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**Case Report**

# Pediatric Keratoplasty: The Success of a Tailor-Made Surgical Management

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**Keywords**
Penetrating keratoplasty · Pediatrics · Congenital opacities · Adult graft

**Abstract**
A Romanian 5-month-old girl was referred to our hospital after being diagnosed with congenital corneal opacities. She was sent in order to undergo penetrating keratoplasty (PKP) surgery on her left eye. The patient presented a natural tendency to esotropia. We took into account two different surgical techniques: PKP and lamellar keratoplasty. The latter was technically impossible to carry out because of the full-thickness corneal opacity. We conducted several tests to accurately obtain the patient's preoperative parameters and specifically decide the details of the surgical technique to be applied. For each step of the surgical procedure we carefully compared the individual results in the literature in order to ensure a stable and lasting result. In addition to this, we used an innovative suture technique: nylon thread, interrupted suture, alternating 11-0/10-0 threads. Six months after the operation, the functional result obtained was 4–5/10, with recovery of the fixation. Pediatric PKP, therefore, cannot follow a surgical standard, but requires careful case-by-case evaluation from the pre- to the postoperative phase, with the aim of maximizing stable visual acuity.



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## Introduction

Congenital corneal opacities (CCO) are a rare abnormality of the eye. According to the published literature, the reported prevalence of CCO is 6 in 100,000 newborns. The importance of making the correct diagnosis goes without saying; nevertheless, it is of vital importance to have a data sharing network between the centers that manage the above-mentioned disease. The common goal should be to shorten the lag time between the onset of symptoms and the diagnosis and to shorten the preparation time before surgery; this would lead to minimization of the risk of developing lifelong visual impairment.

## Case Presentation

A Romanian 5-month-old girl was referred to our hospital after being diagnosed with CCO in her country of origin. She was sent to the University Clinic of Ophthalmology of Turin in order to undergo penetrating keratoplasty (PKP) surgery on her left eye. We performed a complete physical examination of the patient through autorefractor, puff tonometer, slit lamp examination, as well as direct and indirect ophthalmoscopy under anesthesia. We managed to carry out the whole examination only on the left eye, which was emmetropic; the right eye had such a significant opacity as to prevent a complete analysis. Upon examination, the left eye, the healthy one, had a corneal diameter within the limits of age, 12.5 mm, pupil reflexes were normal, and the red fundi reflex was present. The right eye had a complete full-thickness corneal opacity; its diameter measured 10 mm and there were no irregularities detectable on the surface. Because of the complete corneal opacity, we were not able to explore the remaining structures. In both eyes there were no structural abnormalities of the ocular adnexa; there was no sclerocornea in the nasal sectors. The patient presented a natural tendency to esotropia; this is why during the preoperative phase, we informed the parents that one of our aims was to make the patient regain, through specific exercises, visual fixation. The patient's tendency to esotropia is not sufficient to uniquely determine the diagnosis of strabismus, but must be considered a wake-up call for the development of amblyopia.

We took into account two different surgical techniques: PKP and lamellar keratoplasty. The latter was technically impossible to carry out because of the full-thickness corneal opacity. PKP was the only technique that could lead to the achievement of the objectives set. The donator was a 27-year-old man. In order to preserve our patient's visual acuity (VA) and avoid the risk of her developing amblyopia, we did not wait for a younger donator. The donor's graft was 6.5 mm, the recipient's bed was 6 mm. The reason for the 0.5-mm difference was to ensure the possibility of growth of the patient's bulb (only 5 months), despite controversies in the literature, and to avoid subsequent surgery or postoperative ocular hypertension.

The whole surgery lasted 60 min. The operating room had been equipped so that we could carry out intraoperative optical coherence tomography (OCT) to confirm the full-thickness corneal opacity. The use of OCT also allowed to check the point of contact between the graft and the receiving cornea to verify correct positioning. During the operating session, the transplant was centered, the patient's iris was regular, there were no signs of Rieger's syndrome, there was a sustained positive vitreous pressure, and the crystalline was transparent. To avoid positive vitreous pressure, we administered mannitol. To avoid postoperative ocular hypertension, we performed iridectomy at 1 o'clock and we chose a viscoelastic with specific characteristics such as no proven correlation with postoperative hypertonicity. After the graft had been centrally placed, we sutured it with an interrupted suture using a nylon thread, alter-

nating 11-0/10-0 threads. The position of the detached points between donor and recipient was adjusted to reduce residual corneal astigmatism. For the calculation of residual astigmatism, an objective examination under anesthesia will be necessary with subsequent prescription of lenses for its correction. In our case, the residual astigmatism was assessed with the operating microscope resulting regular and low grade. Once the sutures were done, we performed another intraoperative OCT of the anterior segment to check the possible remaining astigmatism. The donator's graft was regular without a significant astigmatism.

