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Acute macular neuroretinopathy associated with acute promyelocytic leukemia

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ABSTRACT

Purpose: To describe the first reported case of acute macular neuroretinopathy (AMN) associated with acute promyelocytic leukemia in a young Asian-Indian male.

Observations: We review the clinical and multimodal imaging findings in our patient that are characteristic of AMN.

Conclusions and importance: Ophthalmologists should be aware of the association of leukemia with AMN and consider hematologic work-up when assessing patients with AMN without the prototypical history or risk factors.

1. Introduction

Acute macular neuroretinopathy (AMN), is a relatively rare retinal disease that was first described by Bos and Deutman in 1975 in healthy young females taking oral contraceptives.[1] Affected patients classically present with acute paracentral scotomas, mild vision loss, and perifoveal reddish, wedge-shaped petalloid lesions on exam. Other risk factors commonly reported with AMN include viral prodrome, exposure to vasoconstrictive epinephrine or ephedrine, caffeine intake, and hypotensive shock.[2,3] To date, there has been one other report in the literature describing AMN in the setting of acute lymphoblastic leukemia (ALL).[4] We herein report the first described case of AMN associated with acute promyelocytic leukemia (APL) with multimodal imaging.

2. Case presentation

A 37 year-old Asian-Indian male was admitted for fatigue and fever in the setting of viral pneumonia after routine labs detected pancytopenia (hemoglobin 5.4 g/dL, white cell count 3.0 K/UL, platelet 9.0 K/UL). His hematologic work-up was consistent with APL and all-trans retinoic acid therapy (ATRA) was initiated. His hospital course was complicated by disseminated intravascular coagulation, multifocal pneumonia, and acute respiratory distress requiring intubation. His inpatient treatment course consisted of two doses of idarubicin, arsenic trioxide, and ATRA therapy. Ophthalmology was initially consulted after globe flattening was detected on neuro-imaging. Examination at that time demonstrated significant papilledema indicative of intracranial hypertension secondary to ATRA therapy.

Following extubation, the patient complained of paracentral scotomas in the right eye. Fundus examination demonstrated Roth spots and peripapillary intra-retinal hemorrhages surrounding the nerve in both eyes. After management and stabilization of the patient's complicated hospital course, the patient was discharged. He returned for follow up six weeks after initial onset of symptoms for further work-up and assessment of persistent paracentral scotomas of the right eye. Visual acuity was 20/20 in both eyes. Examination of the right fundus revealed intra-retinal hemorrhage within the superonasal macula and superior to the disc along with pigment mottling within the macula. His left eye revealed intra-retinal hemorrhage nasal to the disc and pigment mottling within the macula (Fig. 1A and B). The near infrared reflectance (NIR) clearly demonstrated well demarcated, wedge-shaped lesions pointing towards the fovea corresponding to the patient's scotomas in the right eye and a single wedge shaped lesion in the left eye (Fig. 2A and C). Spectral domain optical coherence tomography (SD-OCT) imaging (Spectralis HRA + OCT, Heidelberg Engineering) showed thinning of the outer nuclear layer (ONL) and disruption of the ellipsoid zone (EZ) corresponding to the lesions seen on NIR (Fig. 2B and D). OCT angiography (OCT-A) using RTVue- XR Avanti system (Optovue Inc., Fremont, California) revealed loss of the deep capillary plexus (DCP) on 3×3 mm scans with attenuation of signal on both the enface and cross-sectional images in the regions corresponding to the NIR defects in the right and left eye (Fig. 3). Fluorescein and indocyanine green

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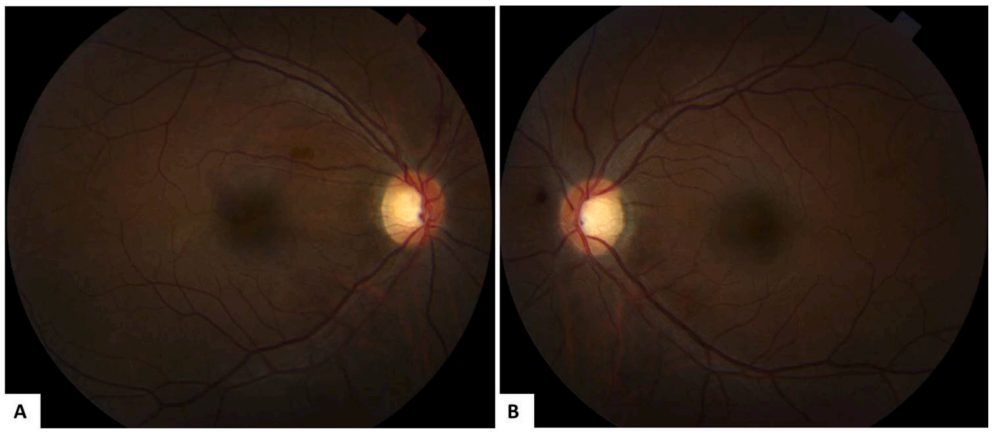

Fig. 1. (A, B). Color fundus photographs of right and left eyes reveal intra-retinal hemorrhages and pigment mottling within macula.

