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Cerebral vasculitis presenting as acute posterior multifocal placoid pigment epitheliopathy in a 16-year-old male

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ABSTRACT

Purpose: To report on a case of the successful treatment of Acute Posterior Multifocal Placoid Pigment Epitheliopathy (APMPPE) in a pediatric patient with a prior diagnosis of cerebral vasculitis.

Observations: A 16-year-old male with a prior diagnosis of cerebral vasculitis presented without ocular complaints. Visual acuity was 20/20, and color vision remained normal. Fundus examination revealed yellowish-white placoid lesions and retinal pigmented epithelial changes involving the posterior pole. A work-up including a rapid plasma reagin test, complete cell blood count, comprehensive metabolic panel, and urinalysis was within normal limits. A head computed tomography angiography without contrast and a brain magnetic resonance imaging scan were compatible with acute and past episodes of ischemia. Ancillary testing was compatible with an assessment APMPPE. Immunosuppressive and monoclonal antibody therapy resulted in the improvement and remission without residual neurologic deficits and with a BCVA of 20/20.

Conclusionand Importance: This case suggests that a diagnosis of cerebral vasculitis should prompt physicians to consider an ophthalmic evaluation that includes a dilated fundus exam, regardless of the presence or absence of ocular symptoms. Ophthalmic findings may affect the diagnostic processes, particularly concerning infectious and non-infectious etiologies, or potentially neoplastic diseases.

1. Introduction

Acute posterior multifocal placoid pigment epitheliopathy (APMPPE) is a rare inflammatory chorioretinopathy; it is characterized by the rapid onset of bilateral blurred vision with associated scotomas and occurs mainly in young adults.[1–3] Within days of their onset, fundus examination reveals multifocal, yellow-white placoid lesions, mostly located in the retinal pigment epithelium (RPE), confirming the diagnosis of the disease[1,2] These lesions are typically self-limiting, fading gradually as visual acuity is restored, often within weeks, yet some macular changes and symptoms may persist after resolution.[3] Some authors have proposed that APMPPE may be accompanied by a preceding infectious or flu-like illness, while others suggest an autoimmune origin; however, the pathogenesis and etiology of the disease remain unclear.[3]

Currently, there are no established guidelines for the treatment of this rare disease; however, systemic corticosteroids and immunosuppressive therapy, as well as a timely diagnosis and early intervention of APMPPE, have been found beneficial, particularly in cases with neurological symptoms.[3] Furthermore, neurological complications, such as headaches, sensorineural hearing loss, cerebrospinal fluid pleocytosis, and systemic manifestations, including strokes and sudden death, all the previous being associated with APMPPE, are uncommon but have been described in the adult population.[3] Although APMPPE has been described extensively in adults since 1968, the literature on the pediatric population remains minimal. We report on a case of a 16-year-old male without ocular symptoms and previously diagnosed with cerebral vasculitis who was successfully treated for both his APMPPE and his vasculitis.

2. Case report

A 16-year-old male with no ocular complaints was referred for a routine ophthalmic evaluation before starting treatment with

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hydroxychloroquine. The patient had a past medical history of hypertension, anxiety, and multiple strokes. He had been diagnosed with cerebral vasculitis associated with two bilateral cerebral infarcts two weeks before the consultation. The patient reported having had headaches for several days before the syncopal episode. He had begun treatment with methylprednisolone (1 g/day for 5 days) and aspirin. His family history was remarkable for diabetes, cancer, hypertension, and heart disease. His review of systems, as well as past social history, was otherwise unremarkable.

