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Pediatric macular hole repair with amniotic membrane graft in a patient with leukemia

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ABSTRACT

Purpose: Idiopathic macular holes are rare in children. The optimal management and surgical technique have not been fully investigated in chronic pediatric macular holes.

Observations: Here we report a pediatric patient with leukemia who presented with non-clearing vitreous hemorrhage and intraoperative identification of a full thickness macular hole. After pars plana vitrectomy and internal limiting membrane peeling, a human amniotic membrane transplant (AMT) was fashioned and tucked under the retina at the edge of macular hole. Silicone oil was used to provide sufficient tamponade to the graft as the patient lived at high elevation. At follow up the graft was properly incorporated in the retina with successful anatomic closure of the macular hole without graft displacement, intraocular inflammation, or retinal detachment. One month after surgery visual acuity was 3/100 with subsequent improvement to 20/70 at final follow up. The graft remained well integrated in the retina after silicone oil removal. Optical coherence tomography demonstrated restoration of foveal contour with disruption in outer retinal layers.

Conclusion and importance: Unlike idiopathic senile macular holes, application of AMT for idiopathic macular holes in children has not been investigated. Our case suggests amniotic membrane graft as an adjunctive tool in management of pediatric macular holes.

1. Introduction

Leukemia is the most common pediatric malignancy, accounting for 30 % of all cases of childhood neoplasia.[1] Leukemic retinopathy is the most common ocular manifestation and it is estimated that up to 69 % of all patients demonstrate fundus changes during the course of their disease.[2] Retinal hemorrhages can occur at all levels, are usually in the posterior pole and may extend into the vitreous.[3]

Pediatric macular holes are rare and are usually associated with blunt trauma.[4] There are few reports in the literature of idiopathic non-traumatic macular hole in a young patient.[5] Pediatric non-traumatic macular holes have been reported as secondary causes of retinopathy of prematurity,[6] Coats disease,[7] Bartonella retinitis,[8] idiopathic juvenile epiretinal membrane,[9] and abnormal vitreomacular traction.[10]

In pediatric macular holes, spontaneous closure is common and more likely in patients with small macular holes with an attached posterior hyaloid.[11] However, pars plana vitrectomy (PPV) with internal limiting membrane (ILM) peeling, and gas tamponade is the standard technique for treating pediatric macular holes that fail spontaneous closure.[12] Amniotic membrane grafts can be used for refractory or persistent adult idiopathic macular holes with acceptable structural and functional outcome.[13] There is very limited data on amniotic membrane transplant (AMT) for management of macular holes in pediatric patients.

Here we present a pediatric patient with leukemia who presented with vitreous hemorrhage and intraoperative identification of a full thickness macular hole that was successfully repaired with amniotic membrane graft.

2. Case report

A 13-year-old male with history of decreased vision for two months

Abbreviations: (OCT), optical coherence tomograohy; (AMT), amniotic membrane transplant; (PPV), pars plana vitrectomy; (ILM), internal limiting membrane; (VA), visual acuity; (OD), right eye; (OS), left eye; (ALL), acute lymphocytic leukemia; (iOCT), intraoperative OCT; (PVD), posterior vitreous detachment; (FTMH), full thickness macular hole.

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was referred to the retina clinic for evaluation of vitreous hemorrhage in the setting of a hemoglobin of 3 g/dL. The patient was diagnosed one year before the onset of visual symptoms with T cell acute lymphocytic leukemia (ALL) and was under maintenance therapy with monthly chemotherapy and weekly methotrexate. Birth and family history were unremarkable. The family and patient denied any history of trauma. On examination, there were no visible signs of trauma externally. Visual acuity (VA) was 20/20 in the right eye (OD) and hand motion in the left eye (OS). Anterior segment examination was unremarkable other than a 3 mm conjunctival pigmented spot nasally consistent with conjunctival nevus in the left eye. Fundus exam of the right eye was normal. Fundus exam of OS showed dense vitreous hemorrhage obscuring the view of the posterior segment (Fig. 1A). OCT macula of OD showed intraretinal hyperreflective material and trace outer retinal attenuation nasal to fovea. B-scan of OS showed vitreous hemorrhage but no retinal detachment (Fig. 1B). Initial close observation was elected as the patient's family wanted to avoid surgery due to the patient's chemotherapy schedule. The patient was followed closely but by month 4, he was noted to have non-clearing vitreous hemorrhage and surgery was recommended.

