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Salmon patch maculopathy: An amblyogenic complication of pediatric sickle cell retinopathy

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ABSTRACT

Purpose: To report a case of a large foveal sub-internal limiting membrane hemorrhage from sickle cell retinopathy in a pediatric patient.

Observations: A five-year-old boy with sickle cell disease (SCD) type SS (HbSS) and numerous complications was referred after a failed vision screening and was found to have a large yellow subacute sub-internal limiting membrane hemorrhage overlying the fovea in his right eye. There were several other peripheral salmon patches noted. Optical coherence tomography (OCT) revealed temporal inner retinal macular thinning in both eyes. Serial imaging showed rapid improvement over time of the hemorrhages, though amblyopia persisted.

Conclusions and importance: We describe an unusual amblyogenic presentation of non-proliferative sickle cell retinopathy in five-year-old patient with HbSS due to a foveal salmon patch. Numerous vision-threatening complications are possible in SCD, highlighting the need for early vision screening.

1. Introduction

Sickle cell retinopathy (SCR) is a well-described complication of sickle cell disease (SCD) and is categorized as non-proliferative (NPSR) or proliferative (PSR). NPSR is characterized by vessel ischemia, dropout, and remodeling. Other features include multi-layered retinal hemorrhages, classically called salmon patches, and their resulting scars known as sunbursts. PSR is characterized by retinal neovascularization and related complications including vitreous hemorrhage and retinal detachment which typically presents in the peripheral retina. Previous studies have shown a higher incidence of PSR and vision loss in patients with SCD type SC (HbSC).[1,2] We describe an instance of bilateral NPSR with a unilateral macular salmon patch in a five-year-old male with HbSS.

2. Case report

A five-year-old unvaccinated boy with HbSS and history of acute chest syndrome and superficial occlusive venous thrombi was referred to optometry clinic following a failed vision screen. His current treatment was with voxelotor initiated one year prior to presentation and folic acid only, as hydroxyurea had been declined. His most recent dilated eye exam prior to presentation was five months prior at an outside optometry office and was reportedly unremarkable besides myopia. The patient denied any visual symptoms on presentation. His best corrected distance visual acuity was 20/30 on eccentric gaze in the right eye with a spherical equivalent of −0.75 diopters (D) and 20/25 in the left eye with a spherical equivalent of −1.2 D. His intraocular pressures with iCare tonometry were 15 mm of mercury (mmHg) in the right eye and 16 mmHg in the left eye. His pupillary exam, motility exam, and alignment exam were unremarkable. He had full Ishihara color plates in both eyes. His anterior segment exam was unremarkable. His initial dilated exam was notable for a superficial yellow layered hemorrhage with old heme overlying the fovea, numerous peripheral salmon patch lesions in similar stages of healing in the right eye, and peripheral arteriovenous anastomoses (Fig. 1A and C). The left eye had an older resolved salmon patch with residual pre-retinal haze and peripheral arteriovenous anastomoses (Fig. 1B).

His laboratory evaluation was notable for microcytic anemia with a hemoglobin of 10.5 g per deciliter, reticulocytosis, and mild thrombocytosis of 455 cells/mm^3. Blood cultures and full examination with hematology ruled out any disease process apart from sickle cell to account for the patient's macular hemorrhage. Due to the relatively advanced retinopathy at a young age, screening magnetic resonance imaging

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(MRI) and magnetic resonance angiography (MRA) of the brain were completed which did not show any evidence of ischemia or vessel narrowing. Treatment was transitioned from voxelotor to hydroxyurea by the hematology service after discussion with family.

Thirteen days after initial presentation, his corrected distance visual acuity worsened to 20/60 in the right eye and remained stable at 20/30 in the left eye. His anterior segment exam remained unremarkable. Dilated fundus examination showed improvement of the pre-foveal hemorrhage (Fig. 1D). Optical coherence tomography (OCT) of the right eye showed large sub-internal limiting membrane (ILM) hemorrhage involving the fovea with foveal shadowing, but preserved foveal contour and temporal inner retinal macular thinning (Fig. 2A). OCT of the left eye also showed significant temporal inner retinal macular thinning (Fig. 2C). Patching was not advised at this time, due to the rapid clearing of blood overlying the fovea.

