A Sandwich-Type Double-Layer Amniotic Membrane Graft for Repairing Myopic Macular Hole-Related Retinal Detachment in a Child with Knobloch Syndrome

Omer Othman Abdullah[1], Ece Özdemir Zeydanlı[2], Şengül Özdek[3]

[1]İbinsina Modern Eye and Retina Center, Erbil, Iraq
[2]Ankara Bilkent City Hospital, Clinic of Ophthalmology, Ankara, Türkiye
[3]Gazi University Faculty of Medicine, Department of Ophthalmology, Ankara, Türkiye

Abstract

This case report describes a surgical technique using double-layer human amniotic membrane (hAM) grafting to repair a high myopic macular hole (MH)-related chronic retinal detachment (RD) with subretinal bands in a child with Knobloch syndrome. A 4-year-old boy diagnosed with Knobloch syndrome presented with macular atrophy in the right eye and chronic total RD with subretinal bands associated with a myopic MH in the left eye. The surgery involved an encircling band, pars plana vitrectomy, and subretinal band extraction through a retinotomy. The retinotomy and MH were sealed using hAM with a 5000 centistoke (cS) silicone oil (SO) tamponade. RD recurred two weeks postoperatively due to hAM contracture, leading to MH reopening. A second intervention included replacing the contracted graft with two larger hAM grafts; the first positioned under the MH and the second over the MH in a sandwich configuration, with 5000 cS SO tamponade. Eighteen months after SO removal, a flat retina, closed MH, and ambulatory vision were achieved. In conclusion, double-layer hAM grafting provides a strong seal for MH in high myopia-associated RD where conventional techniques fail.

Keywords: Pediatric retinal detachment, human amniotic membrane, Knobloch syndrome, macular hole-related retinal detachment, pediatric high myopia

Cite this article as: Abdullah OO, Özdemir Zeydanlı E, Özdek Ş. A Sandwich-Type Double-Layer Amniotic Membrane Graft for Repairing Myopic Macular Hole-Related Retinal Detachment in a Child with Knobloch Syndrome. Turk J Ophthalmol. 2025;55:57-60

This case is presented in EVRS 20th meeting, Cappadocia, Türkiye, as poster presentation. Also presented in MIOC 29 Nov-2 Dec 2023 as video oral presentation.

Address for Correspondence: Omer Othman Abdullah, İbinsina Modern Eye and Retina Center, Erbil, Iraq
E-mail: majidy6@yahoo.com **ORCID-ID:** orcid.org/0000-0003-3589-3227
Received: 05.11.2024 **Accepted:** 26.01.2025

DOI: 10.4274/tjo.galenos.2025.15675

Introduction

Knobloch syndrome, first described in 1971,[1] is a rare genetic disorder caused by mutations in the *COL18A1* gene and characterized by extreme myopia, vitreoretinal degeneration, retinal detachment (RD), and occipital encephalocele.[2] Traditionally, RD in Knobloch syndrome has been attributed to peripheral breaks rather than macular holes (MH).[1] However, recent studies have revealed that RD may occur secondary to full-thickness MH, with standard treatment procedures demonstrating low success rates in these cases.[3]

Herein, we describe a genetically confirmed case of Knobloch syndrome in a 4-year-old patient who underwent vitreoretinal surgery using a double-layer human amniotic membrane (hAM) grafting technique to address recurrent MH-related RD. We discuss the surgical challenges associated with Knobloch syndrome and the potential benefits of this innovative approach in complex cases.

Case Report

A 4-year-old boy with infantile myopia, born full-term without complications, was referred for RD in his left eye. His parents reported first-degree consanguinity but no known familial history of retinal disease. The patient had no siblings. The diagnosis of Knobloch syndrome was confirmed by identifying *COL18A1* mutations.

Visual acuity was counting fingers at 0.5 meters for the right eye and at 1 meter for the left eye. Retinoscopy revealed refractive errors of -5.50 diopters (D) in the right eye and -6.00 D in the left eye. Intraocular pressure was normal and anterior segment examination was unremarkable in both eyes. Fundus examination revealed pigmentary retinopathy and macular atrophy in the right eye, while there was chronic total RD with subretinal bands associated with MH in the left eye (Figure 1).