Upon a comprehensive ophthalmic evaluation, the best-corrected visual acuity (BCVA) was 20/20 in both eyes (OU). The cycloplegic refraction had a spherical power of +1.00 sph OU. Intraocular pressure was 14 mm Hg in the right eye (OD) and 17 mm Hg in the left eye (OS). The pupils were round and reactive to light, and there was no afferent pupillary defect. Color vision, as assessed by the Ishihara color plate test, was 14/14 OU. A confrontational visual field test was unremarkable OU. A sensory-motor test revealed no strabismus or limitations of ductions and versions. A slit-lamp examination was unremarkable, with no evidence of keratic precipitates, signs of inflammation in the anterior chamber, or vitreous cells OU. An examination of the right fundus revealed confluent yellowish-white placoid lesions along the superotemporal arcade and a smaller placoid lesion superior to the fovea (Fig. 1A and B). The left fundus examination showed atrophic chorioretinal lesions, RPE changes inferior to the fovea, and very faint localized periarteriolar sheathing within the associated arteriole (Fig. 1C and D). No signs of optic disc edema or atrophy, retinal hemorrhage, exudates, or detachment were observed bilaterally. A spectral-domain optical coherence tomography examination revealed RPE atrophy in the

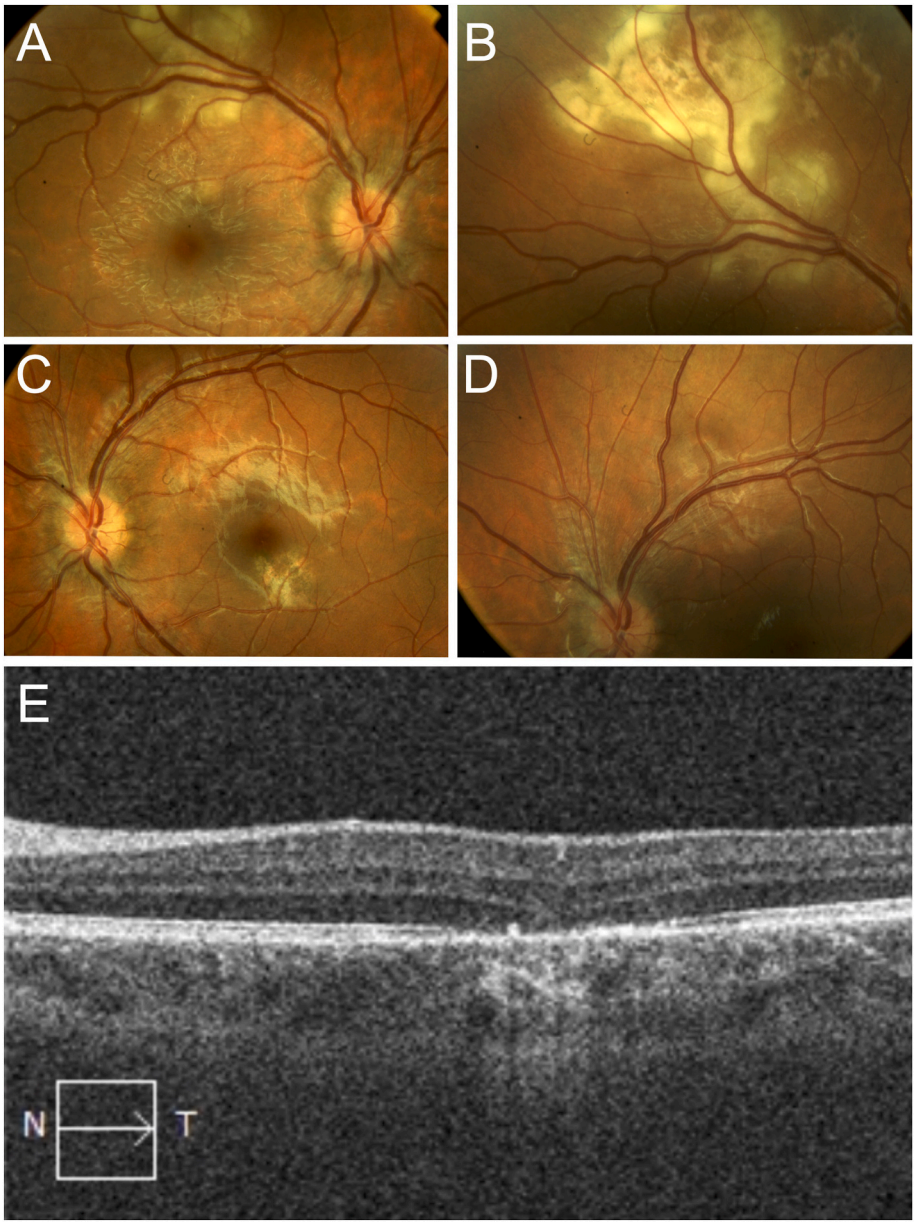

Fig. 1. Color fundus photographs of both eyes and optical coherence tomography of the left eye at presentation. Color fundus photographs of the right eye (A and B) reveal confluent yellowish-white placoid lesions along the superotemporal arcade and a smaller placoid lesion superior to the fovea. Color fundus photographs of the left eye (C and D) reveal an atrophic chorioretinal lesion with associated retinal pigment epithelium changes inferior to the fovea, along with very faint localized periarteriolar sheathing within the associated arteriole, as well as a single placoid lesion along the superotemporal arcade. Spectral-domain optical coherence tomography of the left eye (E) reveals retinal pigment epithelium atrophy in the juxtafoveal region and disruption of the photoreceptor inner segment/outer segment layer. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

juxtafoveal region and disruption of the photoreceptor inner segment/outer segment layer OS (Fig. 1E). There was no evidence of intraretinal cystoid macular edema or subretinal fluid OU. The patient's mother denied consent for fluorescein angiography (FA) on the day of the initial evaluation, as the patient felt unwell.

