Association of Pediatric Choroidal Neovascular Membranes at the Temporal Edge of Optic Nerve and Retinochoroidal Coloboma

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• PURPOSE: To describe the characteristics of pediatric choroidal neovascular membranes (CNVs) associated with retinochoroidal and optic nerve coloboma using optical coherence tomography (OCT) and their response to treatment.

• DESIGN: Retrospective case series.

• METHODS: Retrospective review of children <16 years of age with CNV and retinochoroidal and optic nerve coloboma from 1995–2015 who underwent OCT imaging using either handheld (Bioptigen, Morrisville, NC) or tabletop OCT (Spectralis; Heidelberg, Carlsbad, CA).

• RESULTS: Eight eyes of 8 patients (3 males, 5 females) with a mean age of 4.1 ± 3.9 years (range 6 months–10 years) at diagnosis were included. Mean follow-up was 21.4 ± 12.1 months (range 7–38 months). An optic nerve coloboma was present in 2 eyes and combined optic nerve and retinochoroidal coloboma in 6 eyes. In all eyes, CNVs were located at the temporal margin of the coloboma closest to the macula. Fluorescein angiogram characteristics included staining without leakage suggesting inactivity (n = 6) and leakage (n = 2). OCT characteristics included subretinal fluid (n = 5), intraretinal fluid and cysts (n = 1), and subretinal hyperreflective material (n = 7). Two eyes received intravitreal bevacizumab (range 3–6) injections, one of which also underwent focal peripapillary laser. Both eyes showed improvement in subretinal or intraretinal fluid on OCT. Vision at presentation among those quantified ranged from 20/200 to 20/40 and at final follow-up from 20/400 to 20/30. Genetic or systemic abnormalities were seen in 6 patients.

• CONCLUSIONS: Association of pediatric CNV occurrence at the temporal margin of retinochoroidal and optic nerve colobomas closest to the fovea has not been established before and careful OCT and angiographic assessment of this region is warranted. The CNV lesions exhibit a varied degree of response to treatment. (Am J Ophthalmol 2017;174:104–112. © 2016 Elsevier Inc. All rights reserved.)

RETINOCHOROIDAL AND OPTIC NERVE COLOBOMA results from the abnormal closure of the embryonic fissure during weeks 5–7 of fetal life and may involve the iris, lens zonules, ciliary body, choroid, retina, and optic nerve.[1,2] They may be associated with serous retinal detachments, lenticonus, persistent hyaloid arteries, and optic disk pits.[2] Genetic and environmental causes have been suggested to cause an intrauterine insult with a defective embryonal fissure closure leading to coloboma of the fundus.[3] Histologically, there is no normal choroid, retinal pigment epithelium, or retina overlying a retinochoroidal coloboma, and the overlying tissue is an extension of the neurosensory retina called the intercalary membrane.[2] Colobomas can vary from small defects located in the equatorial region that do not interfere with vision to larger ones involving the disc and macula with severe impairment of vision. Vision impairment may also be caused by retinal detachment, which has been estimated to occur in ≤40% of these eyes, or choroidal neovascular membranes (CNVs), which are a rare cause of decreased vision in children with retinochoroidal colobomas.[4,5]

Optical coherence tomography (OCT) findings across a spectrum of coloboma severity have been described.[2] In cases with retinal detachment, OCT has allowed for identification of the precise site of communication between the subintercalary membrane space and subretinal space.[6] In some cases, subclinical retinal detachments have been identified along the margin of the coloboma.

OCT characteristics of CNVs associated with pediatric optic nerve and retinochoroidal colobomas and their response to treatment have, however, not been well described before and are limited to isolated case reports. In these patients, it has been suggested that discontinuities of Bruch membrane and retinal pigment epithelium (RPE) at the margin of the coloboma may allow choroidal vessels to enter the subretinal space, resulting in CNV formation at the margin. This region at the coloboma margin has not yet been studied using high-resolution OCT in children.

In this report, we describe the largest series of pediatric CNV associated with optic nerve and retinochoroidal

