Case Report

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Visual rehabilitation in laryngo-onycho-cutaneous (LOC) syndrome

Abstract

Background: Laryngo-onycho-cutaneous syndrome (LOC) is a sub type of Junctional Epidermolysis Bullosa (JEB). Patients, who are mostly from the Punjabi Muslim population, exhibit a homozygous recessive mutation in the LAMA3 gene with subsequent N-terminal deletion of the laminin α3a isoform. Ocular involvement with extensive granulation tissues often results in intractable blindness early in life.

Case report: A male Punjabi patient suffered from a LOC syndrome and subsequent progressive ocular surface disease. At the age of one, he presented with bilateral symblephara. Repeated excision of granulation tissues managed to keep his central cornea clear for a considerable period of time. Different immunosuppressant agents were tried to stop recurrence followed by three amniotic membrane grafts with no long term success. At the age of 19, patient had osteo-odonto-keratoprosthesis (OOKP) surgery done for his left eye, which successfully restored his vision to 6/9.

Conclusion: We are reporting the first patient with LOC syndrome who had his vision successfully restored following surgical intervention. OOKP remains the last resort for visual rehabilitations in cases with severe dry eyes where all other surgeries doomed to fail. We recommend a combined approach for patients with LOC syndrome, which involves early granulation tissues debridement and ocular surface reconstruction, which can be repeated as needed, to be followed by OOKP surgery at the age of 18. Surgical care of these patients should be done in one of the specialist centres, where complexity of such cases could be handled, and patients should be counselled on the need for life-long follow up.

Keywords: LOC syndrome, LOGIC syndrome, JEB, OOKP

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Abbreviations: LOC, laryngo-onycho-cutaneous syndrome; JEB, junctional epidermolysis bullosa; OOKP, osteo-odonto-keratoprosthesis

Visual rehabilitation in LOC syndrome

Background

Laryngo-onycho-cutaneous syndrome (LOC) is a subtype of Junctional Epidermolysis Bullosa (JEB).[1] This rare autosomal disorder was first described by Shabbir in 1986.[2] Patients, who are mostly from the Punjabi Muslim population, exhibit a homozygous recessive mutation in the LAMA3 gene with subsequent N-terminal deletion of the laminin α3a isoform. Miscommunication between basal keratinocytes, where laminin α3a is produced, and the mesenchyme is postulated to be the main mechanism of the disease. The tissue localization of the laminin α3a corresponds to the clinical manifestations of LOC.[1,3] In a recent study, conjunctival granulation tissue was found to be mainly fibroblastic in origin and to have reduced p63 expression. This supports the Keratinocyte-Mesenchymal miscommunication theory.[4]

Clinically, neonates with LOC syndrome presents soon after birth with a hoarse cry. They develop extensive granulation tissue in the mucosal regions, nail bed and the larynx. In later life, they develop skin ulcers and ocular involvement which often leads to intractable blindness. The conjunctival lesions usually start temporally, with subsequent symblepharon and local adhesions which can result in total palpebral occlusion. Patients also have marked dental hypoplasia due to failure of tooth enamel formation. Many patients diagnosed with LOC syndrome do not live beyond childhood, the most common cause of premature death being acute or chronic respiratory obstruction with secondary pulmonary sepsis. However, patients who survive the early neonatal period often survive to adulthood and symptoms of hoarseness and ulceration slowly improve with age. As granulation tissue accumulates in the larynx, a permanent tracheostomy often becomes necessary to ensure a clear respiratory passageway.[1–3,5] Clinical criteria for diagnosis of LOC syndrome can be found in Table 1.[3]

Table 1 Clinical Criteria for diagnosis of LOC syndrome

Sl no	Clinical Criteria for diagnosis of LOC syndrome[3]
1	Hoarse cry in first few weeks of life or evidence of laryngeal granulation tissue, scarring or stenosis in the first few years of life.
2	Nail dystrophy
3	Ocular involvement including aggressive conjunctival pannus formation.
4	Dental anomalies (hypodontia, poor enamel formation, excessive caries)
5	Slow-healing cutaneous erosions.
6	Absence of a history of skin fragility or blistering at any stage

Case report

A male Punjabi patient suffered from a LOC syndrome and subsequent progressive ocular surface disease. He was born in Northern Ireland to parents who are first cousins. At the age of one, he presented with bilateral symblephara. Prior to this, he had had several problems in the form of multiple subungual granulomata (Figures 1 & 2) and his umbilicus has taken over 6 months to heal after birth. Initial examination under anaesthesia revealed extensive granulation tissues growing from both upper and lower fornices which resulted in adhesion of lids to the external eye. Repeated excision of granulation tissues managed to keep his central cornea clear for a considerable period of time. He was seen by an immunologist who tried multiple immunosuppressants including mitomycin, topical cyclosporin and even thalidomide with no effect. He underwent an emergency tracheostomy because of laryngeal granulomata. Three amniotic membrane grafts were done to stop recurrence of granulation without long term success. In 2003, examination under anaesthesia was carried out at Moorfields Eye Hospital, London. Obliteration of fornices was detected in both sides with the left side being severely affected. Impression cytology was done and showed dry eye-related conjunctival squamous metaplasia, more prominent in the left eye. No further action was taken at that time as the prognosis of any further reconstructive surgery was doomed to failure due to severe tear deficiency and recurrent granulation tissue growth. He was counselled about future keratoprothesis surgery and asked to see a specialist dentist to keep his oral hygiene.

