Case Report

Ocular Surface Disease in a Young Boy with Laryngo-Onycho-Cutaneous Syndrome: A Case Report

PJO – Official Journal of Ophthalmological Society of Pakistan

Saman Gulzar[1], Shehr Bano Abbas[2], Hajra Arshad Malik[3], Najia Uzair[4]
[1-4]Al-Shifa Trust Eye Hospital, Rawalpindi

ABSTRACT

Laryngo-Onycho-Cutaneous (LOC) syndrome is a rare variant of autosomal recessive junctional epidermolysis bullosa (JEB), predominantly affecting individuals from consanguineous families within the Muslim Punjabi community. A 12-year-old boy presented with a progressive decline in visual acuity over four years, accompanied by photophobia and excessive tearing. His visual acuity was severely impaired, with light perception in the right eye and 6/60 vision in the left eye. Slit-lamp biomicroscopy revealed symblepharon in both eyes, corneal conjunctivalization, and restricted ocular motility in all directions. Systemic examination identified additional features, including nail clubbing, cheek ulcerations, stridor, hoarseness, vitiligo, and dental anomalies. The patient underwent symblepharectomy with an amniotic membrane graft. Cycloplegic refraction was performed 1 month postoperatively which resulted in considerable improvement in visual acuity and symptomatic relief

Keywords: Symblepharon, Amniotic membrane Graft, Laryngo-Onycho-Cutaneous syndrome.

How to Cite this Article: Gulzar S, Abbas SB, Malik HA, Uzair N. Ocular Surface Disease in a Young Boy with Laryngo-Onycho-Cutaneous Syndrome: A Case Report. 2025;41(3):328-330. **Doi:** 10.36351/pjo.v41i3.2007

Correspondence: Shehr Bano Abbas
Al-Shifa Trust Eye Hospital, Rawalpindi
Email: saimasalarabbas@gmail.com

Received: January 14, 2025
Revised: April 28, 2025
Accepted: April 30, 2025

INTRODUCTION

Laryngo-onycho-cutaneous (LOC) syndrome was first described in 1986 by a Pakistani dermatologist Dr. Ghulam Shabbir, who identified the condition in 22 children from 12 Punjabi Muslim families.[1] This disorder is marked by an altered vocal cry at birth, along with cutaneous erosions, nail dystrophy, and the excessive development of granulation tissue that leads to lesions in the conjunctiva and larynx. In early childhood, the affected individuals display erosive lesions on the face, conjunctivae, and dental abnormalities, accompanied by minimal blister formation but extensive development of granulation tissue. The conjunctival lesions result in symblepharon and palpebral occlusion, often causing blindness, which distinguishes this variant from other JEB subtypes.[2]

The condition arises due to genetic mutations in the LAMA3 gene, which encodes a component of the laminin protein complex. The laminin 332 protein is essential for enhancing the structural integrity and stability of the skin by enabling the firm attachment of the epidermis to the underlying tissue layers. The laminins containing the altered subunits are unable to efficiently anchor the epidermis to the underlying skin layers or effectively regulate the wound healing process. The genetic defects in laminin 332 cause the key manifestations of Shabbir syndrome, including skin erosions, excessive granulation tissue, and nail and dental anomalies.2In the majority of cases, JEB-LOC is attributed to a homozygous recessive mutation in the LAMA3A gene, causing shortening of a crucial segment at the N-terminus of the alpha 3 subunit within the laminin-332 protein complex.[3,4]

Case Presentation

A12-year-old boy presented to the Pediatric Ophthalmology Department with progressive

reduction in visual acuity for four years, accompanied by photophobia and excessive tearing. The patient had best corrected visual acuity of light perception in the right eye and 6/60 in the left. Examination of the anterior and posterior segment was hindered by limited visibility. Slit-lamp biomicroscopy revealed symblephara in both eyes, corneal conjunctivalization, and restricted eye movements in all directions. Systemic examination showed nail clubbing, ulcerations on skin of cheek, stridor, hoarse voice, vitiligo, and dental anomalies. The patient was referred to the dermatologist for management.

