Treatment of corneal dermoid with lenticules from small incision lenticule extraction surgery: a surgery assisted by fibrin glue

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Abstract

AIM: To observe the clinical efficacy of the combined use of small incision lenticule extraction (SMILE)-derived lenticule patches in corneal dermoid excision, with fixation of the lenticule patches assisted by fibrin glue.

METHODS: Seventeen eyes of 17 patients with corneal dermoid were treated with dermoid removal combined with SMILE-derived lenticule transplantation. All lenticule patches were fixed by fibrin glue. Ocular changes were assessed using slit lamp microscopy and anterior-segmental optical coherence tomography. The best-corrected visual acuity (BCVA) and ocular dioptric variations were examined preoperatively and postoperatively. Intraocular pressure (IOP) was also monitored in all visited time.

RESULTS: Totally, 18 lenticule patches were used on 17 eyes of 17 cornea dermoid patients. The mean follow-up time was 11.47±5.28mo. All lenticule patches were successfully glued, kept on its location and maintained transparent during the follow-up time, with a consecutive epithelial cover for 1wk. Nine of the patients could coordinate visual and optometry exam well. Their preoperative BCVA is 0.60±0.35 in decimal, significantly improved to 0.80±0.26 in decimal at 6mo postoperatively \(Z=2.392, P=0.017\), but the changes of their corneal astigmatism diopters showed no significance, with 2.22±1.91 D preoperatively, and 2.28±1.31 D at 6mo postoperatively \(Z=-0.135, P=0.893\). Limbal pannus formation occurred in 4 (23.52%) cases and decreased with the application of tacrolimus eyedrops. IOP increased in 2 (11.76%) cases, but well decreased by timolol maleate eyedrops. All the adult patients or guardians of minor patients were satisfied with the cosmetic improvement.

CONCLUSION: Dermoid excision combined with transplantation of SMILE-derived lenticule patches using fibrin glue is a safe and effective novel tectonic keratoplasty procedure for corneal dermoid.

KEYWORDS: corneal dermoid; small incision lenticule extraction; fibrin glue

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INTRODUCTION

Corneal dermoids, composed of ectodermal and mesodermal original tissues, are common congenital benign choristomas in children. They are seen sporadically, with an incidence varying from 1 to 3 in 10,000\(^{[1]}\). They most commonly occur in the inferotemporal quadrant of the bulbar, straddling the limbus and often having a keratinized surface with hair follicles on its surface\(^{[1-2]}\). They may grow into cornea slowly or maintain stationary, but can result in astigmatism, amblyopia, and even monocular blindness if pupil is covered\(^{[3-4]}\). Corneal dermoid shows abnormal ocular appearance. It has been reported that approximately 26.7% of the congenital corneal opacities were caused by corneal dermoid\(^{[5]}\).

According to the site and extent of affected cornea area, corneal dermoid is anatomically classified into 3 grades\(^{[2,6]}\). The grade I is superficial lesion less than 5 mm. The grade II is larger and deeper. The grade III often affects entire anterior structures,
including whole cornea and pigmented epithelium of iris. The main management of corneal dermoid is surgical treatment. Although different surgical techniques have been used, combination of the dermoid dissection and keratoplasty is the main recommended procedure\cite{6-8}. Though cornea is the most common transplant worldwide, it is still lacked worldwide for their huge demand at conservatively 12.7 million, while only 180 000 cases corneal transplantations were performed each year\cite{9}. What’s more, for the lack of cornea donors, only 536 corneal tumor cases could be treated with the keratoplasty surgery in China\cite{10}. This meant that seeking more keratoplasty materials or safe substitutes was imminent.

In recent years, the corneal intrastromal lenticule, which could be derived from small-incision refractive lenticule extraction (SMILE) in femtosecond laser refraction surgery, has been concerned on its role of corneal graft substitute\cite{11-14}. It was reported to be used as corneal graft for treatment of corneal diseases such as corneal ulcer with or without perforations\cite{15-18}. Although SMILE-derived lenticule has been applied as corneal graft in several corneal dermoid surgeries, its safety and feasibility is not clear till now\cite{19}. It means, whether the SMILE-derived lenticule could be served as new corneal graft substitute on corneal dermoid surgery or not, should be verified by more research.

Besides, a new blood-derived product—fibrin glue, which has a unique mechanism of action that mimics the common pathway of coagulation, has been widely used in clinical surgical treatment for its character of adhesion, preventing wound hemostasis and low biological toxicity\cite{20-22}. It has been also used in many ophthalmic surgeries, such as amniotic membrane (AM) transplantation, pterygium or strabismus surgery, and even vitreoretinal or cataract surgeries, etc\cite{23-27}. However, its safety and benefits in ophthalmic surgeries need to be further verified.

