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Case report

Orbital and chorioretinal manifestations of Erdheim-Chester disease treated with vemurafenib

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ABSTRACT

Purpose: We report a patient with severe multi-organ dysfunction of unknown origin who presented with bilateral orbital and chorioretinal manifestations that led to the diagnosis of Erdheim-Chester Disease (ECD).
Observations: ECD is a rare, histiocytic, proliferative disorder characterized by multi-systemic organ involvement that has historically lacked effective therapy. Our patient underwent genetic testing that was positive for the *BRAF* V600E mutation; therefore, the patient was treated with vemurafenib.
Conclusions and importance: This case demonstrates the rare orbital and intraocular manifestations of ECD and the unfortunate impact of a delayed diagnosis, the importance of early gene therapy testing for management decisions, and the utilization of targeted directed therapy to improve visual outcomes and quality of life.

1. Introduction

We report an unusual bilateral chorioretinal and orbital presentation of Erdheim-Chester disease (ECD), which is a rare, non-Langerhans' cell histiocytosis with various clinical manifestations that can involve many organs, including the skeleton, pericardium, lungs, endocrine, and central nervous systems. The pathogenesis of the disease is part of a dysregulated mechanism in which mutations in the mitogen-activated protein kinase (MAPK) pathway result in uncontrolled cell survival and proliferation of histiocytes. This produces a xanthomatous infiltration into various organs, resulting in multi-systemic involvement leading to end-organ dysfunction.[1]

2. Case report

Our patient is a 52-year-old Vietnamese woman with history of hypothyroidism as well as multiple medical problems that lacked a unifying diagnosis. She initially presented at age 33 with anemia and leukocytosis and was diagnosed with JAK-2 negative, calreticulin positive, essential thrombocythemia (ET). She subsequently underwent numerous surgical procedures for pancreatitis, hepatomegaly, multiple portal, splenic, and mesenteric vein thromboses, recurrent chronic pleural and pericardial effusions, constrictive cardiomyopathy, and severe restrictive lung disease. Her work up was negative for infectious, rheumatologic, or malignant etiology and numerous biopsies showed multi-organ fibrosis. She suffered from severe chronic dyspnea and abdominal bloating. Her chronic and debilitating condition with oxygen requirements resulted in multiple hospital admissions for medical complications. She was noted to have depression with intermittent suicidal ideation.

She presented to the ophthalmology clinic at age 51 with proptosis of the left eye. Ocular exam was significant for visual acuity 20/30 OD, 20/40 OS, normal intraocular pressure, no afferent pupillary defect, full extraocular movements with left upper eyelid retraction, resistance to retropulsion, and 3.5 mm of proptosis on Hertel. Dilated fundus exam revealed normal optic nerves and bilateral inferior placoid orange subretinal lesions with subretinal fluid (Fig. 1A–B). Humphrey visual field testing showed an enlarged blind spot with a superior arcuate defect (Fig. 2A). Spectral-domain optical coherence tomography (SD-OCT) of her macula demonstrated a sub-retinal pigment epithelium (RPE) hypolucent mass associated with foveal subretinal fluid in the right eye and a similar sub-RPE hypolucent mass with choroidal elevation without subretinal fluid in the left eye (Fig. 3A–B). Fluorescein angiography demonstrated associated hyperfluorescence of the placoid lesions with late staining consistent with non-exudative, multifocal choroidal infiltrates in both eyes (Fig. 4A–E). Magnetic resonance

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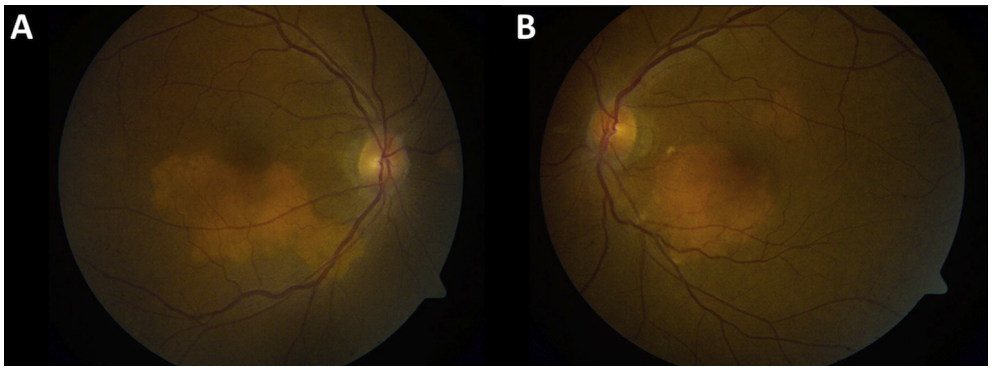