The first day after surgery there were no reactions of any sort: the donor's graft was well connected to the recipient's bed, the anterior chamber was formed, the lens was in place, and the red fundi reflex was present. The patient's postoperative treatment included netilmicin + dexamethasone (1 drop 3 times a day), dorzolamide (1 drop 3 times a day per the first 7 days and then 1 drop every other day for another 7 days). To avoid the patient from touching her eye we wrapped a dressing over it for 24 h. Then we replaced the bandage with a little plastic cup. During the second day after surgery the eye was exactly like the day before, there were no signs of complications. At the 1-week follow up visit the patient had lost the tendency to touch her eye, there were no signs of reactions of any sort, the graft was always well supported, and all the remaining structures were within normal limits. During the visit we explained to the patient's family the management to regain fixation with the right eye. We gave them a covering plaster to put on the left eye for an increasing amount of time: first 4, then 6, then 8 h, up to 10 h a day within 1 month of surgery.

We performed another visit 20 days after surgery: the patient had a 3/10 VA in the operated eye. At the 1-month visit the improvement of the preferential VA reached 4/10. At the 4-month follow-up visit the patient's VA was 4–5/10; since the latter examination, the patient had been treated with dorzolamide (1 drop per day) and clobetasol (2 drops per day).

## Discussion

The patient was 5 months old when she reached our health center; she had already been diagnosed with CCO, nevertheless we confirmed the diagnosis. In the literature there is no unique consent on which is the best age to perform keratoplasty surgery, although it is of vital importance to predict the patient's prognosis. Some authors reported a lower graft survival in patients who were <5 years old when keratoplasty surgery was performed [1]. On the other hand, other authors suggest that, in terms of survival, there are no differences between patients who underwent surgery before the first year of age and those who were >1 year old at the time of surgery [2]. Lin et al. [3] are among the few authors who considered in his study functional success as an outcome instead of survival rate: through their analysis they conclude that, considering visual activity as an outcome, the earlier keratoplasty surgery is performed the better.

PKP in infants and toddlers is extremely challenging because of the elastic sclera, the shallow anterior chamber, the smaller size of the eyeball, and the risk of lens-iris diaphragm anterior displacement during surgery because of positive vitreous pressure. In addition to the technical difficulties of keratoplasty, there are other elements that worsen the outcomes when keratoplasty is performed in adults rather than in children, e.g., the more robust adaptative immune system. This often implies rapid graft rejection; the almost instantaneous and ferocious inflammatory response, along with a robust fibrin reaction, often results in significant scarring with subsequent ocular surface irregularity and instability [4]. Despite these difficulties, surgery is the first-line treatment of CCO in order to ensure the patient's VA [5].

According to Miao et al. [6], PKP is inevitable in all those cases in whom corneal opacity does not allow the surgeon to explore all the structures of the eye. For instance, the red fundi reflex indicates that the nervous structures receive the external luminous signals; this is of vital importance for the correct development of VA in the affected eye. Our patient met the latter eligibility criteria.

Furthermore, we looked for signs of vascularized cornea, intraocular inflammation, presence of glaucoma, presence of sclerocornea, and a possible need of different simultaneous surgery. These signs have been proved to be related with worse outcomes; none of them were present in our patient [7]. It is of vital importance to assess the absence of sclerocornea in the preoperative phase because it is one of the most negative prognostic factors [7] as well as a sign of other conditions such as Peter's anomaly and Rieger's syndrome. In fact, patients with unilateral sclerocornea have lower outcomes and worse deprivation amblyopia [3]. Besides CCO our patient tended to esotropia, which is the most important indication to start therapy against amblyopia. Some authors underline how the presence of visual asymmetry was found to have a statistically significant association with the development of strabismus ($p = 0.002$); esotropia was the main diagnosis [8]. In these patients the goal is to surgically provide a clear pupil (which may require PKP), frequent refractions, as well as early and aggressive amblyopia therapy. In fact, between the fifth and sixth month of life, the incoordination of the extrinsic ocular musculature gradually disappears; because of the high risk of amblyopia, it is therefore important to start treatment as soon as possible [8].