In this corneal dermoid study, we used the SMILE-derived lenticule graft as the substitute of traditional donated cornea after corneal dermoid removal, and then utilized the fibrin glue instead of traditional sutures to fix the lenticule graft patches. Corneal grafts’ growth and location, changes of visual acuity, intraocular pressure (IOP) as well as ocular appearance were observed. The safety and feasibility of the utilization of SMILE-derived lenticule grafts and the fibrin glue in the corneal dermoid surgery was evaluated.

**SUBJECTS AND METHODS**

**Ethical Approval** This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (No.2018KY022). Informed written consent was obtained from the patients’ legal guardians before operation.

**Subjects and Follow-ups** The corneal lenticule donors in this study were healthy individuals between 20 and 30 years old, and all of them scheduled to undergo SMILE surgery. All donors signed the consent for lenticule donation and underwent serological testing to exclude syphilis, hepatitis B, hepatitis C, and human immunodeficiency virus infection. Totally 17 patients diagnosed as corneal dermoid were included. The corneal involvement of the dermoid was less than 1/3 corneal thickness. All the adult patients or guardians of minor patients were told of this novel tectonic lenticule-keratoplasty using fibrin glue instead of traditional corneal suture to fix the lenticule graft and signed the written informed consent for agreement.

The follow-ups were weekly for the first two weeks, then monthly for 6mo, and every 3 to 6mo. The best corrected visual acuity (BCVA), IOP, as well as refractive changes were recorded. Corneal transparency and pannus formation were observed with the slit lamp microscopy. Anterior segment photography and optical coherence tomography were completed if possible. For the 4-year-old or younger children who couldn’t cooperate with the eye examination, a handheld slit lamp was used to complete the anterior segment examination while IOP was monitored by fingers or Hugh’s tonometer if it was needed.

**Lenticule Acquisition and Transplant** Corneal lenticules were extracted from SMILE procedures by a single skilled surgeon (Jiang LZ) with standard technique, using VisuMax FS laser system (Carl Zeiss Meditec, Jena, Germany). The cap thickness was 120 μm, optical zone varied from 6.0 to 6.5 mm and the superior incision was 2 mm. When separated, fresh lenticule grafts were transferred into a sterile tube with glycerol and stored at -20°C. The lenticule graft must be used in one week to avoid contamination and put into the diluted amikacin solution (1:40) at room temperature to rewarm for 5min before use.

All the lenticule transplant operations were performed by an experienced corneal surgeon (Zeng J) under intravenous anesthesia. Bulbar conjunctiva at the edge of the lesion was pruned and the area of the corneal dermoid was marked by a corneal trephine of suitable size. Rewarmed lenticule graft was trimmed with a suitable corneal trephine according to the lesion size. Then, the graft was immersed in solution A (external human fibrin solution, diluted by sterile water for injection, 50 mg/mL) of the fibrin glue (Human Fibrin Sealant Kit, Shanghai RAAS Blood Products Co., Ltd., China), and laid flat on recipient corneal bed. An appropriate amount of solution B (external human thrombin solution, diluted by CaCl₂ solution, 500 IU/mL) of the fibrin glue (Human Fibrin Sealant Kit, Shanghai RAAS Blood Products Co., Ltd., China) was dropped between the graft and recipient corneal bed for 1min or longer. A corneal bandage contact lens (diameter...
Statistical Analysis

IOP was higher than 21 mm Hg.

ocular surface irritation. Timolol maleate eyedrops was used if Sodium hyaluronate was administrated appropriately to reduce twice a day initially and gradually decreased in the last 2wk.

limbal pannus formation or corneal edema were observed, with stopped. Tacrolimus eyedrops was added for totally 1 to 3mo if applied when the tobramycin dexamethasone eyedrops was 1wk later, for 2wk in total. Fluorometholone eyedrops was applied when the tobramycin dexamethasone eyedrops was stopped. Tacrolimus eyedrops was added for totally 1 to 3mo if limbal pannus formation or corneal edema were observed, with sodium hyaluronate was administrated appropriately to reduce ocular surface irritation. Timolol maleate eyedrops was used if IOP was higher than 21 mm Hg.