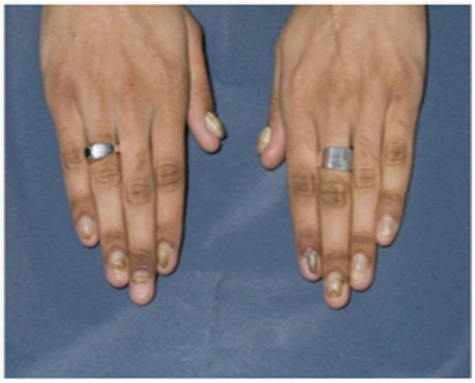

Figure 1 Patient's nails showing dystrophy (extraocular features of LOC syndrome).

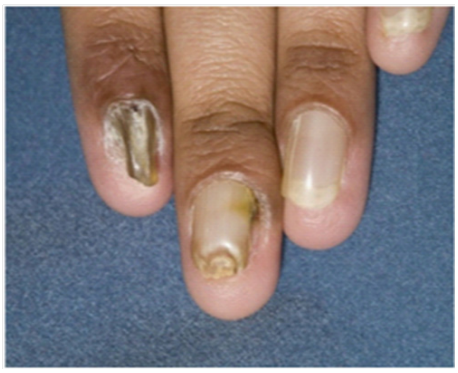

Figure 2 Patient's nails showing dystrophy (extraocular features of LOC syndrome).

In 2008, aging 19, he was seen at the Sussex Eye Hospital, Brighton, the UK national referral centre for OOKP surgery for initial consultation. Examination revealed counting finger vision right and perception of light vision left with accurate projection in all four quadrants in both eyes. Though showing extensive symblepharon (Figure 3), some view of his cornea was possible. Both eyes were dry with the left being bone dry. The right eye IOP was normal to palpation whereas the left eye felt firm. Ultrasound revealed axial lengths of 26.1 mm on the right and 25.9 on the left. Both eyes were phakic and were without retinal detachment. Following oro-surgical and psychological assessments, the decision was to prepare him for left eye OOKP surgery. Stage 1 OOKP surgery was done in Figures 4 (A&B); the right lower canine tooth was used. Scar tissues were removed from the ocular surface. Intraoperatively, the anterior chamber was found to be deep with a round pupil. The surface of the left eye was covered with mucous membrane harvested from the inside of the right cheek. The inside of the upper and lower lids were also relined. A conformer was placed and the patient asked to apply ointment through the central opening. Following stage 1 surgery it was difficult to retain the shell, and patient had to come down to Brighton to get it repositioned. He developed central thinning in mucous membrane which needed no further management. Three months later, Stage 2 OOKP surgery was done; the lamina was retrieved from the right lower lid and surgery was done as per OOKP protocol. Immediately following his stage 2 OOKP, he had severe photophobia which resolved over three months. Three months later he was able to see 6/24 part unaided correcting with glasses to 6/9 (Figure 5).

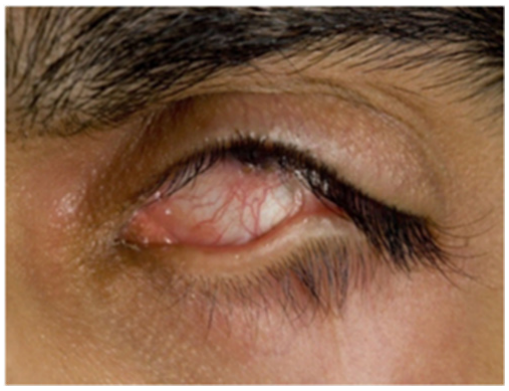

Figure 3 Left eye preoperative ocular appearance.

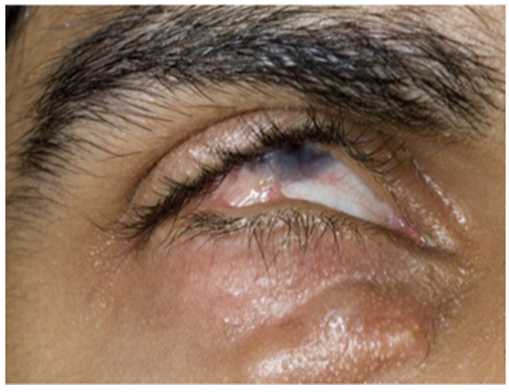

Figure 4 (A) Same patient following stage 1OOKP, Right eye (lamina in the lower lid).