The surgery involved an encircling buckle combined with pars plana vitrectomy. Inducing posterior hyaloid detachment was highly challenging due to unusually strong vitreomacular adherence and required bimanual maneuvers. As the tight subretinal bands were preventing attachment of the retina, we performed a small retinotomy at the most robust portion of the bands, located inferonasally near the optic nerve head, to cut and remove as much of the bands as possible. Staining and peeling of the internal limiting membrane (ILM) could not be performed despite multiple attempts. Therefore, a hAM graft was utilized. Both the retinotomy and the MH were sealed by placing a piece of hAM into the holes (under the retina) with the aid of perfluorocarbon liquid (PFCL). This was followed by fluid-air-silicone oil (SO) 5000 centistoke exchange. No laser was applied to the retinotomy (Video 1).

The retina was flat on the first postoperative day. However, recurrent RD with re-opening of the MH occurred by the second postoperative week due to graft contracture (Figure 1F).

Subsequently, a second intervention was performed under general anesthesia. The retinotomy site was well-sealed with graft in place. The graft was also in place at the macula, adhering to the retinal pigment epithelium (RPE), but had contracted. This created a space for fluid leakage that led to MH reopening and RD recurrence. A fluid-air exchange was performed to flatten the retina under air and PFCL was used to keep it in place. Two separate amniotic grafts, both larger than the MH size, were prepared. The first graft was implanted under the neurosensory retina to cover the floor of the hole, with the chorionic side facing the RPE. The second graft was placed over the surface of the retina (epimacular) with the chorionic side facing downward, creating a sandwich-like covering under and over the MH. Care was taken during the removal of the PFCL to avoid displacement of the grafts, particularly the epimacular graft. The PFCL was aspirated cautiously with a low-vacuum mode from around the margins of the heavy liquid. Upon confirmation of dryness and stability of the grafts, SO was injected, concluding the surgical procedure (Video 1). The SO was removed at postoperative 3 months. The retina remained attached, and the MH stayed closed during the 18-month follow-up period (Figure 2).

Discussion

Pars plana vitrectomy in pediatric and inherited retinal diseases differs significantly from that in the general population, both in the procedure itself and the unique challenges it presents. Vitreoretinal surgeons face additional difficulties during surgical steps such as posterior hyaloid separation, and the chronic nature of RD in pediatric cases further complicates the procedure.[1] Vitreoretinal adhesion is even stronger in Knobloch syndrome, often making posterior hyaloid detachment nearly impossible without inducing new retinal breaks, thereby making the surgery very challenging. Additionally, ILM peeling is always an issue in high myopic eyes. Since the ILM is underdeveloped in young children, routine MH repair techniques are often insufficient, requiring additional measures such as the use of

