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Posterior placoid-like maculopathy and macular hole associated with vitamin A deficiency

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ABSTRACT

Purpose: To report a case of bilateral posterior placoid-like maculopathy and a macular hole associated with vitamin A deficiency.

Observations: A 72-year-old male presented with nyctalopia and progressive vision loss in both eyes. Examination and multimodal imaging were consistent with posterior placoid-like maculopathy bilaterally and a macular hole in the right eye. A workup for infectious, inflammatory, and paraneoplastic etiologies revealed a severely low serum vitamin A level. Two months after initiation of vitamin A repletion, there was improvement in best-corrected Snellen visual acuity as well as macular hole closure. A diagnosis of posterior placoid-like maculopathy in the setting of vitamin A deficiency (VAD) was made.

Conclusions and importance: VAD should be considered when symmetric posterior pole placoid-like lesions are observed and other, more common etiologies have been ruled out.

1. Introduction

Posterior placoid maculopathy is a rare clinical finding characterized by large confluent areas of retinal whitening or yellow-white lesions predominantly affecting the outer retinal layers in the posterior pole.[1] These lesions have been described to be hyperautofluorescent, sometimes with speckled punctate hypoautofluorescence, and have characteristic early hypofluorescence with late "fill-in" or staining on fluorescein angiography.[2] Optical coherence tomography (OCT) shows thickening of the neurosensory retina with disruption of the ellipsoid zone, thickening and granular hyperreflectivity of the retinal pigment epithelium (RPE), and nodular elevations.[3]

When discrete placoid lesions are observed in the macula and posterior pole in a patient with visual impairment, infectious causes, particularly syphilitic retinitis, remain high on the differential diagnosis.[4,5] Other conditions to consider include inflammatory, autoimmune, toxic/metabolic, and paraneoplastic etiologies. We report a unique case of a patient with a history of hepatic malignancy in remission who presented with progressive nyctalopia and decreased vision with findings of bilateral posterior placoid-like maculopathy and a macular hole in the right eye due to underlying VAD, with marked improvement once supplementation of vitamin A was initiated.

2. Case report

A 72-year-old Caucasian male with hepatocellular carcinoma (HCC) in remission, pseudophakia of both eyes (OU), and strabismic amblyopia OU was referred for a macular hole in the right eye (OD) and age-related macular degeneration OU. He reported experiencing worsening vision over the year prior to presentation, decreased night vision, and severe dry eyes. On examination, his best corrected Snellen visual acuity (BCVA) was 20/60 OD and 20/50 in the left eye (OS). Both eyes had significant punctate epithelial erosions. On fundus examination, both eyes revealed well-circumscribed, stippled hypopigmented placoid-like lesions in the posterior pole. There was a stage 2 full-thickness macular hole with trace cystoid macular edema (CME) OD and a small focal RPE detachment OS seen on OCT, as well as diffuse outer photoreceptor layer attenuation, external limiting membrane disruption, ellipsoid zone loss, and RPE mottling and thickening. Peripherally, there were numerous scattered yellow-white punctate drusenoid deposits OU. OCT, ultrawide-field fundus photos, and autofluorescence corroborated fundus findings, and fluorescein angiogram (FA) showed disc leakage with stippled hyperfluorescence throughout the posterior pole with distinct margins (Figs. 1–3). Indocyanine green angiography was unremarkable.