Perioperative Management and Evaluation

For all patients, levofloxacin eyedrops was administrated 4 times a day before surgery for 2d. Bovine basic fibroblast growth factor eye gel as well as olofoxacin eye ointment was used postoperatively for 2ws. Tobramycin dexamethasone eyedrops was administrated after the surgery 4 times a day for 3d, and reduced gradually 1wk later, for 2wk in total. Fluorometholone eyedrops was applied when the tobramycin dexamethasone eyedrops was stopped. Tacrolimus eyedrops was added for totally 1 to 3mo if limbal pannus formation or corneal edema were observed, with twice a day initially and gradually decreased in the last 2wk. Sodium hyaluronate was administrated appropriately to reduce ocular surface irritation. Timolol maleate eyedrops was used if IOP was higher than 21 mm Hg.

Statistical Analysis

Data analyses were performed using SPSS software (version 25.0; IBM Inc., USA). Numerical data were presented as mean±standard deviation (SD). The BCVA and corneal astigmatism diopters were assessed by correlated samples Wilcoxon signed-rank test. A value of P<0.05 was considered statistically significant.

RESULTS

Seventeen eyes of 17 patients were included in the study (Table 1). Except for a 35-year-old adult patient, the age of the minor patients ranged from 3mo to 15y, and the average follow-up time was 11.47±5.28mo (range 5 to 19mo). In these 17 patients, 6 (35.3%) were grade I with lesions less than 5.5×5.0 mm, 11 (64.7%) patients suffered grade II with larger dermoid lesions, which ranged from 5.5×5.5 to 7.5×7.5 mm². Lenticule grafts were all successfully adhered to the corneal surface using fibrin glue, without any dislocation or lost. AM was combined in three patients (cases 5, 7, and 16).

Table 1 Demographics and clinical characteristics of 17 cases of corneal dermoid

<table>
<thead>
<tr>
<th>Case</th>
<th>Age/gender</th>
<th>Dermoid size, mm²</th>
<th>Eye/location</th>
<th>Lenticule (thickness/diameter)</th>
<th>AM assisted</th>
<th>Follow-up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4y/M</td>
<td>6.0×6.0</td>
<td>OD/IT</td>
<td>146 μm/6.5 mm</td>
<td>No</td>
<td>19mo</td>
</tr>
<tr>
<td>2</td>
<td>7y/F</td>
<td>5.5×5.5</td>
<td>OD/IT</td>
<td>130 μm/6.0 mm</td>
<td>No</td>
<td>10mo</td>
</tr>
<tr>
<td>3</td>
<td>6mo/F</td>
<td>4.5×5.0</td>
<td>OD/IT</td>
<td>138 μm/5.0 mm</td>
<td>No</td>
<td>19mo</td>
</tr>
<tr>
<td>4</td>
<td>14y/F</td>
<td>5.5×5.0</td>
<td>OD/IT</td>
<td>143 μm/6.5 mm</td>
<td>No</td>
<td>10mo</td>
</tr>
<tr>
<td>5</td>
<td>15y/F</td>
<td>7.5×7.5</td>
<td>OS/IT</td>
<td>138 μm/6.5 mm</td>
<td>Yes</td>
<td>18mo</td>
</tr>
<tr>
<td>6</td>
<td>11mo/F</td>
<td>6.5×6.5</td>
<td>OS/IT</td>
<td>154 μm/6.5 mm</td>
<td>No</td>
<td>19mo</td>
</tr>
<tr>
<td>7</td>
<td>4y/M</td>
<td>2.5×3.5, 5.5×5.5</td>
<td>OD/IT/ST</td>
<td>145 μm/6.5 mm</td>
<td>Yes</td>
<td>16mo</td>
</tr>
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<td>8</td>
<td>2y/M</td>
<td>6.0×5.5</td>
<td>OS/IT</td>
<td>143 μm/6.3 mm</td>
<td>No</td>
<td>16mo</td>
</tr>
<tr>
<td>9</td>
<td>18mo/M</td>
<td>5.5×6.0</td>
<td>OD/IT</td>
<td>148 μm/6.5 mm</td>
<td>No</td>
<td>13mo</td>
</tr>
<tr>
<td>10</td>
<td>3mo/M</td>
<td>6.0×5.5</td>
<td>OD/IT</td>
<td>148 μm/6.5 mm</td>
<td>No</td>
<td>8mo</td>
</tr>
<tr>
<td>11</td>
<td>4y/M</td>
<td>5.5×5.0</td>
<td>OS/IT</td>
<td>136 μm/6.5 mm</td>
<td>No</td>
<td>9mo</td>
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<tr>
<td>12</td>
<td>6mo/M</td>
<td>5.5×5.5</td>
<td>OS/IT</td>
<td>130 μm/6.5 mm</td>
<td>No</td>
<td>8mo</td>
</tr>
<tr>
<td>13</td>
<td>35y/F</td>
<td>4.5×4.5</td>
<td>OD/IT</td>
<td>145 μm/5.0 mm</td>
<td>No</td>
<td>8mo</td>
</tr>
<tr>
<td>14</td>
<td>11y/F</td>
<td>6.5×5.5</td>
<td>OD/IT</td>
<td>(139+145) μm/6.5 mm</td>
<td>No</td>
<td>6mo</td>
</tr>
<tr>
<td>15</td>
<td>6y/F</td>
<td>5.0×5.0</td>
<td>OS/IT</td>
<td>142 μm/6.5 mm</td>
<td>No</td>
<td>6mo</td>
</tr>
<tr>
<td>16</td>
<td>1y/M</td>
<td>6.0×5.0</td>
<td>OD/IT</td>
<td>146 μm/6.5 mm</td>
<td>Yes</td>
<td>5mo</td>
</tr>
<tr>
<td>17</td>
<td>10mo/F</td>
<td>5.5×5.0</td>
<td>OD/IT</td>
<td>139 μm/6.5 mm</td>
<td>No</td>
<td>5mo</td>
</tr>
</tbody>
</table>