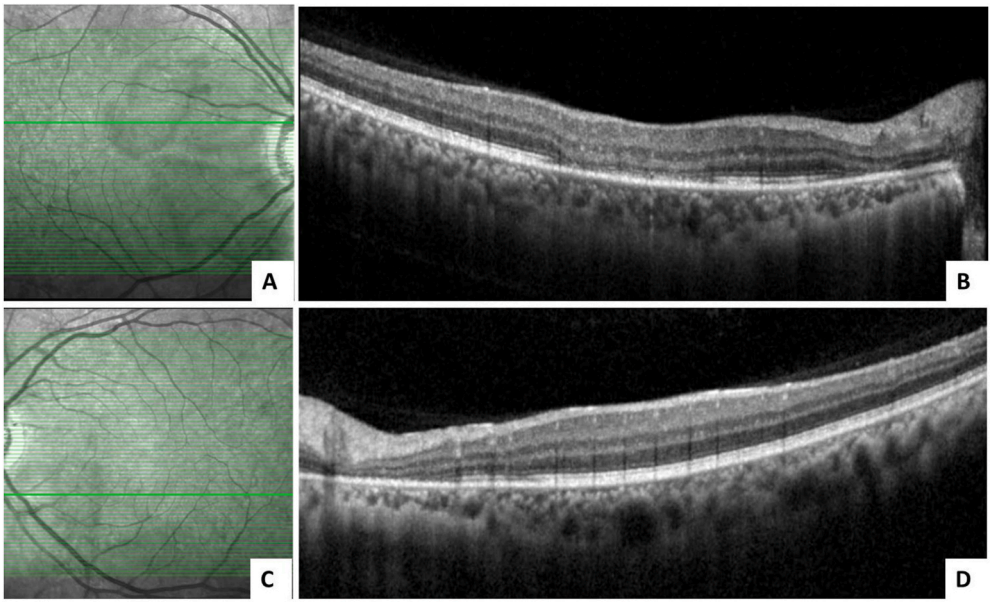

Fig. 2. (A, C) Near infrared reflectance (NIR) of the right and left eye showing perifoveal wedge-shaped lesions (B, D) Spectral domain optical coherence tomography (SD-OCT) imaging reveals thinning of the outer nuclear layer (ONL) and disruption of the ellipsoid zone (EZ) corresponding to the lesions on NIR.

angiography were unremarkable. Humphrey Visual Field 24–2 of the right eye demonstrated central and paracentral depression. Collectively these findings were consistent with a diagnosis of AMN.

At last follow-up, 4.5 months since initial presentation, the patient had achieved complete remission after induction and was on consolidation therapy. He reported improvement of his scotomas. His visual acuity remained 20/20 in both eyes with near resolution of previously noted intra-retinal hemorrhage in both eyes (Fig. 4A and D). NIR showed some improvement of the wedge-shaped defects (Fig. 4B and E) while SD-OCT demonstrated some reconstitution of the ellipsoid zone in both eyes (Fig. 4C and F). OCT-A of the right eye showed relatively stable loss of the DCP on 6 × 6 mm enface images (Fig. 5A and B). The patient's anemia and thrombocytopenia were also improved (hemoglobin 13.4 g/dL and platelets 252 K/μL. He had borderline leukopenia (white cell count 3.7 K/μL).

3. Discussion

AMN is a rare entity generally occurring in young females with risk factors such as flu-like illness or use of oral contraceptives.[2,3] In a recent comprehensive review of AMN by Bhavsar et al., 84% of affected patients were female and 80% were non-Latino Caucasians.[2]

Several conditions have also been described in association with AMN, including use of vasoconstrictive agents, trauma, hypovolemic shock, anemia, and thrombocytopenia.[2,4] Our report is the first reported case of AMN associated with acute promyelocytic leukemia in a young, Asian-Indian male.

