurofibromatosis type 1 (NF-1). This was confirmed with genetic testing which showed a pathologic mutation 1246C > T in *NF1* gene. She is the only one in her family to have confirmed NF-1. Two and a half years post diagnosis and debulking of the laryngeal plexiform neurofibroma, the patient had increased airway resistance syndrome and additional debulking was performed by otolaryngology. At follow up one month after this procedure, the patient's parents noted that her breathing had improved. The intracranial MRI findings have not changed. The patient's retinal detachment in the right eye and peripheral nonperfusion of the left eye are unchanged with no other problems with IOP. The patient is now 6 years old and the retina in the left eye has remained stable and avascular with no evidence of neovascularization by fluorescein angiography. We plan on performing fluorescein angiography every 6–12 months, with interval in-office peripheral retina examinations in between each FA.

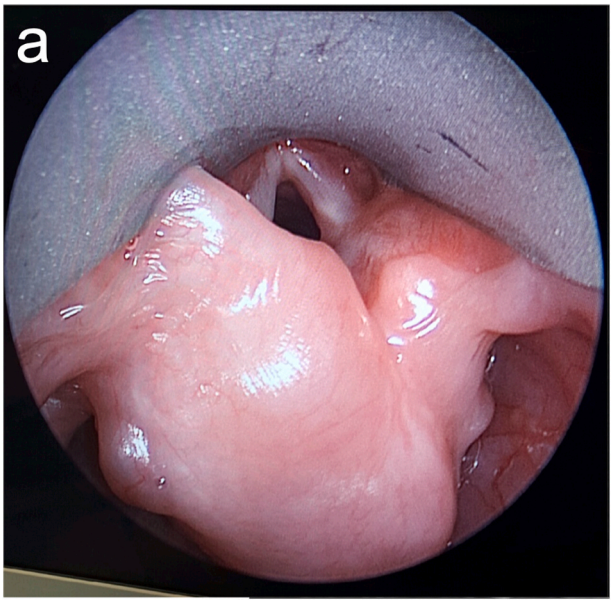

Fig. 2a. Posterior laryngeal cystic mass noted during intubation during exam under anesthesia.

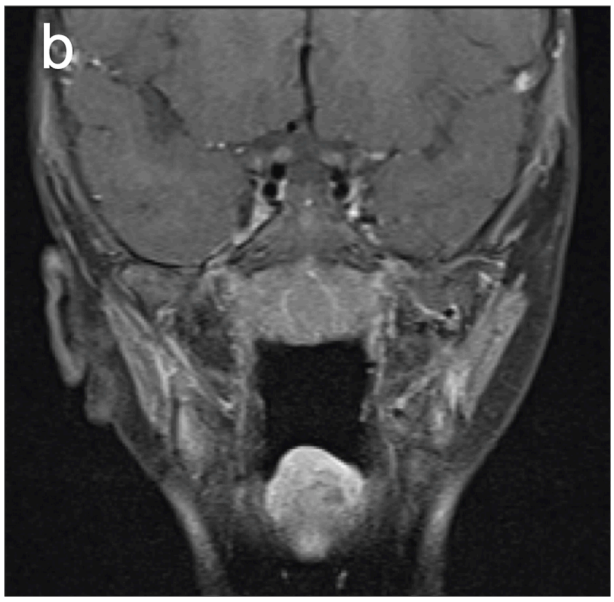

Fig. 2b. Magnetic Resonance Imaging of the brain, T1 post-gadolinium, demonstrating enhancing lobulated hypopharyngeal mass that measures 1.6 × 1.9 × 2.2 cm with mass effect on the supraglottic larynx causing severe narrowing and anterior displacement. The airway is patent although severely narrowed.

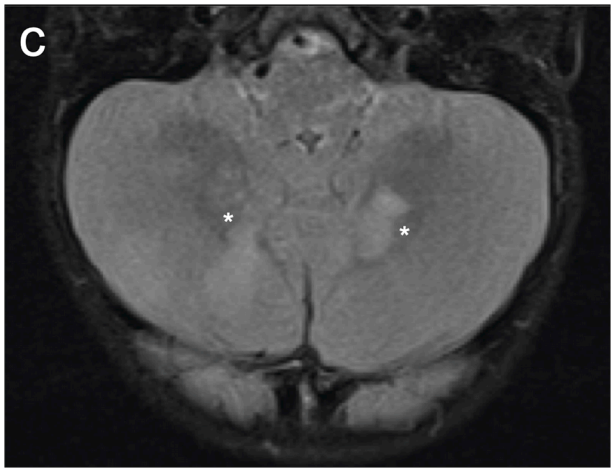

Fig. 2c. Foci (asterisk*) of T2 FLuid Attenuated Inversion Recovery hyperintensity in the bilateral cerebellar white matter, representing areas of dysplastic myelin which has been described in patients with NF-1.