On three month follow up, the patient's best corrected distance visual acuity was 20/40 in the right eye and 20/20 in the left eye. Dilated fundus examination showed near complete resolution of the macular hemorrhage with no heme obscuring the fovea in the right eye (Fig. 1E). OCT showed resolving sub-ILM hemorrhage with persistent temporal inner retinal macular thinning in the right eye (Fig. 2B) and stable temporal inner retinal macular thinning in the left eye. Fluorescein angiography showed blocking from residual heme in the right eye (Fig. 1F) and capillary nonperfusion temporally in the left eye (Fig. 1G). Due to persistent acuity difference without residual media opacity, patching therapy of the left eye was initiated for 2 h per day. After three months of patching of the left eye, the patient's vision improved to 20/30 in the right eye; his fundus exam showed no gross abnormalities and OCT at that time showed resolution of the foveal hemorrhage.

3. Discussion

We describe here a patient with HbSS who presented at five years of age with bilateral NPSR and a large foveal salmon patch in the right eye. The duration of the foveal hemorrhage was unknown, and rapid resolution in our care argued against surgical intervention. Nonetheless duration of the hemorrhage was sufficient to induce amblyopia requiring patch therapy. This disease severity is unusual in such a young patient, as the prevalence of SCR has been shown to increase with age; additionally, screening for retinopathy begins at ten years of age in the United States.[1,3] While it has been shown that close to half of patients had peripheral vessel occlusion by six years and more than 90 % by 12