In the literature the outcomes of pediatric PKP surgery are heterogeneous [3, 5]. Previous research showed that 32.6–78.6% of grafts performed for CCO remain clear for >1 year [5]. However, when stratification criteria are applied, for example the underlying disease and the age of the patient, the outcomes are very different.

Advances in lamellar keratoplasty techniques have made the use of this method of corneal transplantation in children possible [9]. We did not choose to perform deep anterior lamellar keratoplasty (DALK) surgery due to the full-thickness opacification of the cornea. DALK surgery has specific pediatric complications to consider: the risk of displacement of the anterior lamella during growth, in addition to technical difficulties due to pediatric anatomy [9]. From these complications it may become necessary to carry out a second replacement of the displaced lamella or to proceed with a PKP [10]. DALK is not the only alternative to PKP in children. Because of the promising results seen in Descemet stripping endothelial automated keratoplasty (DSEAK) for diseases characterized by endothelial dysfunction such as pseudophakic bullous keratopathy and failed grafts, DSEAK offers advantages over PKP in terms of fewer postoperative astigmatism, decreased risk of suture-related complications, and quicker visual rehabilitation with lower risk of amblyopia [11]. The functional results obtained using these techniques are comparable with those obtained with PKP [12], but the surgery indications for the former are restricted and our patient did not meet them. Our patient did not present corneal decompensation but a diffuse congenital full-thickness opacification of the cornea, thus DSEAK or Descemet membrane endothelial keratoplasty were not indicated. Therefore, we decided to carry out keratoplasty surgery. In addition to this, it was our experience that made us lean towards the decision to perform PKP: the casuistry of our center showed a greater risk of displacement and thus of complications in superficial grafts transplanted with a lamellar technique.

The multitude of different results, as for graft survival, reflects the variety of clinical presentations of patients requiring PKP or DALK intervention [12]. It is essential that in the setting and preparation of the surgery phase the main operator assess all the patient's distinctive features; by careful examination of the anatomical details, all the variants of the different

surgical steps to be performed can be weighted [3, 5]. It is precisely through this careful analysis that the nonoptimal results presented in the literature can be improved. Pediatric keratoplasty surgery cannot be presented only with an all-inclusive guideline that unambiguously clarifies the technique with the greatest success; the surgeon must be ready to vary his technique and adapt it to the individual patient.

PKP or DALK are both the interventions of choice in the event of failure or abnormal growth of the eye. Studies with a very long follow-up (>5 years) [10] highlight how the need to reoperate for rejection and graft failure reaches 25–45% depending on cases. In these patients, reoperation greatly reduces the survival of the second transplanted graft and reduces it even more for the third implant [13]. This is why it is essential to ensure maximum longevity for the first intervention.

The first detail that must be checked is the compatibility between the donor and the recipient. In the literature there are no works that assess the need of an anagraphic compatibility; this supports our decision to accept a 27-year-old donator for our patient. Once the donator has been identified, the correct preparation of the graft requires a dimensional difference in favor of the donator: such precaution ensures a better outcome. In a prospective, nonrandomized clinical trial in which donor corneal buttons oversized by 1 mm were grafted in 40 pediatric patients with a variety of uni- or bilateral corneal diseases [14], 85% of these grafts remained clear and provided adequate anterior chamber depth, helping to prevent post-keratoplasty glaucoma. A multicenter study reports a wide range of donor and recipient characteristics, with graft sizes ranging from 5.5 to 12.0 mm (mean 7.6 mm) and host bed size ranging from 5.0 to 11.0 mm for recipients (mean 7.1 mm). Moreover, it reports tissue-donor age ranging from 1 to 41 years, with an endothelial cell count ranging from 2,200 to 4,600 cells/mm$^2$ [15]. The best explanation for this difference seems to be that fewer endothelial cells migrate from smaller grafts, leading to graft failure. In the literature the most frequent difference in the grafts' dimensions is between 0.5 and 1.0 mm [4] or between 0.25 and 0.5 mm [2]. For the aforementioned reasons, after calculating the growth prospects of the bulb, we decided to use a 6.5-mm graft against the 6.0 mm of the receiving host bed. We furthermore believe that use of a bigger graft not only leads to better outcomes, but by ensuring a deeper anterior chamber and an easier outflow, it also prevents the development of intraocular hypertension in the postoperative phase. The present literature does not clarify the growth possibilities of the human bulb [16]. The various models for predicting corneal size at the end of growth show inaccuracies due to marked interpersonal variety [16]. The authors agree that neonatal corneal growth is, in reality, the strong slowdown of the fetal one; they also agree that the end of the growth is in any case towards the first year of life [16], therefore in our case, at 5 months, it had to still be planned in the preoperative phase. This underlines how tailor-made management of the individual patient can make a difference.