3. Discussion

We present a case of pediatric retinal detachment that led to a diagnosis of neurofibromatosis 1 (NF-1) using a multispecialty examination during an EUA. There are seven criteria, of which a patient must have two, for a patient to meet a diagnosis of NF-1.[1] Our patient meets the following two: 6 or more café-au-lait macules and a plexiform neurofibroma. Common ophthalmic manifestations of NF-1 include iris Lisch nodules, optic pathway gliomas, myopia, glaucoma, choroidal nodules, retinal hamartomas, orbital-periorbital-plexiform neurofibromas.[1]

In our case, our patient presented with a retinal detachment in the right eye and peripheral non-perfusion in the left eye. Retinal involvement of NF-1 is rare; however, retinal vascular abnormalities in NF-1 have been prior described in the literature.[2,3] In our case, Fig. 1b demonstrates peripheral non-perfusion with abnormal tortuous vessels. There are four other cases of patients with NF-1, which note abnormal tortuous retinal vessels on exam or FA.[2–4] Furthermore, there are several well-documented cases of peripheral retinal ischemia in cases of NF-1.[2–6] In two of these cases, neovascular glaucoma was attributed to peripheral ischemia and patients were treated with panretinal photocoagulation (PRP); one of these patients needed an Ahmed valve for pressure control.[3,5] In another, the patient was found to have neovascularization noted on fluorescein angiography—attributed to peripheral ischemia—and was also treated with PRP. With our case, peripheral perfusion was present with no angiographic evidence of neovascularization, so the decision was made to observe. Though the mechanism of vascular occlusion in NF-1 is not yet certain, Ozerdem et al. offer that hyperproliferation of pericytes and endothelial cells may cause vascular occlusion and neovascularization.[7]

In our patient's right eye with a total funnel retinal detachment (RD), B-scan echography demonstrated a funnel retinal detachment with cystic formation. There was no evidence of calcification. It is certainly possible that the peripheral non-perfusion seen on fluorescein angiography predisposed her to retinal detachment or she had a combined hamartoma of the retina and RPE inducing traction. Other possibilities include retinal dysplasia, which can mimic intraocular tumors.[10] Of course, these are assumptions given there was no view to the fundus.

She was initially given a diagnosis of an inflammatory process given the redness, pain, and pupillary synechia by the referring ophthalmologist. The thought at the time was possible toxocariasis, unfortunately tests at the time were not conclusive. Once she presented to Bascom Palmer Eye Institute she underwent testing for *Toxocara* that was negative.

In a case series of NF-1 patients, Destro et al. describe two cases of astrocytic hamartomas leading to retinal detachments as well as two cases of congenital hypertrophy of the retina and retina pigment epithelium causing macular distortion and vitreous hemorrhage.[8] We propose that this may be one possible etiology of the detachment in the right eye of our patient.

As with most neurofibromatosis type 1 patients, the most intriguing aspect of our patient's case involves the multidisciplinary care. Were it not for the cystic mass noted with intubation during EUA, there likely would have been further delay in the of diagnosis of NF-1. Laryngeal plexiform neurofibroma, is an uncommon manifestation of NF-1. A literature review by Kasapoglu et al. records 31 cases.[10] They grow very slowly and therefore can present later in life with symptoms of hoarse voice, dysphagia, dysphonia, and stridor. Our patient's early presentation with laryngeal neurofibroma is unusual.

4. Conclusion

This case is an unusual presentation of NF-1 with neovascular glaucoma, inflammation and total retinal detachment. We recommend careful review of systems, family history, and physical exam for pediatric patients who present with retinal detachment, peripheral non-perfusion, or microvascular abnormalities of the retina. We cannot stress enough the importance of angiographic studies of the non-involved eyes of children who present with retinal detachments in one eye. Furthermore, pediatric patients who present with retinal detachment should warrant thorough work up for systemic etiology of retinal detachment, as highlighted in our case and others.[12] Additionally, NF-1 patients should have diligent monitoring with fluorescein angiographic assessing the possibility of peripheral ischemia and/or neovascularization for the prevention of retinal detachments.

Patient consent

Written consent to publish case information, such as details of the case and photographs, was obtained from the patient(s) or their legal guardian(s).

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

The authors have no financial or proprietary interest in the materials presented herein.

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