A work-up including a QuantiFERON-TB gold, rapid plasma reagin test, comprehensive metabolic panel, and urinalysis was within normal limits. A complete cell blood count revealed mild leukocytosis. Further studies, including a head computed tomography angiography without contrast obtained a month before the initial ophthalmic evaluation, revealed an area of hypoattenuation consistent with subacute to chronic ischemia in the territory of the right middle cerebral artery. A brain magnetic resonance imaging scan, obtained less than a week before the initial ophthalmic evaluation, was remarkable for restricted diffusion in the left parietal superior convexity and multiple areas of restricted diffusion in the supratentorial brain compatible with acute ischemia and acute lacunar strokes, respectively (Fig. 2)(). A duplex carotid artery scan showed no clinically significant carotid stenosis, and the venous duplex scan obtained was unremarkable, with no evidence of venous thrombosis or clinically significant retrograde flow.

Based on the results, an assessment of APMPPE was made. A course of methylprednisolone was completed, and the patient was started on intravenous rituximab (375 mg/m^2, weekly for four weeks) and prednisone (60 mg oral, daily). At the one-week follow-up visit, his visual acuity remained 20/20 OU. A right fundus examination revealed multiple chorioretinal lesions with mild residual activity and some cicatrized lesions, while the left fundus examination showed RPE changes and scarring in the subfoveal region (Fig. 3A–C). An FA showed early blockage and late staining of lesions in the superotemporal and extrafoveal regions OD and juxtafoveal transmission defects consistent with RPE changes OS (Fig. 3D–F).

At the one-month follow-up visit, his BCVA was 20/20 OU. A right fundus examination revealed multiple chorioretinal lesions along the superior arcade and in the inferior macula. The patient continued prednisolone (60 mg oral, daily) for approximately three months and then was gradually tapered.

Five months following his initial presentation, the patient's visual acuity was 20/20, and the slit-lamp examination remained unchanged OU. A fundus examination revealed a single active lesion superior to the fovea OD and well-demarcated chorioretinal scarring with pigmentation OS. The subacute lesions alongside the fovea that were present OS at his first appointment remained quiescent. An FA showed early blockage with late staining of these lesions OD and RPE changes OS. The patient remained on prednisolone (40 mg oral, daily) and started on mycophenolate mofetil (1000 mg oral, twice daily).

At his follow-up four years after the initial evaluation, the patient remained in remission without residual neurologic deficits and with a BCVA of 20/20.