A standard 3 port 25-gauge PPV was performed. During the surgery, after removal of the dense vitreous hemorrhage, a full thickness macular hole was seen and confirmed with intraoperative OCT (iOCT) (Fig. 2). Brilliant blue G was used, and the posterior hyaloid and ILM were easily peeled (**Supplementary video**) using a Flex loop (FINESSE® Flex Loop, Alcon). Given the chronic appearing large macular hole, the decision was made to use a human amniotic membrane graft. A 1 mm amniotic membrane graft was fashioned and tucked under the macular hole edges. 1000 cs silicone oil (SO) was used for tamponade as the patient lived at high elevation. One month after surgery, VA was 3/100 OS and the macular hole was closed with good incorporation of the amniotic membrane graft, confirmed by SD-OCT (Fig. 3A, 3B, 3C). Three months after the initial surgery, silicone oil removal was performed. At final follow up, seven months after silicone oil removal, the visual acuity improved to 20/70 OS, the retina showed an area of parafoveal pigmentary change inferiorly but retina was attached without retinal tears, holes or detachment (Fig. 3D). OCT showed that the macular hole remained closed and AMT was in good position, however, atrophy of outer retinal layers was noted in foveal B-scans (Fig. 3E and 3F).

3. Discussion

Here we report a pediatric patient with leukemia who presented with vitreous hemorrhage, full thickness macular hole and spontaneous ILM/posterior hyaloid separation that was successfully managed with standard PPV and adjunctive AMT. Posterior segment involvement in the form of intraretinal hemorrhages is thought to be the most common ophthalmic manifestation in leukemia.[14] In this case, the primary clinical manifestation was vitreous hemorrhage in the left eye. However, on OCT, the right eye demonstrated intraretinal exudates which may have been signs of old intraretinal hemorrhages. In a series of 81 subjects with ALL, Bukhari et al. reported ophthalmic manifestations in 23 patients with a prevalence of 28.4 %. Retinal hemorrhages were the most common exam findings (six subjects) and vitreous hemorrhage was noted in 2 patients (8.7 %).[3] In a series of 24 eyes with ocular leukemia, vitreous hemorrhage was described in 2 eyes.[14]

Inducing posterior vitreous detachment (PVD) in pediatric patients can be one of the more challenging steps during vitreoretinal surgery. Interestingly, the hyaloid and what appeared to be ILM were already separated from the retina in this patient as visualized with brilliant blue which typically stains ILM. Given this finding, we hypothesized that sub-ILM and/or sub-hyaloid hemorrhage was the initial ocular pathology leading to detachment of ILM and posterior hyaloid with subsequent progression to secondary vitreous hemorrhage and macular hole. Or perhaps abnormal vitreomacular traction also contributed to the formation of the macular hole as the hyaloid/ILM separated from the macula. Sub-hyaloid and sub-ILM hemorrhages were previously reported in leukemic patients.[15]

Ocular trauma must be considered in a patient with the combination of macular hole and vitreous hemorrhage. While we cannot completely rule out blunt trauma, the family and patient denied trauma and there were no other ocular manifestations of trauma in this patient.

Unlike adult macular holes, pediatric macular holes are very rare and mostly traumatic in nature and the best practice for their management have not been established. Brennan et al. has reported anatomic macular hole closure in all 12 of 13 pediatric traumatic macular holes treated with combination of vitrectomy, ILM peel, and gas tamponade.[16] In one of the largest series on treatment of pediatric macular holes, Kothari et al. investigated multicenter microincisional vitrectomy surgical outcome for pediatric macular holes.[12] Their series included 31 eyes with traumatic or laser induced macular holes. All patients underwent standard vitrectomy with gas or silicone oil for internal tamponade. They have reported 81 % primary closure rate after the first vitrectomy. Although they have used various adjuvants for staining ILM, no surgical adjuvant for facilitating closure or cellular proliferation was used.