APL is a specific subtype of acute myeloid leukemia characterized by translocation of the retinoic acid receptor gene between chromosomes 15 and 17 leading to accumulation of atypical and immature promyelocytes in the bone marrow and peripheral blood causing pancytopenia.[5] Ocular manifestations of leukemia are a result of either direct tissue infiltration or indirect sequelae. Direct infiltration may involve the orbit, anterior segment, posterior segment, choroid, or optic nerve.[6,7] Our patient had signs of leukemic retinopathy, a common indirect manifestation, that appears as retinal vessel tortuosity, dilation, and hemorrhages as a result of anemia, thrombocytopenia, and hyperviscosity from underlying disease.[6,7]

On SD-OCT imaging, our patient had outer retinal changes including disruption of the EZ and thinning of the ONL that are typical of AMN particularly after the acute phase of the disease.[2,8] Although the exact pathophysiology of AMN has yet to be fully elucidated, ischemia of the

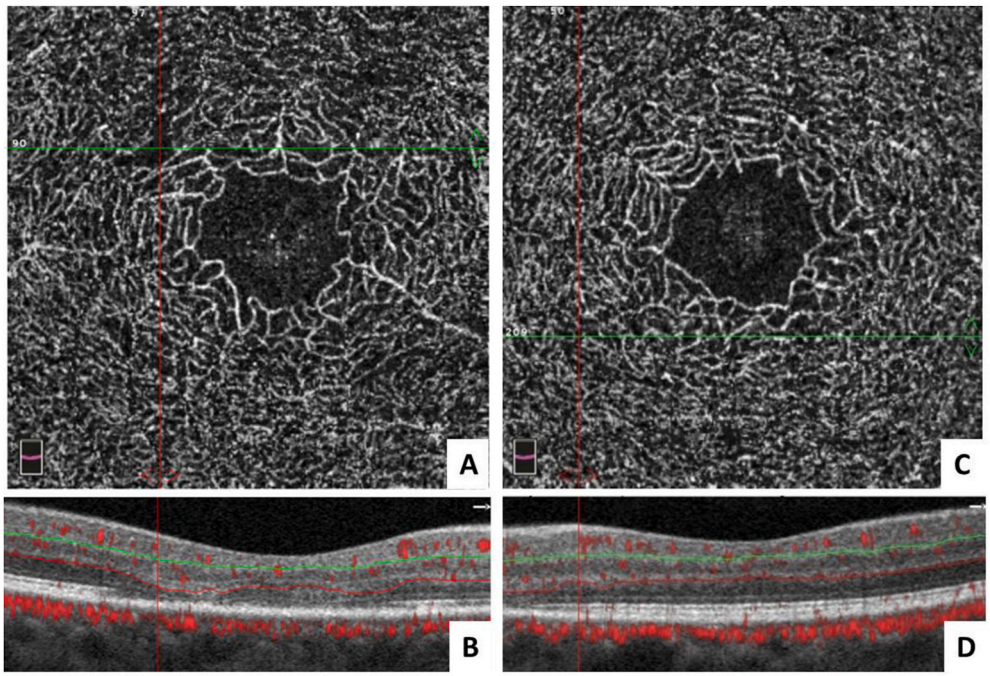

Fig. 3. Right eye (A,B) and left eye (C,D), optical coherence tomography angiography (OCT-A), 3 mm × 3 mm scan shows drop-out of deep capillary plexus with attenuation of signal on both enface and cross-sectional images.

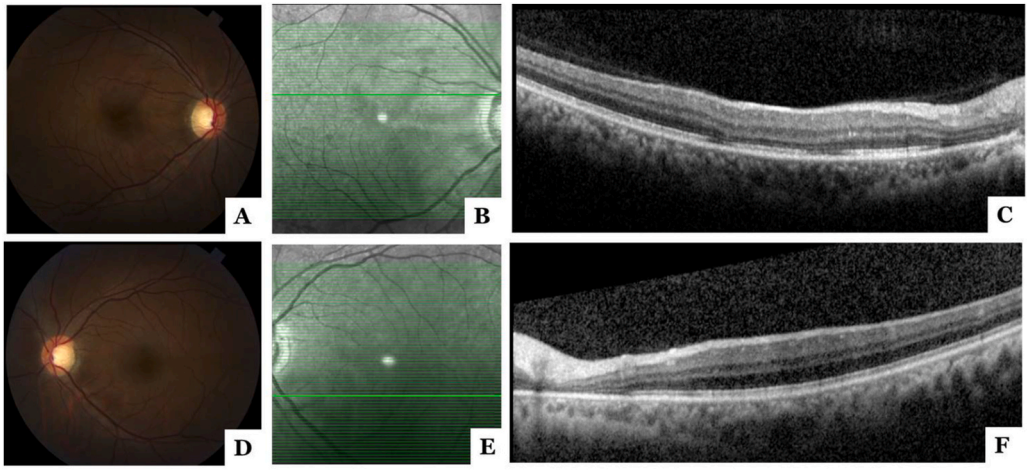

Fig. 4. (A, D) Color fundus photographs of the right and left eye at 4.5 month follow-up reveals resolution of intra-retinal hemorrhages (B, E) NIR shows modest improvement of wedge-shaped defects in both eyes (C, F) SD-OCT shows partial recovery of ellipsoid zone in both eyes.