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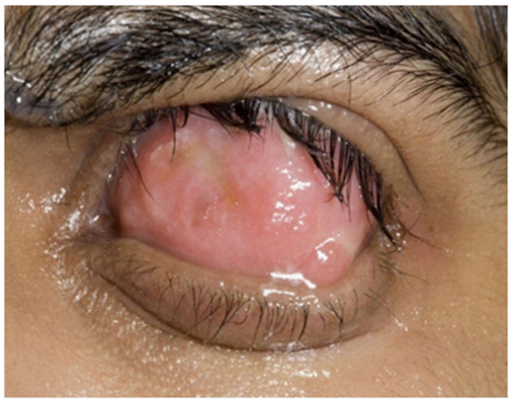

Figure 4 (B) Same patient following stage 1OOKP, Left eye (mucous membrane graft covering the ocular surface).

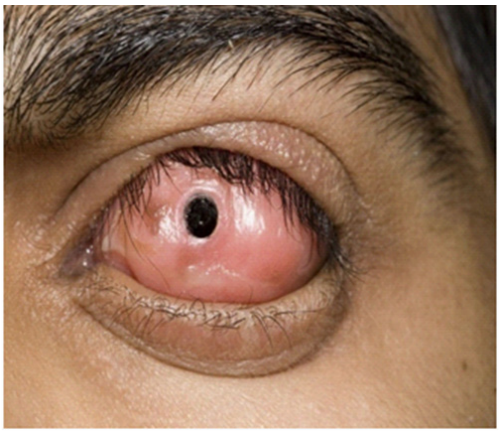

Figure 5 Left eye following stage 2OOKP.

Comment

OOKP surgery, using the patient's own tooth, remains the treatment of choice for visual rehabilitation in patients with end stage ocular surface disease with severe tear deficiency. It has the longest follow up reported among other keratoprothesis.[6,7] Specific issues which should be considered while preparing a LOC patient for OOKP surgery include patient age at time of surgery, tooth size and oral hygiene. OOKP surgery is not recommended for patients under 18 years of age to lessen rapid resorption of the lamina. LOC syndrome usually develops shortly after birth with the eye affected within the first year. The challenge will be to provide the patient with good vision to avoid deep amblyopia while awaiting OOKP surgery at a later stage. Thus while all surgeries done for our patient was doomed to fail, yet it provided him with the potential to have good visual acuity following OOKP surgery. Kadyan et al.,[8] reported their modified surgical technique of ocular surface reconstruction which has been tried in a cohort of 4 patients with LOC syndrome. Their technique involved meticulous removal of granulation tissues from the ocular surface. Dissection of tissues covering the corneal surface was facilitated by ethanol-assisted delamination and then superficial keratectomy. Coverage of the cornea and sclera can be achieved with either multiple layers of amniotic membrane grafts (AMG), typically 3 stacked one on top of the other, or sutureless AMG with ProKera implant (Bio-Tissue, Inc, Miami, FL).

They reported good success in relieving the ocular discomfort related to tethered lids with moderate visual improvement limited by corneal scarring. They also recommended concurrent immunomodulation with potent anti-tumor necrosis factor agent, Infliximab (Remicade, Centacor, Malvern, PA), with initial good response. Other immunosupressants which have been tried before did not show significant success.[8] We recommend a combined approach for patients with LOC syndrome, which involves early granulation tissues debridement and ocular surface reconstruction, which can be repeated as needed, to be followed by OOKP surgery at the age of 18. This approach can reduce the risk of deep amblyopia with good visual rehabilitation following OOKP surgery. Patients with LOC syndrome should learn to keep good oral hygiene at an early stage of their childhood. In our patient, the tooth size was not a hindrance for surgery, thus despite the small crown size the root was of good size. This was also noted in his preoperative x-ray. This is done routinely prior to scheduling any patient for OOKP surgery. Following OOKP surgery, patients will need lifelong follow-up with risk of complications which are mainly resorption and glaucoma. The risk can be more significant in LOC patients, if we consider their relative youth at time of surgery. On the other hand, survival of patients with LOC syndrome is also something to consider. Compared to our OOKP cohort, time needed for visual recovery in this patient was longer. We are reporting the first patient with LOC syndrome who had his vision successfully restored following surgical intervention. OOKP remains the last resort for visual rehabilitations in cases with severe dry eyes where all other surgeries doomed to fail. Surgical care of these patients should be done in one of the specialist centres, where complexity of such cases could be handled, and patients should be counselled on the need for life-long follow up.

Acknowledgments

None.

Conflicts of interest

Author declares that there is no conflict of interest.

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