There is not a consensus on optimal timing of surgical intervention in

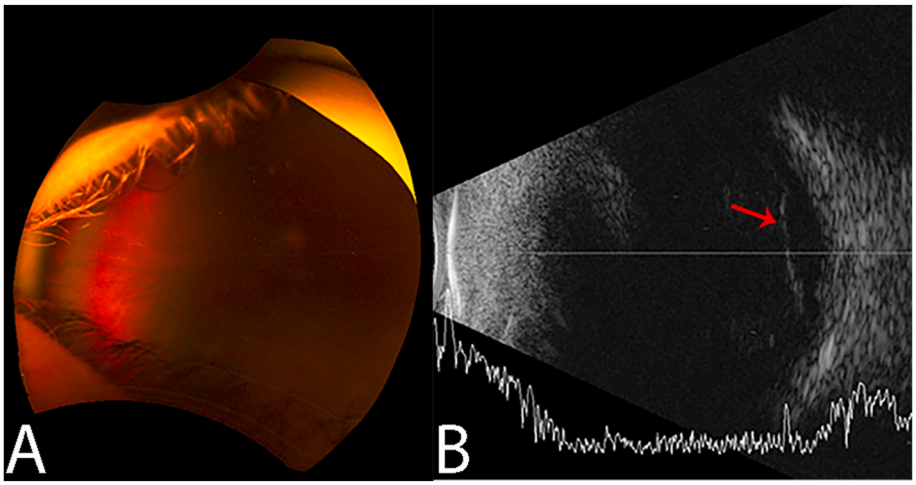

Fig. 1. Widefield fundus photo (Optos plc) OS, showing dense vitreous hemorrhage obscuring view of the posterior pole (**A**). B-scan OS demonstrates vitreous hemorrhage and posterior hyaloid elevation without retinal detachment (**B,** red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

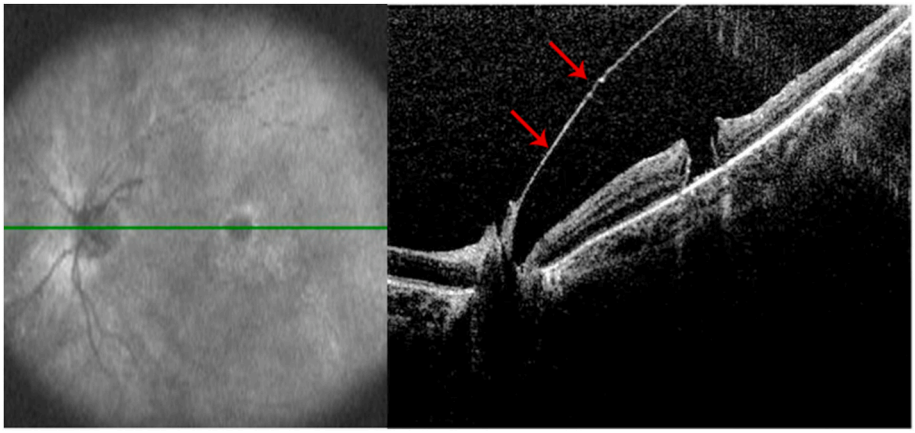

Fig. 2. Partially detached posterior hyaloid (red arrows) and FTMH is evident on iOCT image OS (Envisu, Leica microsystems). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