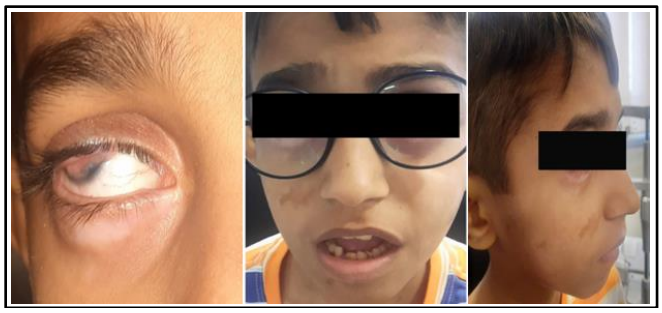

Figure 1(A): Symblepharon; **(B):**Ulcerative lesion on the right cheek and dental anomalies; **(C):** Ulcerative lesions on the right cheek.

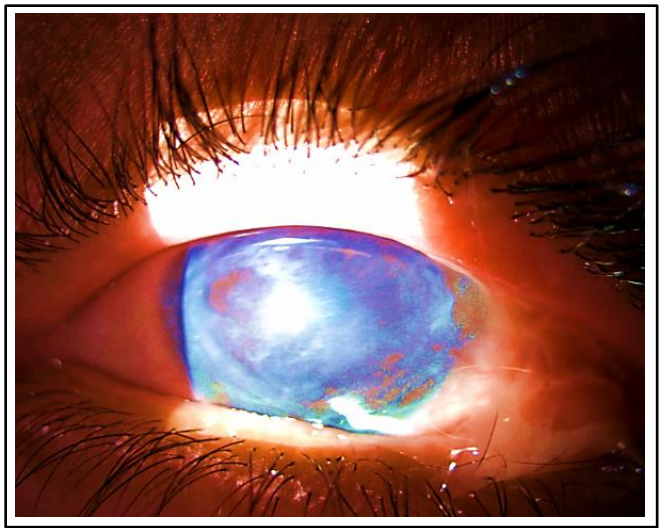

Figure 2: Bandage contact lens (BCL) and Amniotic membrane graft (AMG) on first post-operative day.

Symblepharectomy with an amniotic membrane graft (AMG) was performed. The surgical approach involved excision of abnormal granulation tissue from the conjunctiva, cornea, and fornices. Corneal dissection and superficial keratectomy were performed. The cornea was then covered with a double-layered AMG, placed with epithelial surface oriented upward and secured using 10-0 nylon sutures. Postoperatively, the patient was prescribed tobramycin 0.3% and moxifloxacin 0.5% eye drops every two hours, coupled with lubricants and a large-diameter bandage contact lens (BCL). The BCL and AMG were well placed on the first postoperative day. The BCL was subsequently removed 1 week postoperatively, and the frequency of the medications was reduced to four times a day.

Cycloplegic refraction was performed one month postoperatively which improved visual acuity from 20/200 to 20/120, with significant symptomatic relief. However, at the 2-month postoperative visit, regrowth of granulation tissue was observed in the temporal area, and the frequency of steroid administration was increased. A symblepharectomy with an AMG is planned in the fellow eye.

DISCUSSION

Laryngo-onycho-cutaneous (LOC) syndrome is an extremely rare disorder, with fewer than 50 documented cases worldwide.[5] The condition is characterized by the chronic formation of vascular granulation tissue, which infiltrates and compromises specific epithelial structures, particularly the conjunctiva, anterior corneal epithelium, and respiratory mucous membranes. Many affected individuals succumb to respiratory complications in childhood, while survivors often experience vision impairment and require tracheostomy.

The underlying genetic cause of LOC syndrome is a mutation in exon 39 of the LAMA3 gene, which delays the initiation of translation. The LAMA3A gene's initial exon encodes the laminin α3a subunit, a key component of the laminin 5 protein complex.[6] Laminin 5 is a critical basement membrane protein uniquely synthesized by basal keratinocytes in the skin and other multilayered epithelial structures, including those of the respiratory tract and ocular surface.[4]

Previous therapeutic approaches employing a range of immunomodulatory and anti-inflammatory pharmacotherapies, such as anti-tubercular drugs, corticosteroids, cyclophosphamide, dapsone, cyclosporine, mitomycin, thalidomide, and 5-fluorouracilhave demonstrated limited to partial effectiveness.[7,8] The rationale for this therapeutic approach is to suppress the inflammatory pathways,

and preliminary findings indicate a reduction in inflammation and vascularity of the granulation tissue on the ocular surface. Amniotic membrane transplantation has been utilized to mitigate ocular fibrosis and cicatrization. In the present case, we also performed a symblepharectomy procedure with AMG, which was successful.