To avoid intraoperative hypertension, we administered mannitol and used an appropriate viscoelastic. To avoid postoperative hypertension, use of an oversized graft is not the only method; a helpful decision could be the execution of prophylactic iridectomy. In fact, what causes intraocular postoperative hypertension is the development of peripheral anterior synechiae. Although many authors choose not to perform iridectomies [17], some studies reported the execution of three iridectomies [18]. We performed a single iridectomy (h XII).

Once the graft has been placed, the surgeon may proceed with its suture. We used an innovative suture technique: nylon thread, interrupted suture, and alternating 11-0/10-0 threads. In the literature many authors used interrupted sutures with a 10-0 nylon thread [2] for a total of 12–16 stitches [3].

Once surgery is over, we choose to administer netilmicin + dexamethasone + dorzolamide. In the literature many authors suggest a multidrug therapy which includes prednisolone, tobramycin, and dexamethasone; these should be continued until the stitches are removed. In addition to these, it is suggested to add full-dose topical calcineurin for the first 3 months and then taper the dose in the following 21 months [3].

The management of amblyopia aims to promote a uniform development of VA in both eyes. As mentioned before, our patient had a tendency to esotropia. While giving informed consent, we enlightened the patient's family as to the need to start a postoperative specific therapy in order to avoid amblyopia. The occlusion treatment was aimed at facilitating and supporting the correct development of the sensorineural pattern of the operated eye. The therapy performed consisted of covering the left eye (the healthy one) for an increasing amount of time: 4 h the first week, 6 h the second, 8 h the third. The fixation exercise intervals should be performed with the aid of rattles in order to attract the patient's glance. Apart from the procedures and the techniques used to prevent complications, all the authors agree on the fact that amblyopy reversibility should always be considered regardless of the patient's age [19]. Furthermore, visual improvement would promote global development even if the grafts failed 1 or 2 years after PKP.

At the follow-up 3 months after surgery, our patient already had a 3/10 VA on the right eye. At the 4-month follow-up visit her VA was 4–5/10. The achievement remained stable even after 6 months, as shown in Figure 1. Orthoptic treatment currently continues with 8 h of occlusion per day. Postoperative monitoring and continuation of the occlusion therapy are of fundamental importance to maintain the best visual recovery achieved.

## Conclusions

Correct evaluation of the surgical technique and all the associated details is of vital importance to ensure the best possible results. A tailor-made choice of surgical details and the presence of an experienced surgeon during the operation are key to obtaining successful outcomes, thus disproving the discouraging data currently published in the scientific literature. Pediatric PKP, therefore, cannot follow a surgical standard, but requires careful case-by-case evaluation from the pre- to the postoperative phase, with the aim of maximizing stable VA.

## Statement of Ethics

Informed consent for the procedure reported in this case report was obtained from the subject's parents in written form. In addition to this another informed consent for reporting the case and publishing the picture taken was signed by both parents. Our institution states that no formal ethical approval was needed for this case report.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

R. Nuzzi and A. Rossi contributed to the design of the research, to the analysis of the results, and to the writing of the manuscript.