deep capillary plexus has been proposed as the mechanism.[4,8,9] In our case, the patient's significant thrombocytopenia and anemia may have contributed to focal ischemia at the level of the deep capillary plexus.[4] Additionally, the increased production of immature leukoblasts enhances overall hyperviscosity thereby leading to venous stasis and ultimately exacerbating the patient's underlying hypoxia.[4,10] Finally, APL is associated with disseminated intravascular coagulation (DIC) as there is an irregular production of procoagulants including tissue factor, cancer procoagulant, and microparticles.[11] In our patient, the development of DIC with associated thrombocytopenia and thrombotic microangiopathy may have further exacerbated retinal microvascular ischemia. In fact, as hypothesized by Munk et al. it may be that any pathophysiologic process leading to chorioretinal hypoxia in the setting of thrombocytopenia and anemia may cause AMN. As shown in our patient, however, prognosis can be favorable with improvement of subjective visual symptoms and recovery of photoreceptors over time. We suspect that successful treatment of the underlying leukemia, achieving remission, played an important role in this outcome.

In conclusion, this case raises awareness of the association between leukemia with AMN. Clinicians should consider work-up for hematologic malignancies in patients that lack other conditions more commonly described with AMN and include AMN in the differential diagnosis of vision loss in a patient with known history of leukemia.

Patient consent

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

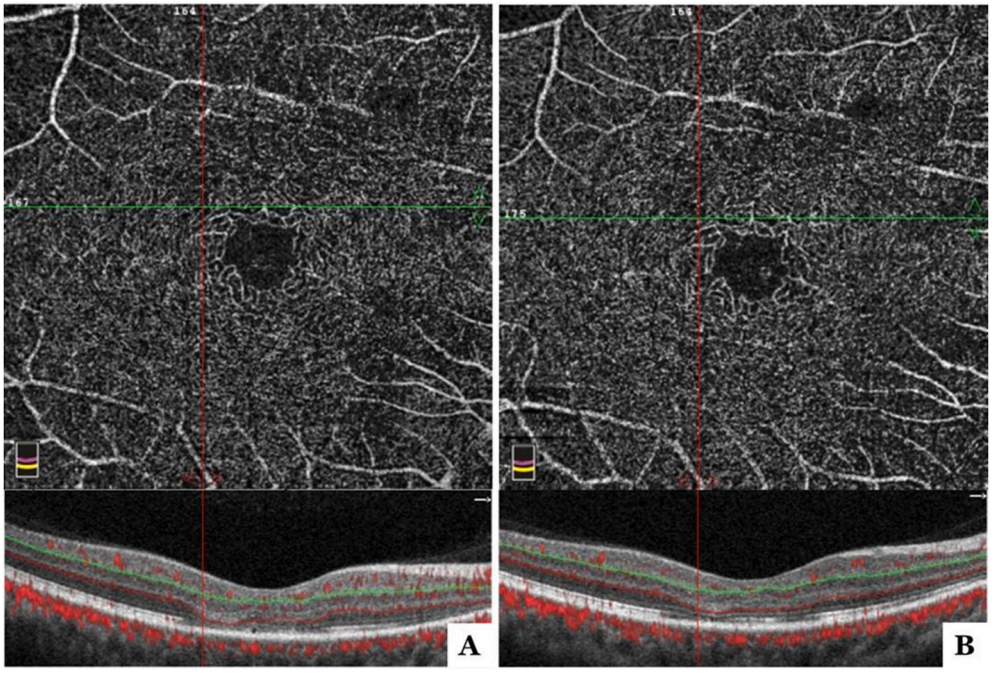

Fig. 5. OCT-A 6 mm × 6 mm scan of the right eye (A) at initial presentation shows deep capillary plexus dropout with attenuation of signal on both the enface and cross-sectional images (B) at 4.5 months follow-up with relatively stable capillary dropout and attenuation of signal on enface and cross-sectional images.

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Authorship

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

Declaration of competing interest

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