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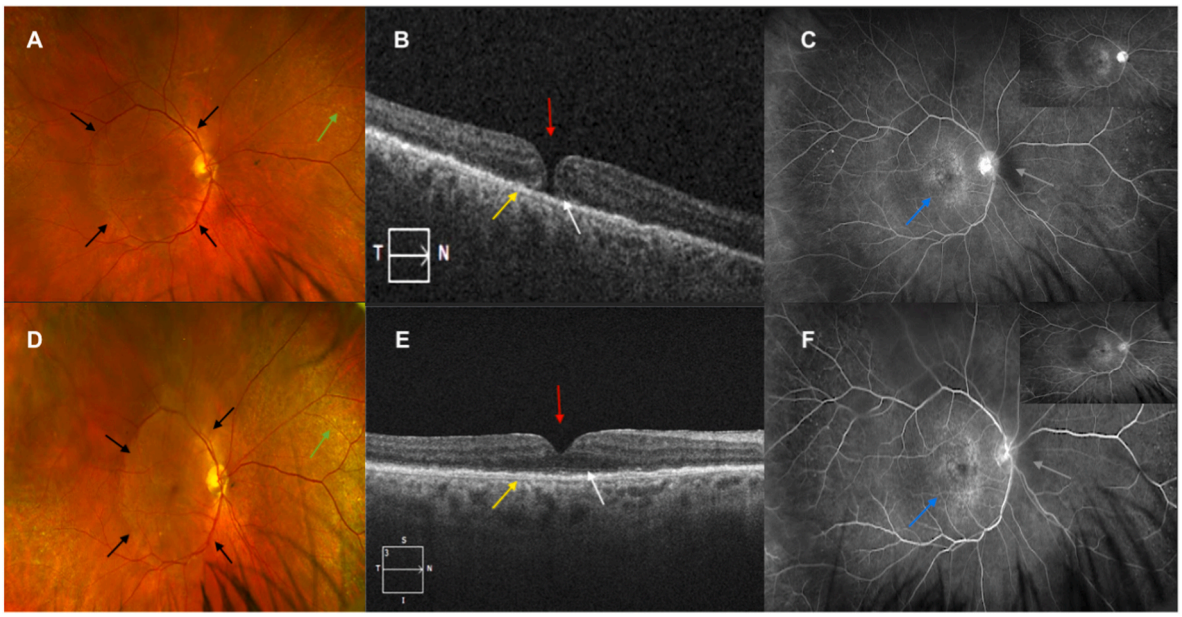

Fig. 1. Fundus photo, OCT macula, and FA of the right eye at presentation (A–C) compared to two months post-vitamin A supplementation (D–F). Fundus photo demonstrates well-circumscribed, placoid-like lesion (A, black arrows) in posterior pole as well as peripheral yellow-white lesions (A, green arrow) with improvement after vitamin A supplementation (D, corresponding line & arrow). OCT macula shows a stage 2 full-thickness macular hole with trace CME (B, red arrow), as well as diffuse outer layer attenuation (B, white arrow), ELM disruption, ellipsoid zone loss, and RPE mottling and thickening (B, yellow arrow). After vitamin A supplementation, the OCT findings significantly improved, and the macular hole resolved (E, corresponding arrows). FA in the early phase, displayed in the upper right hand corner, and late phase, in the central picture, shows disc leakage (C, gray arrow) with stippled hyperfluorescence and staining throughout posterior pole (C, navy arrow), with less distinct margins and less disc leakage **after** supplementation was initiated (F, corresponding arrows). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

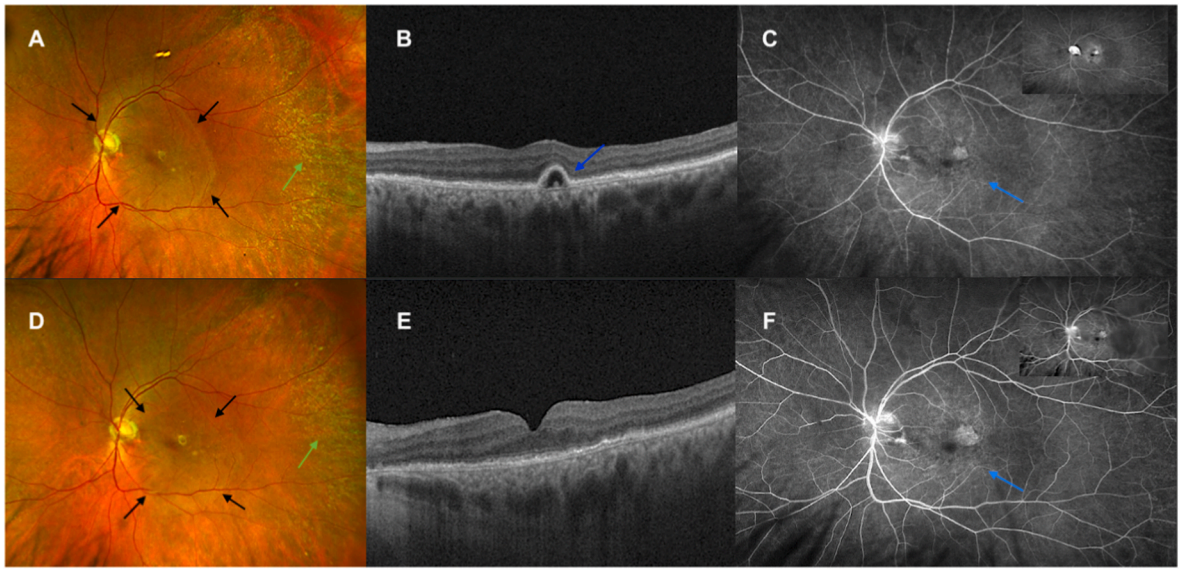

Fig. 2. Fundus photo, OCT macula, and FA of the left eye at presentation (A–C) compared to two months post-vitamin A supplementation (D–F) show similar findings and improvements as described in Fig. 1. OCT macula shows a serous pigment epithelium detachment (B, blue arrow) that improved with supplementation (E). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