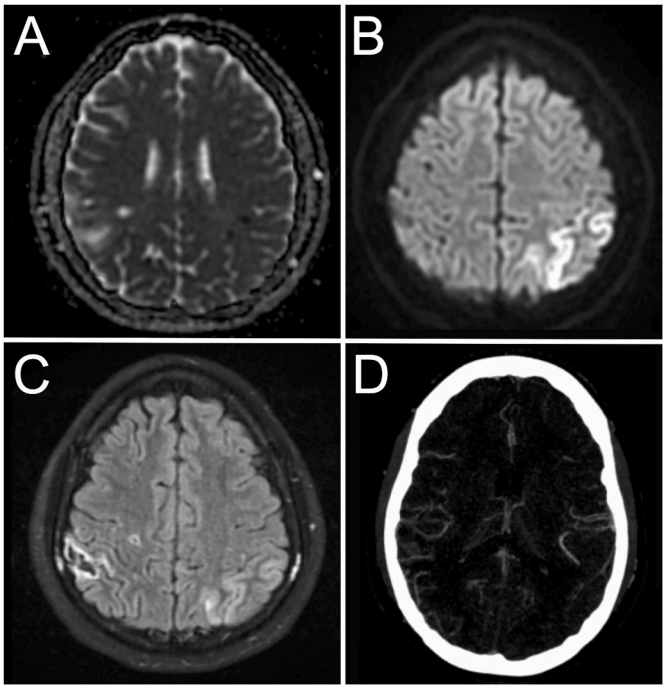

Fig. 2. Axial diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) images (A and B) demonstrate numerous scattered areas of restricted diffusion in the left parietal and high right frontal lobes indicating acute ischemia. The right parietal lobe (C) demonstrates decreased DWI signal with corresponding increased ADC signal intensity consistent with an older chronic infarct. Axial computed tomography angiography head image (D) shows asymmetry involving the M3 branches of the bilateral middle cerebral artery with severe stenosis of the right branch, the left being of normal caliber.

3. Discussion

To our knowledge, this is the third pediatric case of APMPPE associated with cerebral vasculitis in reported literature. The disease has been reported primarily in adults of twenty to forty years of age.[3] Patients' most common symptoms include blurry vision, photopsia, and metamorphopsia; however, our patient did not have any ocular complaints, thereby heightening the complexity of the diagnosis.[1–5] It is most likely that the patient was asymptomatic due to the extrafoveal location of the lesions. Also not present in this patient were prodromal headaches and flu-like manifestations, both of which have been previously associated with APMPEE.[4,5] In this case, the patient inadvertently presented for an ophthalmological evaluation before starting treatment with hydroxychloroquine. His neurologist initially considered hydroxychloroquine as it is a low-morbidity treatment option for cerebral vasculitis and its use is thought to result in fewer relapses, reduced need for glucocorticoids as well as improved symptoms.[6]

The diagnosis of APMPPE in this patient was supported by a funduscopic examination that revealed multiple cream-colored lesions at the RPE and choroid.[1–5] Fluorescein angiography and indocyanine green angiography also characterize the extent of APMPPE.[1–5] Furthermore, the course of APMPPE is most commonly self-limiting, and the fundus lesions generally fade within two weeks.[1,3] Although this condition has a positive prognosis, optimal management is still uncertain due to its rarity and limited data availability. When considering the treatment of APMPPE, the crucial direction for said treatment may be determined by the presence or absence of underlying life-threatening associations, such as neurologic symptoms. Some author have suggested that systemic steroids may shorten the course of uncomplicated disease and limit outer retinal loss; however, this treatment must be guided by the cerebral vasculitis.

The identification and characterization of APMPPE are crucial to enhance and facilitate the study of this rare condition. Prompt ophthalmic workup and surveillance may allow patients with cerebral vasculitis to identify the initial stages of APMPPE and receive expedited treatment, monitoring, and support. The diagnosis of cerebral vasculitis should lead physicians to consider that the patient may require a prompt ophthalmologic workup. Ocular findings could impact the diagnostic process, specifically concerning infectious and non-infectious etiologies or potentially neoplastic diseases. A dilated fundus examination is particularly important regardless of the presence or absence of ocular symptoms. Due to the ocular and life-threatening implications associated with APMPPE, such as cerebral vasculitis described in this patient, it is crucial to prioritize timely attention and intervention. Implementing effective management strategies, including immunosuppressive and monoclonal antibody therapies, can significantly enhance visual outcomes and potentially safeguard a patient's life.[3] Is important to emphasize that patients with cerebral vasculitis should receive appropriate treatment, regardless of the self-limiting nature of APMPPE.