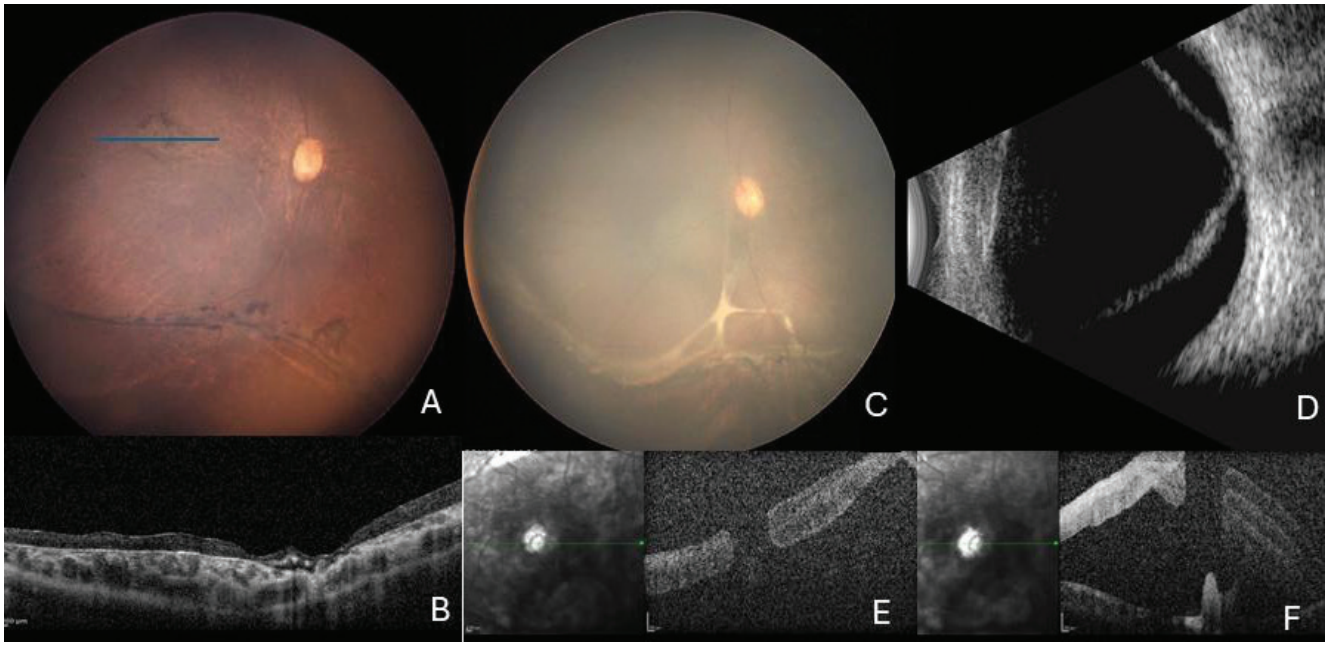

Figure 1. A) Colored fundus image of the right eye showing retinal pigmentary changes and central atrophy. B) Central optical coherence tomography (OCT) of the right eye showing the macular atrophy (cross-section from blue line in panel A). C) Fundus image of the left eye showing macula-off retinal detachment (RD) and inferiorly located thick subretinal bands. D) B-scan of the left eye revealing V-shaped total RD. E) OCT demonstrating macula-off RD with full-thickness macular hole in the left eye. F) Reopened macular hole 2 weeks after surgery in the left eye

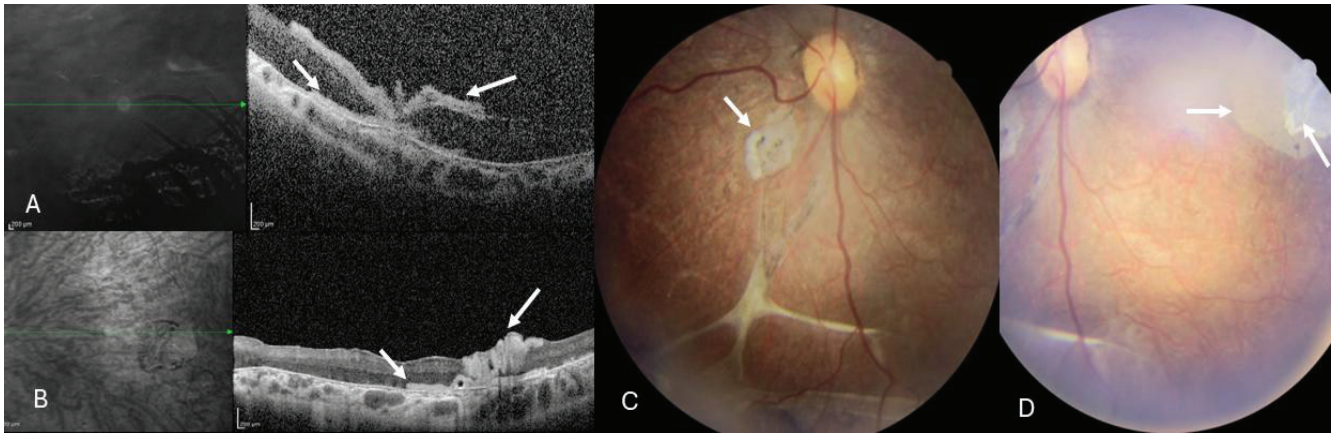

Figure 2. Optical coherence tomography images obtained 3 months (A) and 12 months (B) after the second surgery revealing attached retina with closure of the full-thickness macular hole sealed with inner and outer human amniotic membrane (hAM) grafts (arrows). C) Colored fundus image showing the retina is attached and the retinotomy is well-sealed with the hAM graft (arrow). Also note the residual subretinal bands inferiorly. D) Partial image of the macula (due to poor cooperation of the child) showing the closure of the full-thickness macular hole with 2 hAM grafts, one under and one over the macula (arrows)