A limitation of this case report is the absence of genetic analysis due to resource constraints.

CONCLUSION

This case highlights the characteristic ocular and systemic manifestations of Laryngo-Onycho-Cutaneous (LOC) syndrome, a rare autosomal recessive variant of junctional epidermolysis bullosa (JEB). The progressive nature of ocular involvement underscores the importance of early diagnosis and intervention. Surgical management, including symblepharectomy with an amniotic membrane graft, can significantly improve visual acuity and alleviate symptoms, enhancing the patient's quality of life.

Patient's Consent: Researchers followed the guide lines set forth in the Declaration of Helsinki.

Conflict of Interest: Authors declared no conflict of interest.

REFERENCES

1. **Shabbir G, Hassan M, Kazmi A.** Laryngo-onycho-cutaneous syndrome: a study of 22 cases. Biomedica. 1986;**2:**15-25.
2. **Cohn HI, Murrell DF.** Laryngo-onycho-cutaneous syndrome. Dermatol Clin. 2010 Jan;**28(1):**89-92. Doi: 10.1016/j.det.2009.10.010.
3. **Ullah A, Syed F, Khan S.** c.151dup variant in*LAMA*3 in Pakistani patients affected with Shabbir Syndrome but showing mild symptoms. Pak J Med Sci. 2023;**39(4):**1124-1128. Doi: 10.12669/pjms.39.4.6926.
4. **McLean WH, Irvine AD, Hamill KJ, Whittock NV, Coleman-Campbell CM, Mellerio JE, et al.** An unusual N-terminal deletion of the laminin alpha3a isoform leads to the chronic granulation tissue disorder laryngo-onycho-cutaneous syndrome. Hum Mol Genet. 2003;**12(18):**2395-2409. Doi: 10.1093/hmg/ddg234. Epub 2003 Jul 15. Erratum in: Hum Mol Genet. 2004 Feb 1;13(3):365.
5. **Prodinger C, Chottianchaiwat S, Mellerio JE, McGrath JA, Ozoemena L, Liu L, et al.** The natural history of laryngo-onycho-cutaneous syndrome: A case series of six pediatric patients and literature review. Pediatr Dermatol. 2021;**38(5):**1094-1101. Doi: 10.1111/pde.14790.
6. **Barzegar M, Mozafari N, Kariminejad A, Asadikani Z, Ozoemena L, McGrath JA.** A new homozygous nonsense mutation in LAMA3A underlying laryngo-onycho-cutaneous syndrome. Br J Dermatol. 2013;**169(6):**1353-1356. Doi: 10.1111/bjd.12522.
7. **Song D, Wang S.** A Child with Hoarseness and Recurrent Cheek Erosions: A Quiz. Acta Derm Venereol. 2024;**104:**adv31737. Doi: 10.2340/actadv.v104.31737.
8. **Figueira EC, Crotty A, Challinor CJ, Coroneo MT, Murrell DF.** Granulation tissue in the eyelid margin and conjunctiva in junctional epidermolysis bullosa with features of laryngo-onycho-cutaneous syndrome. Clin Exp Ophthalmol. 2007;**35(2):**163-166. Doi: 10.1111/j.1442-9071.2006.01436.x.

Authors Designation and Contribution

Saman Gulzar; Postgraduate Trainee: *Concepts, Design, Literature Search, Data Acquisition, Data Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Shehr Bano Abbas; Postgraduate Trainee: *Concepts, Literature Search, Data Acquisition, Data Analysis, Manuscript Preparation, Manuscript Editing, Manuscript Review.*

Hajra Arshad Malik; Postgraduate Trainee: *Concepts, Literature Search, Data Acquisition.*

Najia Uzair; Assistant Professor: *Concepts, Literature Search, Manuscript Editing, Manuscript Review.*