Fig. 1. (A–B): Title: Fundus photos on presentation. Caption: A, Color fundus photo of the right eye on presentation demonstrating a yellow placoid subretinal lesion along the inferior arcade extending towards the fovea and a smaller yellow lesion nasal to the optic disc. B, The left eye demonstrates similar yellow subretinal lesion along the inferior arcade with extension into the fovea and a smaller subretinal yellow lesion superotemporal to fovea. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

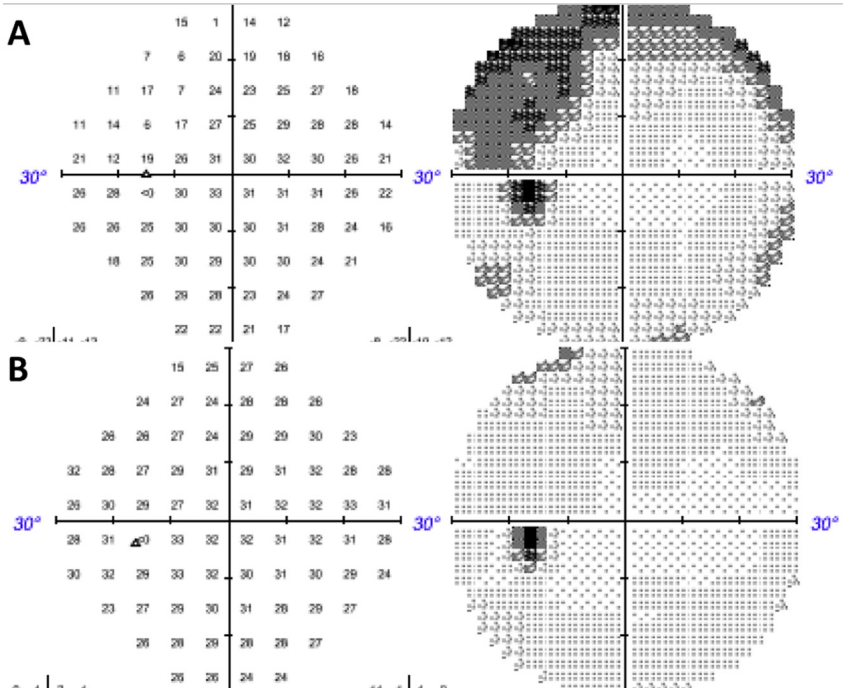

Fig. 2. (A–B): Title: Humphrey visual field 30-2 on presentation and after treatment with vemurafenib. Caption: A, HVF 30-2 left eye on presentation with superior arcuate defects. B, HVF 30-2 left eye performed 6 weeks after initiation of treatment demonstrates improved reliability and resolution of prior defects.

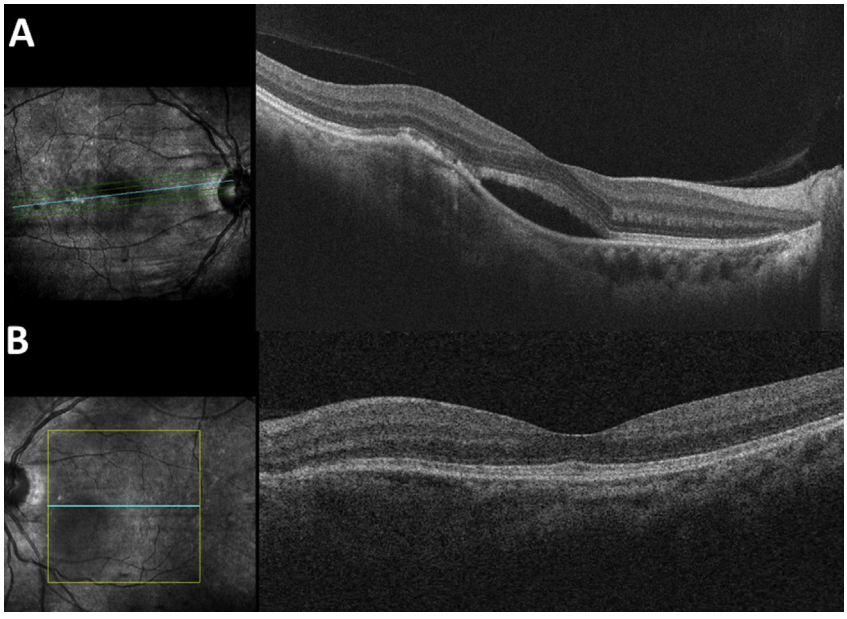

Fig. 3. (A–B): Title: OCT macula on presentation. Caption: A, OCT macula of the right eye demonstrates irregularity and disruption of the RPE with sub-RPE hyperlucent mass. There is subretinal fluid within the fovea. B, The left eye demonstrates a similar choroidal elevation with sub-RPE hyperlucent mass. There is no edema.