a sealing material like hAM grafts. These grafts have been utilized successfully to treat challenging and recurrent RD cases associated with high myopic MH, yielding satisfactory visual and structural outcomes.[4] They are proposed to stimulate the regeneration of the exterior retinal layers, including the external limiting membrane and the ellipsoid zone, facilitating hole closure and leading to favorable visual and anatomical outcomes.[5] However, hAM grafts may migrate or contract, leading to failure of the surgery. A sub-neurosensory graft larger than the MH increases the likelihood of closure, but placing a larger graft under the retina requires more complex maneuvers and may risk damaging the RPE. Additionally, placing the graft with the chorionic surface facing the RPE is very important to achieve good adhesion, but it is not always easy to discriminate the correct side of the graft. In our experience, the risk of contraction is much higher when the graft is not placed in the proper orientation. If the graft is placed over the retina, then the risk of migration during or after the operation increases even more.

In the presented case, the first hAM graft probably contracted due to incorrect graft orientation. As a result, the graft could not seal the MH, leading to recurrent RD. During the second operation, a new technique of sandwich-like double layer grafting was attempted. A large hAM graft was placed under the MH, with another graft positioned over the hole, sandwiching the edges of the hole between the two layers. The hAM acts as a scaffold for tissue regeneration, potentially facilitating both MH repair and reattachment of the retina. The anti-inflammatory and anti-scarring properties of the membrane may also assist in reducing postoperative complications. Some studies have recommended subretinal placement of hAM with an aim to promote RPE regrowth,[6] while others suggest that epimacular grafts may offer better outcomes.[7] The combined use of both grafts may stimulate a dual process which could assist stronger healing. However, a potential disadvantage might be slightly impaired macular function due to the double-layered graft. Therefore, this double-layer sandwich technique may be reserved for challenging MH cases associated with high myopia and RD. To the best of our knowledge, this is the first case in the literature treated with this technique.

Ethics

Informed Consent: Obtained.

Declarations

Authorship Contributions

Surgical and Medical Practices: Ş.Ö., E.Ö.Z., Concept: O.O.A., Ş.Ö., E.Ö.Z., Design: E.Ö.Z., Ş.Ö., Data Collection or Processing: O.O.A., E.Ö.Z., Analysis or Interpretation: O.O.A., Literature Search: O.O.A., Writing: O.O.A., E.Ö.Z., Ş.Ö.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Knobloch WH, Layer JM. Retinal detachment and encephalocele. J Pediatr Ophthalmol Strabismus. 1971;8:181-184.
2. Sertié AL, Sossi V, Camargo AA, Zatz M, Brahe C, Passos-Bueno MR. Collagen XVIII, containing an endogenous inhibitor of angiogenesis and tumor growth, plays a critical role in the maintenance of retinal structure and in neural tube closure (Knobloch syndrome). Hum Mol Genet. 2000;9:2051-2058.
3. Alsulaiman SM, Al-Abdullah AA, Alakeely A, Aldhibi H, Engelbrecht L, Ghazi NG, Mura M. Macular hole-related retinal detachment in children with knobloch syndrome. Ophthalmol Retina. 2020;4:498-503.
4. Alzaben KA, Mousa A, Al-Abdi L, Alkuraya FS, Alsulaiman SM. Surgical outcomes of retinal detachment in knobloch syndrome. Ophthalmol Retina. 2024;8:898-904.

5. Caporossi T, Tartaro R, Bacherini D, Pacini B, De Angelis L, Governatori L, Di Leo L, Oliverio L, Rizzo S. Applications of the amniotic membrane in vitreoretinal surgery. J Clin Med. 2020;9:2675.
6. Capeáns C, Piñeiro A, Pardo M, Sueiro-López C, Blanco MJ, Domínguez F, Sánchez-Salorio M. Amniotic membrane as support for human retinal pigment epithelium (RPE) cell growth. Acta Ophthalmol Scand. 2003;81:271-277.
7. Moharram HM, Moustafa MT, Mortada HA, Abdelkader MF. Use of epimacular amniotic membrane graft in cases of recurrent retinal detachment due to failure of myopic macular hole closure. Ophthalmic Surg Lasers Imaging Retina. 2020;51:101-108.

Video 1. Displaying the details of both operations and the outcomes sequentially

https://www.youtube.com/watch?v=UkaPaXKlF8U&feature=youtu.be