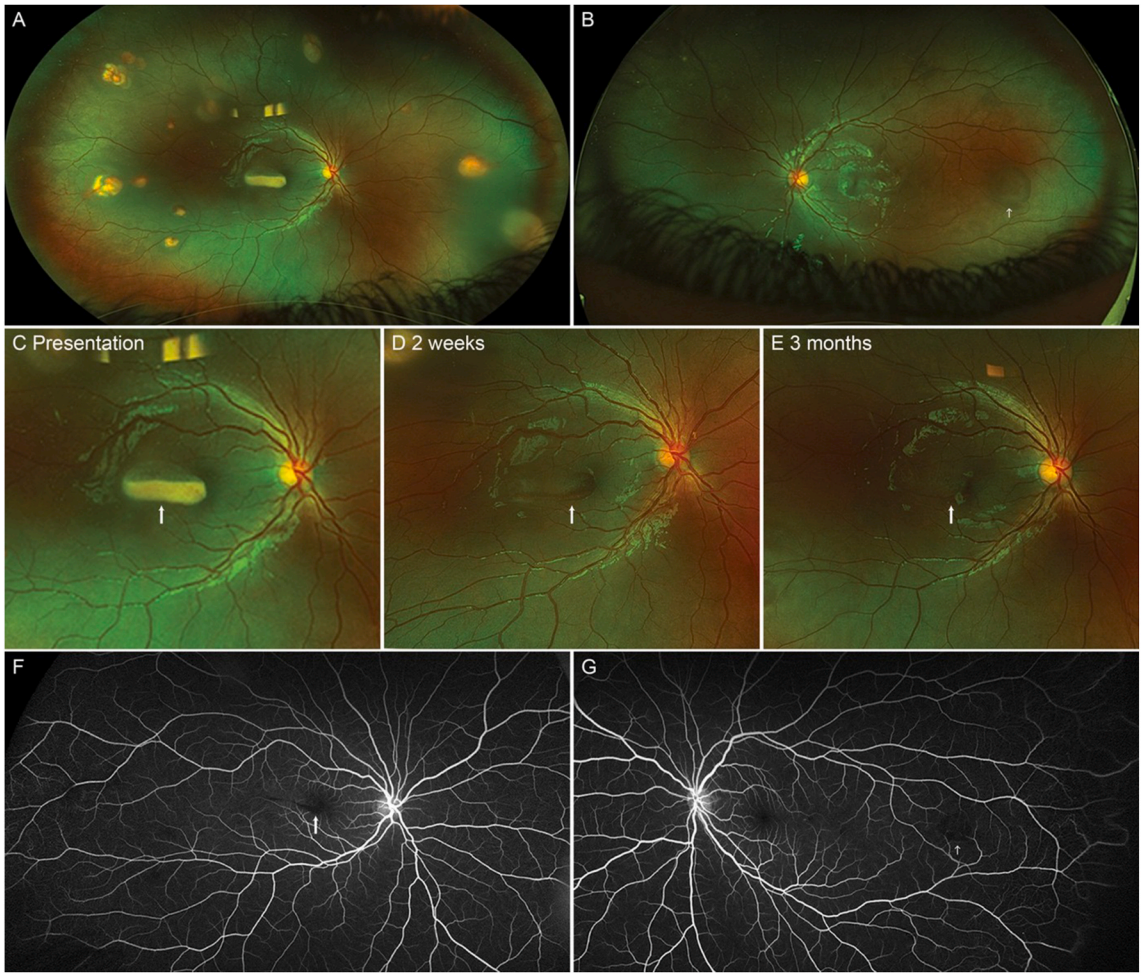

Fig. 1. (A) Color photo of the right eye on presentation showing large sub-internal limiting membrane (ILM) hemorrhage centered over the fovea, numerous peripheral resolving salmon patches, and peripheral arteriovenous anastomoses. (B) Color photo of the left eye on presentation showing a resolved salmon patch temporally (white arrow). (C) Color photo of the right eye at presentation showing large sub-ILM hemorrhage centered over the fovea (white arrow). (D) Color photo of the right eye two weeks after presentation showing interval improvement of a sub-ILM hemorrhage centered over the fovea (white arrow). (E) Color photo of the right eye three months after presentation showing near complete resolution of the sub-ILM hemorrhage (white arrow). (F) Fluorescein angiography of the right eye three months after presentation showing blocking in the macula from residual hemorrhage (white arrow). (G) Fluorescein angiography of the left eye three months after presentation showing capillary non-perfusion in the temporal macula (white arrow). (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

