Peripheral combined hamartoma of the retina and retinal pigment epithelium with remote peripapillary choroidal neovascular membrane

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ABSTRACT

Purpose: To describe the first reported case of combined hamartoma of the retina and retinal pigment epithelium (CHRPE) associated with a remote choroidal neovascular membrane (CNVM).
Observations: A 19-month-old girl with a normal prenatal and infantile history presented with esotropia of the left eye. Fundus examination demonstrated a large, elevated, charcoal-colored lesion in the nasal equatorial retina. There was dragging of the nasal retinal vessels and a retinal fold, presumed to have resulted from nasal traction from the lesion. There was also subretinal hemorrhage in the peripapillary macula. Multimodal imaging demonstrated a peripapillary choroidal neovascular membrane (CNVM) underlying the retinal fold. There was no leakage within the tumor or secondary retinal neovascularization. Examination of the fellow eye was unremarkable. The patient was diagnosed with peripheral CHRRPE with associated peripapillary CNVM. She was treated with serial intravitreal bevacizumab to the affected eye which resulted in a reduction in leakage from the CNVM and resolution of the subretinal hemorrhage. The CHRRPE remained stable on follow-up.
Conclusions: Peripheral CHRRPE can rarely be associated with a remote CNVM.

1. Introduction

Combined hamartoma of the retina and retinal pigment epithelium (CHRPE) was first described by Gass in 1973 as a benign, congenital, slightly elevated retinal lesion easily confused on funduscopy with choroidal melanoma or retinoblastoma. Given their relative rarity and mimicry of life-threatening pathology, CHRPE lesions present a diagnostic challenge. CHRPE classically presents early in life, and as many as 75% of patients are not correctly diagnosed until referral to an academic center. When present, choroidal neovascularization has been reported to occur underneath or at the border of the CHRPE with variable exudation and hemorrhage. Herein, we report the first known association of CHRRPE with remote CNVM.

1.1. Case report

A 19-month-old girl with an unremarkable prenatal and infantile history presented to a pediatric ophthalmologist with esotropia of the left eye and was found to have a vascularized retinal mass concerning for retinoblastoma. The patient was referred to Bascom Palmer Eye Institute for evaluation by a pediatric retinal surgeon.

The patient underwent examination under anesthesia with multimodal imaging. Fundus examination demonstrated a large, elevated, charcoal-colored lesion in the nasal equatorial retina. There was dragging of the nasal retinal vessels and a retinal fold, presumed to have resulted from nasal traction from the lesion. There was also subretinal hemorrhage in the peripapillary macula. Multimodal imaging demonstrated a peripapillary choroidal neovascular membrane (CNVM) underlying the retinal fold. There was no leakage within the tumor or secondary retinal neovascularization. Examination of the fellow eye was unremarkable. The patient was diagnosed with peripheral CHRRPE with associated peripapillary CNVM. She was treated with serial intravitreal bevacizumab to the affected eye which resulted in a reduction in leakage from the CNVM and resolution of the subretinal hemorrhage. The CHRRPE remained stable on follow-up.

Conclusions: Peripheral CHRRPE can rarely be associated with a remote CNVM.

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Fig. 1. Baseline multimodal imaging of peripheral combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) with remote peripapillary choroidal neovascular membrane (CNVM).

A: Color fundus photograph montage demonstrating a charcoal grey, well-demarcated, bilobed mass (white arrows) with straightened feeder vessels (blue arrows). In the macula there is a focus of subretinal hemorrhage (red arrow) and areas of mottled retinal pigment epithelium (yellow arrow). B: OCT image through the inferior lobe of the mass (indicated by black dashed line in panel A) demonstrating a prominent epiretinal membrane (white arrow), diffuse thickening of the retina with disorganization of the retinal layers and prominent foci of hyper-reflective reduplications of the RPE (red arrows). C: OCT image through the peripapillary macula demonstrating an elevated retinal fold with intraretinal cystic spaces with a prominent underlying fibrotic lesion (red arrow). There is marked outer retinal and RPE atrophy temporal to the retinal fold (blue arrow) with normalization of the retina more temporally (white arrow). D: Widefield late-phase fluorescein angiography demonstrating corkscrew-shaped intrinsic vessels within the CHRRPE in a filigree pattern that do not leak. There is marked avascularity anterior to the larger, superior lobe of the mass, and late leakage consistent with CNVM in the peripapillary macula (red arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)
lesional tissue. There was nasal dragging of the retinal vasculature resulting in a straightened appearance of the vessels feeding the lesion. Temporal to the disc, there was elevation of the peripapillary retina with a small focus of subretinal hemorrhage with exudation and RPE changes. Anterior to the lesion, the retina was noted to be avascular, and traction between the lesion and the nasal ora serrata led to posterior dragging of the ora. The fellow eye was normal.