## References

1 Waring GO 3rd, Laibson PR. Keratoplasty in infants and children. Trans Sect Ophthalmol Am Acad Ophthalmol Otolaryngol. 1977 Mar–Apr;83(2):283–96.
2 Huang C, O'Hara M, Mannis MJ. Primary pediatric keratoplasty: indications and outcomes. Cornea. 2009 Oct;28(9):1003–8.
3 Lin Q, Shi W, Miao S, Zhang Y, Li L, Pan Z. Visual Outcomes and Prognostic Factors of Successful Penetrating Keratoplasty in 0- to 7-Year-Old Children With Congenital Corneal Opacities. Cornea. 2018 Oct;37(10):1237–42.
4 Beauchamp GR. Pediatric keratoplasty: problems in management. J Pediatr Ophthalmol Strabismus. 1979 Nov–Dec;16(6):388–94.
5 Mun-Wei L, Md Said H, Punitan R, Ibrahim M, Shatriah I. Indications, Clinical Outcomes, and Survival Rate of Pediatric Penetrating Keratoplasty in Suburban Malaysia: A 10-year Experience. Cureus. 2018 Dec;10(12):e3744.
6 Miao S, Lin Q, Liu Y, Song YW, Zhang YN, Pan ZQ. Clinicopathologic features and treatment characteristics of congenital corneal opacity infants and children aged 3 years or less: a retrospective single institution analysis. Med Princ Pract. 2020;29(1):18–24.
7 Gregersen E. Keratoplasty in babies with sclerocornea. To do or not to do? Report of an unsuccessful case. Dev Ophthalmol. 1981;5:52.
8 Najjar DM, Christiansen SP, Bothun ED, Summers CG. Strabismus and amblyopia in bilateral Peters anomaly. J AAPOS. 2006 Jun;10(3):193–7.
9 Kim YW, Choi HJ, Kim MK, Wee WR, Yu YS, Oh JY. Clinical outcome of penetrating keratoplasty in patients 5 years or younger: Peters anomaly versus sclerocornea. Cornea. 2013 Nov;32(11):1432–6.
10 Hovlykke M, Hjortdal J, Ehlers N, Nielsen K. Clinical results of 40 years of paediatric keratoplasty in a single university eye clinic. Acta Ophthalmol. 2014 Jun;92(4):370–7.
11 Lee WB, Jacobs DS, Musch DC, Kaufman SC, Reinhart WJ, Shtein RM. Descemet's stripping endothelial keratoplasty: safety and outcomes: a report by the American Academy of Ophthalmology. Ophthalmology. 2009 Sep;116(9):1818–30.
12 Ashar JN, Madhavi Latha K, Vaddavalli PK. Descemet's stripping endothelial keratoplasty (DSEK) for children with congenital hereditary endothelial dystrophy: surgical challenges and 1-year outcomes. Graefes Arch Clin Exp Ophthalmol. 2012 Sep;250(9):1341–5.
13 Majander A, Kivelä TT, Krootila K. Indications and outcomes of keratoplasties in children during a 40-year period. Acta Ophthalmol. 2016 Sep;94(6):618–24.
14 Vajpayee RB, Ramu M, Panda A, Sharma N, Tabin GC, Anand JR. Oversized grafts in children. Ophthalmology. 1999 Apr;106(4):829–32.
15 Dana MR, Moyes AL, Gomes JA, Rosheim KM, Schaumberg DA, Laibson PR, et al. The indications for and outcome in pediatric keratoplasty. A multicenter study. Ophthalmology. 1995 Aug;102(8):1129–38.
16 Ronneburger A, Basarab J, Howland HC. Growth of the cornea from infancy to adolescence. Ophthalmic Physiol Opt. 2006 Jan;26(1):80–7.
17 Zhu AY, Marquezan MC, Kraus CL, Prescott CR. Pediatric Corneal Transplants: Review of Current Practice Patterns. Cornea. 2018 Aug;37(8):973–80.
18 Di Zazzo A, Bonini S, Crugliano S, Fortunato M. The challenging management of pediatric corneal transplantation: an overview of surgical and clinical experiences. Jpn J Ophthalmol. 2017 May;61(3):207–17.
19 Keech RV, Kutschke PJ. Upper age limit for the development of amblyopia. J Pediatr Ophthalmol Strabismus. 1995 Mar–Apr;32(2):89–93.

**Fig. 1.** Picture of the patient at 6-month follow-up during occlusion treatment.