OD: Right eye; OS: Left eye; IT: Inferior temporal; ST: Superior temporal; AM: Amniotic membrane; F: Female; M: Male.

14 mm, ACUVUE® OASYS Brand Contact Lenses with Hydraclear® Plus, Johnson & Johnson Vision Care Inc., USA) was utilized for two weeks. AM was used if needed, and it was fixed with bulbar conjunctiva by 8-0 absorbable sutures. Lenticule graft with different thickness was chosen according to the depth of corneal involvement. Two lenticules maybe overlapped together by fibrin glue for deeper lesions.

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Cases 5 and 16 had large lesion and AM was used to repair surface using fibrin glue, without any dislocation or lost. AM was combined in three patients (cases 5, 7, and 16). Cases 5 and 16 had large lesion and AM was used to repair conjunctival. Case 7 had two dermoids, which was 2.5×3.5 and 5.5×5.5 mm², only one lenticule patch was used for the larger lesion, while AM was adopted for the smaller lesion. In these three patients, lenticule grafts were pasted by fibrin glue while 8-0 absorbable sutures were used to fix the AM and conjunctiva. Two lenticules were overlapped in case 14 for its deeper corneal involvement. All the lenticule grafts grew well and kept transparent during the follow-up time (Figures 1, 2).

Corneal epithelialization was achieved for one week, with smooth corneal epithelial coverage on the corneal surface and the grafts gradually merged with the recipient corneal stroma for 3mo (Figures 3, 4). Although an interspace was seen between the central area of the graft and recipient corneal bed in case 1, the space disappeared during the two-week follow-up time, and the lenticule graft grew well without any dislocation during the following observation (Figure 5).

Nine patients' BCVA and refractive diopter changed. The BCVA improved statistically, with preoperative 0.60±0.35 in decimal, which improved to 0.80±0.26 in decimal at 6mo postoperative (Z=-2.392, P=0.017), but no significant reduction in postoperative corneal astigmatism occurred, with preoperative 2.22±1.91 D, changed to 2.28±1.31 D at 6mo postoperative (Z=-0.135, P=0.893; Table 2).
Limbal pannus formation occurred in 4 (23.52%) cases, and effectively decreased with application of tacrolimus eyedrops. IOP increased in 2 (11.76%) cases, decreased with the use of timolol maleate eyedrops. All the adult patients or guardians of minor patients were satisfied with the cosmetic improvement. No recurrence occurred in any patient during the follow-up period.