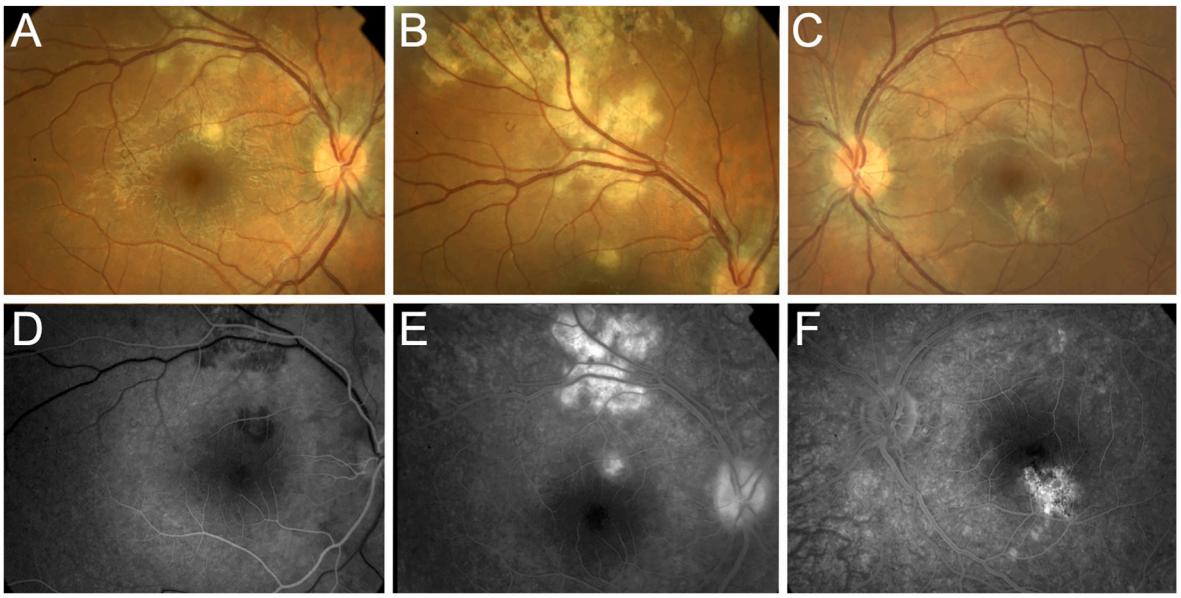

Fig. 3. Color fundus photographs and fluorescein angiography of both eyes at the one-week follow-up visit. Color fundus photographs of the right eye (A and B) reveal multiple white placoid lesions along the superotemporal arcade and a smaller placoid lesion superior to the fovea, while a similar photograph of the left eye (C) reveals an atrophic chorioretinal lesion inferior to the fovea. A fluorescein angiogram of the right eye reveals early-phase blockage (D) and late-phase leakage (E) in the area corresponding to the lesion, both of which are consistent with APMPPE. A late-phase fluorescein angiogram of the left eye (F) reveals a transit defect consistent with an atrophic lesion. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

Additional studies should be conducted to promote the development of improved algorithms for treating APMPPE, as well as its associated life-threatening conditions such as cerebral vasculitis, and preventing significant visual impairment. While it is important to note that findings from a single case are not generalizable, the aim of this study is to stimulate further research of this rare disease.

4. Conclusion

This case highlights the significance of promptly addressing a diagnosis of cerebral vasculitis as this condition can lead to severe ocular complications and even life-threatening outcomes. A diagnosis of cerebral vasculitis should prompt physicians to consider an ophthalmic evaluation that includes a dilated fundus exam, regardless of the presence or absence of ocular symptoms. Ocular findings may influence the diagnostic process, specifically concerning infectious and non-infectious etiologies, or potentially neoplastic diseases.

Patient consent

The patient provided written informed consent to publish this case report. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

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

CRediT authorship contribution statement

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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