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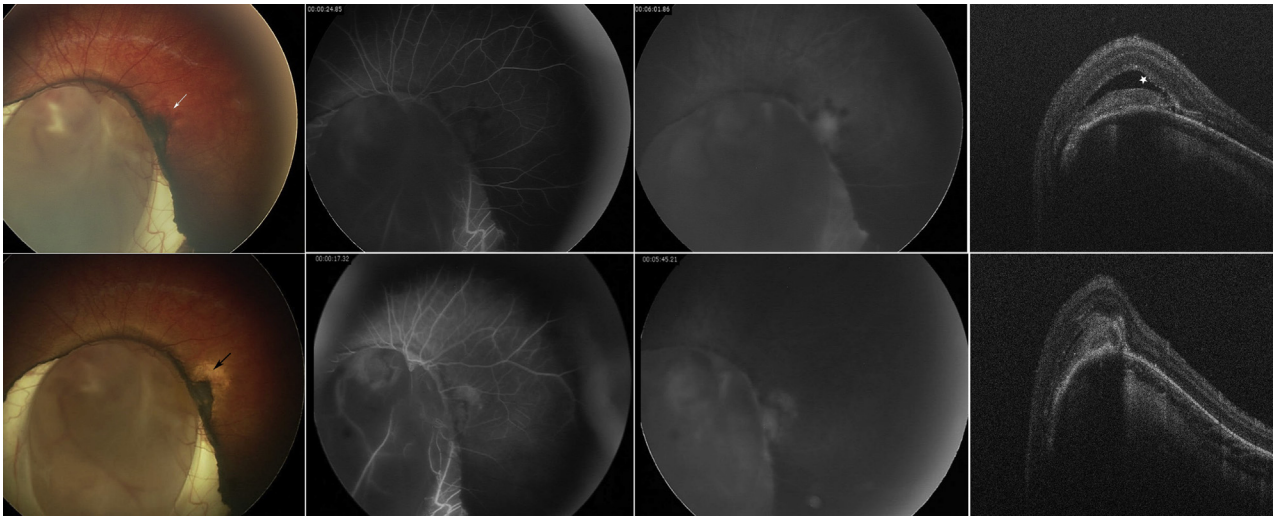

FIGURE 1. A 6-month-old boy with bilateral uveal coloboma involving the iris, retina/choroid, and optic nerve who developed a choroidal neovascular membrane at the temporal margin of the retinochoroidal coloboma with subretinal hemorrhage in the left eye (Top, first column, white arrow) with leakage on fluorescein angiography (Top, second and third column) and overlying subretinal fluid on optical coherence tomography (Top right, white star). After 2 bevacizumab injections there was resolution of the subretinal hemorrhage (Bottom, first column, black arrow), reduction of leakage on fluorescein angiography (Bottom, second and third columns), and resolution of subretinal fluid on optical coherence tomography (Bottom last column).

coloboma reviewed over a period of 20 years, and show the OCT characteristics of CNV and response to treatment.

METHODS

THIS WAS A RETROSPECTIVE ANALYSIS OF CLINICAL RE-cords of patients <16 years of age with retinochoroidal or optic nerve coloboma and associated CNV from March 1995 to March 2015 who were examined at the Pediatric Retina Service, Duke Eye Center (Durham, NC). Imaging was performed under an institutional review board–approved prospective observational study for pediatric retina imaging. Images from this database were analyzed. The study was approved by the Duke University Institutional Review Board and adhered to the tenets of the Declaration of Helsinki. The Duke Enterprise Data Unified Content Explorer (DEDUCE) database was searched for patients diagnosed with retinochoroidal coloboma or optic disc coloboma (based on receipt of *International Classification of Diseases, 9th revision* [ICD-9] codes 743.52 or 743.57) and who had an associated CNV (ICD-9 code 362.16) as identified by billing records.[7] Imaging was performed using either handheld spectral domain OCT during examination under anesthesia (Envisu; Bioptigen Inc, Morrisville, NC) or a tabletop unit in clinic when the child was old enough to co-operate (Spectralis; Heidelberg, Carlsbad, CA). Fluorescein angiography was performed using RETCAM (Clarity Medical Systems, Pleasanton, CA) during examination under anesthesia.

RESULTS

EIGHT EYES OF 8 PATIENTS (3 MALES, 5 FEMALES) WITH A mean age of 4.1 ± 3.9 years (range 6 months-10 years) and with available OCT imaging at diagnosis were included. Mean follow-up was 21.4 ± 12.1 months (range 7–38 months). An associated iris coloboma was present in 5 eyes. None of the eyes had a lens or lens zonule coloboma. One of the patients had microphthalmia.

An optic nerve coloboma was present in 2 eyes and a combined optic nerve and retinochoroidal coloboma in 6 eyes. The fovea was involved within the coloboma in 4 eyes and spared in 4 eyes. In all 8 eyes, the CNV was located at the temporal margin of the coloboma: temporal to the colobomatous nerve (n = 3) and at the temporal edge of the combined optic nerve–retinochoroidal coloboma closest to the fovea (n = 5). Figures 1–4 provide representative examples and OCT characteristics.

Fluorescein angiographic characteristics included window defects in the area of coloboma or staining but no leakage, suggesting inactivity (n = 6; Figure 3), and leakage (n = 2; Figures 1 and 2). Leakage was observed at the temporal edge of optic nerve (n = 1; Figure 2) and retinochoroidal (n = 1; Figure 1) coloboma.

Seven patients underwent imaging with handheld spectral domain OCT during examination under anesthesia, while 1 patient could be imaged using the tabletop OCT unit in the clinic. OCT characteristics included subretinal fluid (n = 5; Figures 1 and 2), intraretinal fluid and intraretinal cysts (n = 1; Figure 3), and subretinal hyperreflective material consistent with a subretinal fibrovascular