DISCUSSION

Corneal dermoid is one of the most common ocular diseases in children, which can seriously affect the appearance of children. Surgical removal of dermoid lesion early can minimize their ocular defects effectively. For the lack of donated cornea, eighteen pieces of SMILE-derived lenticules were used in 17 patients (overlapped lenticules were used in one patient) in our study. With at least 5mo or longer time follow up, all the lenticule grafts grew well. Compared to the preoperative, corneal opacity was reduced in all patients after surgery, adult patients or guardians of minor patients were all satisfied with the cosmetic improvement.
with the improvement of their ocular appearance. Corneal epithelialization was achieved for one week while the grafts merged with recipient corneal stroma for about 3 mo. As the lenticule graft was acellular, this tectonic surgery showed low rejection. Although limbal pannus formation occurred in 4 (23.52%) cases and IOP increased in 2 (11.76%) cases, these complications could be decreased by related eyedrops. Since patients in our research were mainly children, only 9 patients could cooperate with visual acuity and optometry exam well. Although no significant corneal astigmatism reduction was noticed ($P>0.05$), the postoperative BCVA of these 9 patients improved in 6 mo, especially in case 5, whose BCVA was promoted from 0.3 to 0.8 (decimal) at 6 mo postoperative while the corneal astigmatism was apparently decreased at the meanwhile (from +5.5 to +2.75 D). These data indicate that SMILE-derived lenticules are feasible to be used in the new corneal dermoid keratoplasty, and they are safe enough for their well growth and prognosis. It also means that we could make better use of the SMILE-derived corneal lenticules to perform this tectonic procedure as soon as possible if corneal dermoid is diagnosed. It could reduce the loss of visual function effectively in these patients and decrease its abnormal effect on the psychological development.

Although traditional sutures were used to fix the AM in 3 patients who had combined with AM transplantation, all the lenticule patches were pasted onto corneal recipient bed by fibrin glue instead of traditional corneal suture-fixation in our study. All the lenticule grafts were successfully adhered to the corneal surface and maintained transparency in postoperative follow-up, without any dislocation. This proved that fibrin glue could not only stick corneal tissue well, but also show low toxicity to corneal tissue. The utilization of fibrin glue to fix lenticule patches presented many advantages. Without traditional corneal suture, it has shortened the operation time, and economized extra consumption of medical resources for secondary corneal suture removal. It could also avoid extra corneal astigmatism and rejection caused by traditional corneal sutures. Ocular surface irritations also less occurred in these patients. We confirm that it is safe and effective to use fibrin glue in this new tectonic surgery, though a little interspace has been seen between the graft and corneal recipient bed in one

Figure 4 Anterior segment optical coherence tomography of case 5  A: A dermoid change was seen in the inferior cornea and limbus preoperative; B: Postoperative 1wk, the lenticule graft was imbed well with smooth and consecutive corneal epithelium; C: Postoperative 6mo, the lenticule graft grew well on its position; D: Postoperative 10mo, the lenticule graft remained stable.

Figure 5 Anterior segment optical coherence tomography of case 1  A: Preoperative; B: Postoperative 1wk, corneal epithelium was smooth and consecutive with a interspace (white arrow) in the central corneal graft while the peripheral area was tightly adhered; C: Postoperative 2wk, the interspace disappeared; D: Postoperative 3mo, the lenticule graft grew well, and fused with the recipient corneal stromal layer partially; E, F: Postoperative 6 and 9mo, the lenticule graft grew and structured with recipient cornea well.
patient. This interspace disappeared for 2wk, and the corneal tissues pasted and grew well during the follow-up time. We are the first to report the complication of this new surgery and its prognosis. We analyze that this interspace may be caused by uneven distribution of fibrin glue in the central area of corneal graft. As shown in our research, with sufficient fibrin glue covered in the peripheral graft, the central area may finally paste to recipient corneal bed successfully by wearing corneal bandage contact lens for 2wk. It also reminds us that it is necessary to spread the glue as evenly as possible during the operation to avoid dislocation or loss of the graft. Besides, keeping graft as well as the corneal wound dry enough is also necessary since other liquids in the operative area may decrease fibrin glue’s adhesion to a certain extent.

Former studies have showed similar use of SMILE-derived lenticule patches graft assisted by fibrin glue was safe and feasible in corneal dermoid surgery. Sutureless fixation of corneal lenticule patches graft assisted by fibrin glue was safe and feasible in corneal dermoid of grade I and II. This novel tectonic surgical procedure deserves to be carried out more in the treatment of corneal dermoid, for it could save more allogeneic corneal materials for other patients who need penetrated corneal transplantation.

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Authors’ contributions: The study was designed by Zeng J, Ye Q, and Liu JL. Material preparation and data collection were performed by Ye Q, Ji JY, Wei LQ, Liu JL, Zhong X, Zeng J and Jiang LZ. Data analysis was performed by Liu JL. The manuscript was written by Liu JL, reviewed and edited by Zeng J. All authors read and approved the final manuscript.

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Conflicts of Interest: Liu JL, None; Ji JY, None; Ye Q, None; Wei LQ, None; Zhong X, None; Jiang LZ, None; Zeng J, None.

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