The patient had felt unwell for several months and had a new rash of the extremities for three weeks prior to initial presentation. He denied a history of sexually transmitted diseases, autoimmune disorders, or tuberculosis. He was referred to the emergency department for laboratory evaluation to rule out syphilis, although he left against medical advice prior to completing the requested work-up. The initial labs drawn were unremarkable and included: complete blood count, basic metabolic panel, Lyme serologies, and fluorescent treponemal antibody test absorption test/rapid plasma reagin; transaminases were at baseline.

Two months later, the patient was evaluated by a uveitis specialist as his vision and symptoms progressively worsened with a BCVA of 20/125 OD and 20/60 OS. With a stable examination, he was advised to complete the work-up and follow-up with his medical oncologist to ensure stable remission of his HCC. Fortunately, there was no recurrence of hepatic malignancy, although he had ascites that required an abdominal paracentesis.

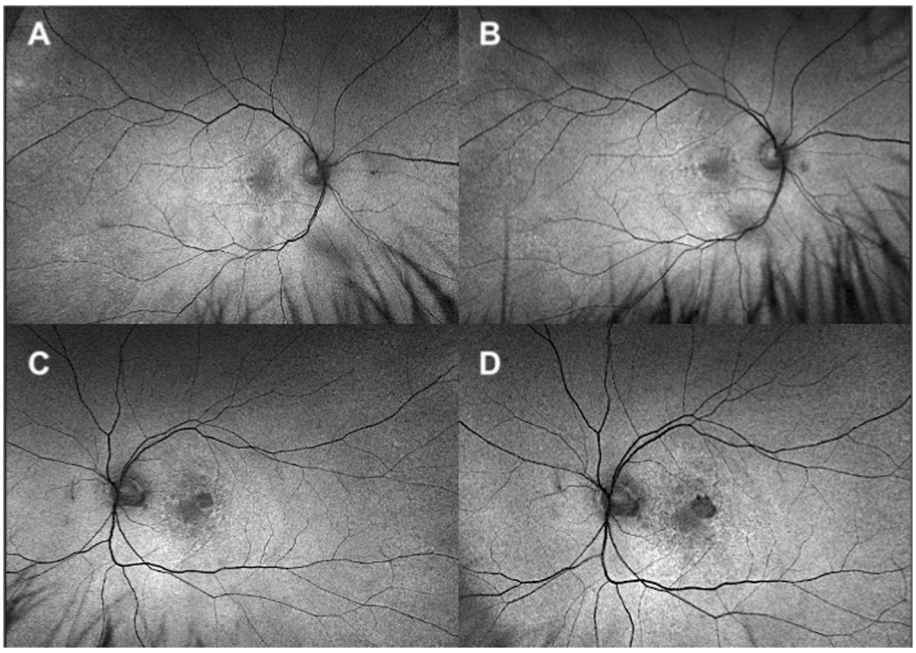

Fig. 3. Fundus autofluorescence photography of the right eye (A) and left eye (C) at presentation compared to two months post-vitamin A supplementation (B, D) shows improvement in hyperautoflourescence in the placoid-like lesion.

Table 1
Timeline of patient's BCVA, color vision, exam findings, and vitamin A levels/supplementation. Vitamin A was dosed at 50,000 units by intramuscular injection once per week.

Date	BCVA OD	BCVA OS	Color vision (Ishihara)	Serum vit A level (μg/dL)	Notes
8/11/21	20/50	20/60	1/15		Referred to emergency department, but left against medical advice prior to complete work-up
12/7/21	20/200	20/100		6.2	Started vitamin A supplementation
1/28/22				11.9	
2/2/22	20/50	20/40			Macular hole OD resolved
3/23/22				22.3	
5/18/22	20/30	20/30	5/15 OU		Continued symptomatic improvement

Legend: BCVA = Best corrected visual acuity; OD = right eye; OS = left eye; OU = both eyes; ERG = electroretinogram; Serum vitamin A reference range: 22.0–69.5 μg/dL.

Further testing revealed negative human leukocyte antigen-A29, alpha fetoprotein tumor marker, and interferon gamma release assay. The patient declined further testing with electroretinograms and cancer-associated retinopathy (CAR) antibodies at the time. Unexpectedly, he was found to have a severely low serum vitamin A level (6.2 μg/dL, reference range 22.0–69.5 μg/dL). His BCVA continued to decline to 20/200 OD and 20/100 OS.