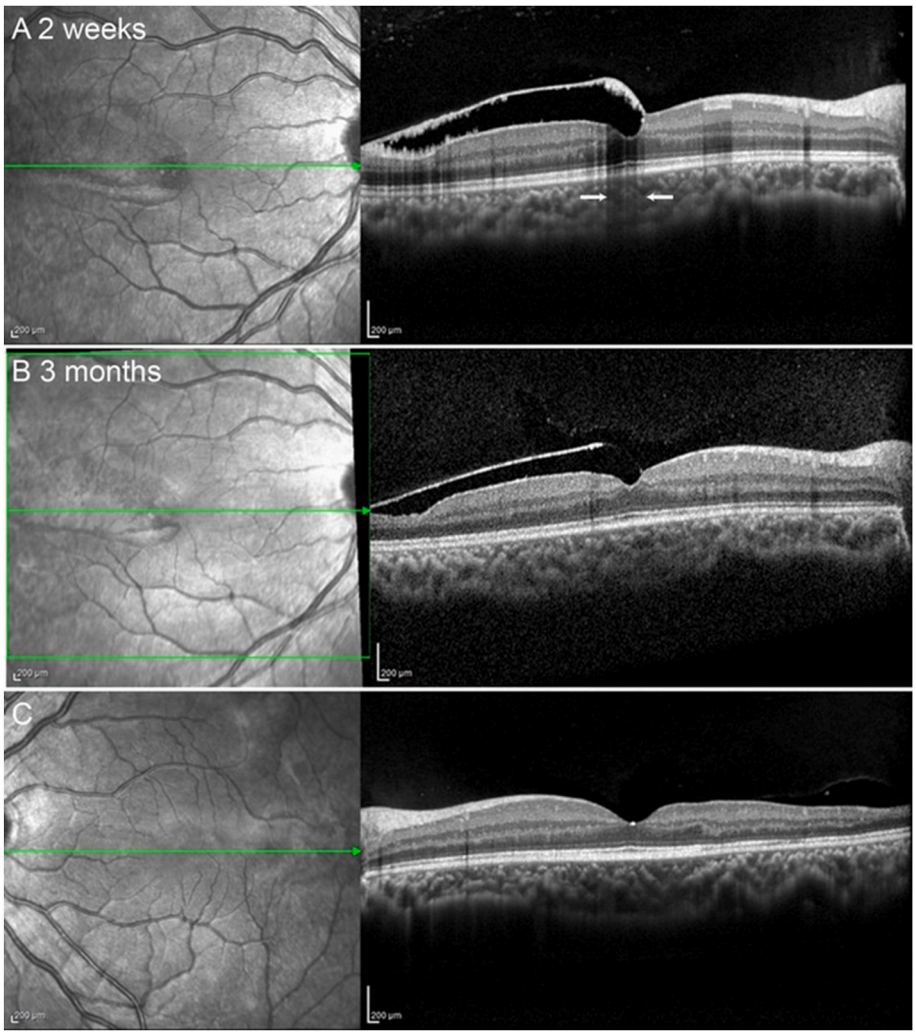

Fig. 2. (A) Optical coherence tomography (OCT) of the right eye thirteen days after presentation showing a large sub-internal limiting membrane (internal limiting membrane (ILM)) hemorrhage involving the fovea with foveal shadowing and temporal inner retinal macular thinning (white arrows). (B) OCT of the right eye three months after presentation showing interval improvement of a large sub-ILM macular hemorrhage with stable temporal inner retinal macular thinning. (C) OCT of the left eye thirteen days after presentation showing temporal inner retinal macular thinning.

years and that NPSR is present in patients as young as four years, data on the incidence of amblyogenic manifestations of SCR is not available.[2,4]

Salmon patches are retinal hemorrhages resulting from rupture of superficial retinal arterioles occluded by sickled erythrocytes. These hemorrhages dehemoglobinize (turning from red to yellow on fundoscopy) over time and then are slowly resorbed often leaving behind characteristic retinal hyperpigmentation or scarring.[5] Notably, salmon patches can less commonly cause vitreous hemorrhage in the absence of proliferative disease and can mimic other retinal pathology including uveitis.[6] Salmon patches are typically described as occurring in the retinal periphery outside of the posterior pole.[5,7]

The peripheral retina is thought to contain a higher proportion of sickled erythrocytes leading to more occlusive events; the increased rate of sickling in the peripheral retinal vasculature likely results from a lower level of oxygenation and narrower lumens in the peripheral vasculature.[8] However, the macula is also affected by sickle cell disease with well-described findings of retinal thinning from ischemia.[9] These findings are more severe in HbSS—as in our patient's case—compared with HbSC where there are more focal and more severe vascular occlusions in the macula.[10–12] We theorize that a more posterior vascular occlusion could analogously lead to vessel rupture and subsequent development of a macular salmon patch with co-localized macular thinning as was seen in our patient.[13,14] Notably, the patient did have more severe macular thinning in the left eye; this interocular asymmetry has been previously described in SCR.[15]

It is important to consider other causes of unexpected retinal hemorrhages in a pediatric patient, specifically accidental or non-accidental trauma.[16,17] Our patient is out of the age range where this would be likely to occur, but nonetheless a full history was obtained. Severe anemia and thrombocytopenia, especially that seen with acute hematologic malignancy can also cause severe retinal hemorrhaging in children, but this was ruled out in our patient with his work-up.

To summarize, while sickle cell maculopathy has been well-described in adult and pediatric patients, it classically presents as macular thinning with enlargement of the foveal avascular zone rather than as hemorrhage.[18,19] To our knowledge, this is the first report of a macular salmon patch in a patient with SCR. The importance of this finding in a pediatric patient is risk the for irreversible amblyopia, and notably this patient was below the age recommended for initiation of SCR screening in the United States of 10 years. While other countries do not have recommended screening ages for SCR, there have been calls to institute an equivalent screening of age of 10 years.[20] It is important to note recent studies have shown relatively high incidence of SCR and sickle cell maculopathy in patients younger than 10 years of age.[2,21–23] Additional research is needed prior to mandating OCT as part of SCR screening for very young patients, but we suggest starting annual eye

chart-based screening for verbal children at four to five years of age with urgent ophthalmology referrals for any failures or concerns. In conclusion, we describe here an instance of a large foveal salmon patch in a very young patient with HbSS and bilateral NPSR; this case highlights the importance of early vision screenings in pediatric patients with SCD.

CRediT authorship contribution statement

Nitya Rao: Writing – review & editing, Writing – original draft, Methodology, Conceptualization. **Therese McKnight:** Writing – review & editing. **Cynthia Norris:** Writing – review & editing. **Drew Scoles:** Writing – review & editing, Writing – original draft, Methodology, Conceptualization.

Statement of informed consent

Informed consent was not sought for the present study because no identifiable patient information was included in the case report.

Ethical approval

Ethical approval was not sought for the present study because there was no medical research involving human subjects.

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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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