Optical coherence tomography (OCT) through the lesion demonstrated a prominent epiretinal membrane, thickened retina without intraretinal cystic spaces, and hyperreflective irregularities in the outer retina (Fig. 1B). OCT through the temporal peripapillary retina demonstrated an elevated retinal fold with cystic intraretinal spaces and an underlying fibrotic lesion with adjacent subretinal fluid (Fig. 1C). Temporal to the lesion there was marked outer retinal and RPE atrophy. Fluorescein angiography (FA) demonstrated straightened feeder vessels leading to the lesion with dilated, corkscrew shaped intrinsic vessels in a filigree pattern. (Fig. 1D). The peripheral retina anterior to the lesion was avascular without secondary neovascularization. There was no leakage of fluorescein within the lesion. In the peripapillary retina there was a focus of late leakage in the area of the subretinal hemorrhage consistent with a choroidal neovascular membrane (CNVM) (Fig. 2A and B). OCT angiography through the temporal peripapillary retina re-demonstrated the large subretinal lesion seen on OCT, confirmed flow within the lesion (Fig. 2C), and revealed an irregular vascular network in the same area (Fig. 3A). OCT angiography through the peripheral CHRRPE revealed a filigree pattern of the intrinsic vasculature (Fig. 3B).

The patient was diagnosed with combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) with an associated peripapillary CNVM causing subretinal hemorrhage and exudation. She was treated with intravitreal bevacizumab and sub-Tenon’s injection of triamcinolone in the affected eye.

On follow-up examination under anesthesia six weeks later, there was interval improvement in the subretinal hemorrhage and exudation. She was again treated with intravitreal bevacizumab. At follow-up evaluation 6 weeks later, the subretinal hemorrhage and subretinal fluid had resolved. The CHRRPE lesion itself did not change in lateral size, thickness, or appearance over 3 months of follow-up. The patient continues daily patching of the right eye for amblyopia management.

2. Discussion

Combined hamartoma of the retina and retinal pigment epithelium (CHRRPE) is a rare but well-described congenital retinal lesion frequently confused with retinoblastoma or choroidal melanoma that can be present in the macula, peripapillary retina, or periphery. Histopathological analysis of eyes with CHRRPE enucleated out of concern for malignancy demonstrate a mass consisting of disorganized, thickened retina and dysplastic glial tissue with vasculature and infiltration by sheets of RPE. The underlying RPE demonstrates reduplication rather than a monolayer of cells.

Funduscopic examination findings of our patient’s lesion and features present on multimodal imaging were consistent with the diagnosis of CHRRPE. The charcoal grey coloration is classic for CHRRPE and dragged feeder vessels are present in a majority of cases. The elongated, bilobed configuration of the patient’s lesion has not been previously reported in the literature but is not suggestive of alternative pathology. The intrinsic vessels within the lesion, highlighted on fluorescein angiography, were tortuous and corkscrewed from contraction of the inner surface of the tumor and organized in a filigree pattern. Typical OCT findings including retinal thickening, prominent epiretinal membrane, and reduplication of the retinal pigment epithelium were present.

Choroidal neovascularization is a known sequela of CHRRPE and has been described in macular and extramacular lesions. In all previously reported cases, CNVM secondary to CHRRPE occurs at the border of the lesion.
To our knowledge, this is the first reported case of remote CNVM associated with CHRRPE. Owing to the elongated, circumferential orientation of the patient’s lesion, tractional forces were exerted radially over a large area of retina leading to dragging of nasal retinal vessels, a dragged disc appearance, and a shallow tractional retinal detachment. The nasal traction in the macula was disrupted by the optic disc, which served as a stationary bulwark and redistributed the radial forces into vertical projection of the temporal peripapillary retina resulting in an impressive retinal fold. We believe that the traction caused by the large nasal CHRRPE which caused the peripapillary retinal fold is likely responsible for the development of the secondary CNVM.

Through clinical-pathological correlation, Sarks demonstrated that primary and secondary peripapillary CNVMs reach the sub-RPE space through one of two pathways: via a defect in Bruchs’ membrane or by growing around the peripapillary termination of Bruchs’ membrane. The OCT and OCTa images (Figs. 1C and 2C) indicate that the fibrovascular CNVM is located in the subretinal space adjacent the optic nerve. On the basis of multi-modal angiography including OCTa and FA, it was not possible to determine the exact ingress of the CNVM stalk into the subretinal space to conclude which pattern of peripapillary CNVM development had occurred. The outer retinal and RPE atrophy temporal to the area of subretinal fluid suggested chronicity.

There is one reported case of an atypical stalk of persistent fetal vasculature (PFV) in the nasal periphery leading to tractional retinal changes and associated with a remote CNVM in the temporal peripapillary retina. The patient with PFV did not have a dragged disc appearance or a retinal fold; however the similarities are suggestive that it is possible for retinal traction to be sufficient to lead to remote CNVM formation. We were unable to identify any other examples of peripheral traction associated with remote CNVM.

3. Conclusions

While secondary CNVM associated with CHRRPE has been previously reported, we believe that the present case is the first reported case of peripheral CHRRPE associated with a remote CNVM. This finding has implications regarding the surveillance of peripheral CHRRPE lesions, which are typically thought of as benign, as well as other conditions associated with radial retinal traction and dragged disc configuration.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information or photographs that could lead to the identification of the patient.

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Authorship

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

Disclosures

None
Intellectual property

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Research ethics

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of all relevant bodies and that such approvals are acknowledged within the manuscript.

Declaration of competing interest

Dr Audina M. Berrocal reports the following disclosures: Administrative board member for Allergan PLC and Bayer; Consultant for Alcon, Dorc (Dutch Ophthalmic Research Center International BV), Visunex, and Phoenix.

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