The patient began to receive vitamin A supplementation (50,000 international units, intramuscular, weekly), and two weeks later, he reported experiencing a subjective improvement in nyctalopia, dry eyes, and visual acuity. Six weeks later, repeat testing of the serum vitamin A level indicated an improvement to 11.9 μg/dL, and his findings dramatically improved with BCVA of 20/50 OD and 20/40 OS. Remarkably, the macular hole in the right eye had closed, and there was decreased disc leakage on FA, as well as less distinct placoid-like macular lesions OU. Three months later, with vitamin A level at 22.3 μg/dL, there was continued improvement to BCVA (20/30 OU), color vision, and a decrease in peripheral scattered yellow-white punctate drusenoid deposits. Table 1 highlights the patient course.

The patient will continue with vitamin A supplementation and retinal monitoring.

3. Discussion

Posterior placoid maculopathy has been documented in association with many diseases including ocular syphilis, COVID-19, vasculitis, serpiginous choroiditis, birdshot retinochoroidopathy, and acute posterior multifocal placoid pigment epitheliopathy.[4,6,7] To our knowledge, this is the first documented case of posterior placoid-like maculopathy with macular hole secondary to VAD.

Vitamin A, a fat-soluble vitamin, may become deficient from insufficient intake or impaired absorption. Malnutrition is the most common cause of VAD worldwide. Conditions causing gastrointestinal and hepatobiliary malabsorption, including cirrhosis, inflammatory bowel disease, Celiac's disease, and bariatric surgery, are common causes of VAD in the developed world.[8] Initial signs of VAD include nyctalopia with visual field defects while other associated symptoms include conjunctival xerosis, Bitot's spots, and keratomalacia.[9,10]

Retinal findings in VAD are typically described as multiple round yellow-white lesions in the macula and midperiphery captured on OCT as drusenoid subretinal deposits.[11–13] These yellow deposits are theorized to represent accumulating shed photoreceptors from a disrupted retinoid cycle layering between the RPE and ellipsoid band, causing blocked hypo-autofluorescence and appearing as hyperreflective deposits on OCT.[12,14] In reports describing VAD retinopathy, treatment with vitamin A supplementation usually improved retinal function,

resolved symptoms, and cleared the yellow deposits.[15,16] In our case, the patient experienced profound subjective improvements in vision within weeks of initiating vitamin A replacement therapy, with notable anatomic improvements as well.

Findings of bilateral posterior placoid maculopathy in the retina often points to an underlying systemic etiology, including infectious, inflammatory, toxic/metabolic, or paraneoplastic. Syphilis is the most common cause and required immediate rule-out, but tuberculosis and fungal infection may also cause similar findings. Posterior placoid maculopathy is also associated with inflammation in the eye, as CME is the most frequent complication in uveitis causing visual impairment.[17] In paraneoplastic syndromes, autoimmune retinopathy (AIR) and CAR are rare, poorly understood retinal diseases that can also present as bilateral, progressive visual deterioration.[18] The patient's history of HCC drew greater concern for other malignancy. Although no autoimmune or paraneoplastic markers returned positive, AIR and CAR should remain on the differential diagnosis in cases with similar presentations. While our patient refused further workup, he agreed to do so in the event that visual and retinal decline continued even after Vitamin A levels normalized.

Macular holes and CME, however, have not been previously described as an association with VAD. Since VAD has been linked to atrophic changes in the RPE,[3,19] it is possible that a similar process could have caused a full-thickness macular hole to form over time. Although spontaneous closure of macular holes is common, given the speed of closure after starting supplementation in our patient without other ocular intervention, we strongly believe that treatment of the underlying hypovitaminosis likely resulted in resolution of the macular hole.

Our report is limited by the patient's hepatologic comorbidities which may impact his metabolism of vitamin A, although he was deemed stable and in remission. It is not possible to prove a causative relationship between therapy and treatment effect, but the temporal association is strongly supportive.

4. Conclusions

Posterior placoid maculopathy is classically associated with infectious and inflammatory etiologies, particular ocular syphilis. We report a unique case of a patient with hepatobiliary disease with severely low vitamin A levels that presented with bilateral posterior placoid-like lesions and a macular hole of the right eye that resolved with vitamin A supplementation.

Patient consent

The patient consented to publication of the case in writing.

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Authorship

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

Declaration of competing interest

The following authors have no financial disclosures: EWL, RD, BKD, SAS.

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