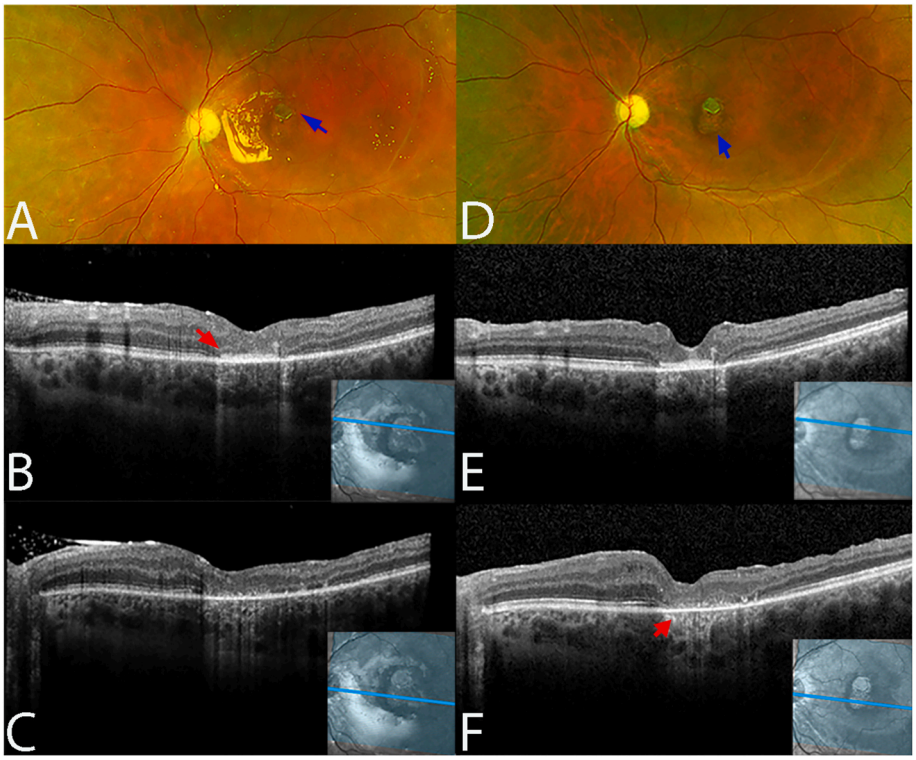

Fig. 3. One month after surgery, under silicone oil, AMT plug is evident on fundus image (Optos plc) (**A,** blue arrow) with good incorporation and closure of overlaying retina layers as visible on macular OCT OS (**B,** red arrow). Fovea B-scan demonstrates appearance of foveal contour with atrophy of outer retinal layers (**C**). Severn months after silicone oil removal, fundus photo exhibits well placed AMT plug and pigmentary change in inferior macula (**D,** blue arrow). Associated OCT shows closed macular hole with residual, integrated AMT and atrophic outer retinal layers at the fovea (**E, F,** red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

pediatric macular holes. In a comparative multicenter study, 66.7 % of the traumatic macular holes were found to close spontaneously after observation for 6 months.[17] Regeneration and spread of glial cells as well as retinal pigment epithelial cells with subsequent recruitment and migration of astrocytes are considered to be the mechanism behind structural and functional recovery in spontaneous closure.[18]

Although surgical adjuncts have been investigated in the management of adult idiopathic recalcitrant macular holes, there is limited data on safety and efficacy of these in pediatric macular holes. Wachtlin et al. has reported successful application of platelet concentrate in 4 cases of traumatic pediatric macular hole with anatomic closure in all cases.[19] Finn et al. described a large traumatic macular hole in a pediatric patient managed with combination of inverted ILM flap and autologous plasma concentrate (APC). This combined technique had the advantage of providing a strong plug and a scaffold for cell proliferation to allow for anatomical closure.[20] To the best of our knowledge this is the first report of introducing AMT to manage a chronic pediatric macular hole. In this case, given the chronic, large appearing macular hole, an ILM peel alone likely would not achieve macular hole closure. Therefore, the decision was made to perform ILM peel with amniotic membrane graft. Nine months after PPV with ILM peel and amniotic membrane graft, the patient's visual acuity improved to 20/70 and OCT showed macular hole closure.

4. Conclusion

This case highlights unique vitreoretinal findings in a pediatric leukemic patient including hyaloid and ILM separation from the fovea, vitreous hemorrhage and underlying chronic appearing macular hole. Intraoperative OCT was helpful in diagnosing and understanding the size/appearance of the macular hole, leading to the decision for an amniotic membrane graft. Amniotic membrane graft can be a good option for a pediatric patient with a large chronic appearing macular hole and can lead to anatomic and functional success.

CRediT authorship contribution statement

Vahid Ownagh: Writing – original draft, Project administration, Methodology, Investigation. **Nita G. Valikodath:** Writing – review & editing, Investigation, Conceptualization. **Lejla Vajzovic:** Writing – review & editing, Supervision, Resources, Project administration, Conceptualization.

Patient consent

Institutional consent for publication has been obtained from the patient or the legal guardian.

Claims of Priority

After conducting a literature review on October 4, 2024 utilizing MEDLINE (via PubMed), Embase (via Elsevier), Web of Science (via Clarivate), Google Scholar, and Scopus (via Elsevier) databases, using the key words (amniotic membrane + macular holes + pediatrics), we did not find any prior reports of utilizing amniotic membrane for repairing pediatric macular holes.

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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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ajoc.2025.102259.

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