Jpn J Ophthalmol (2013) 57:239–244
DOI 10.1007/s10384-012-0217-5

THE OFFICIAL INTERNATIONAL JOURNAL OF THE JAPANESE OPHTHALMOLOGICAL SOCIETY

CLINICAL INVESTIGATION

Amniotic membrane in the management of strabismus reoperations

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Received: 10 January 2012 / Accepted: 1 October 2012 / Published online: 13 December 2012

Abstract

Purpose To reduce postoperative scar formation and to improve duction using amniotic membrane (AM) in strabismus reoperations.

Methods A prospective study of interventional case series comprised of 14 patients with restrictive strabismus. Objective clinical findings (visual acuity, angle of deviations and degree of duction deficits) were recorded in both the pre- and post-operative periods. Strabismus surgery included the excision of adhesions and scar tissue, repositioning of extraocular muscles (according to the degree of deviations) and placement of two sheets, one between muscle and tenon and the other between muscle and sclera. Conjunctival recession with covering of the bare sclera using AM was also performed.

Results The mean preoperative deviation of the patients was 34.3 prism diopters (PD) and mean post-operative deviation was 4.6 PD. The mean pre-operative duction deficit of the patients was 1.7; mean post-operative duction deficit was 0.2. Postoperatively all patients improved in relation to deviation and duction. Less than 8 PD deviations with no duction deficits were achieved in 12 (86 %) of the patients.

Conclusions Amniotic membrane placement around the extraocular muscle improves the duction and decreases the residual angle of deviations by inhibiting postoperative scar formation.

Keywords Amniotic membrane · Reoperation cases · Strabismus surgery

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Introduction

Patients who undergo strabismus surgery may need reoperations. Reoperation can be expected in 5–10 % of the operated patients despite the most meticulous efforts to perform a careful preoperative evaluation and determine appropriate surgical strategy [1]. Common reoperation scenarios include undercorrection, overcorrection, slipped or lost muscles, restrictions after a prior ophthalmic surgical procedure and the development of a new surgical problem. Restrictions usually develop after excessive resections, intraconal fat violation or scar tissue formation, which result in postoperative adhesions [2]. Various approaches have been used to prevent the formation of postsurgical adhesions, including polyamide 6.6 (Supramid; Jackson, Alexandria, VA, USA), silicone sleeves, polyglactin 910 mesh, polypeptide sleeves, sodium hyaluronate, steroids, mitomycin C, 5 fluorouracil and Seprafilm (Genzyme, Cambridge, MA, USA) [3–9]. However, none of these approaches is widely used because of associated complications, unavailability or inconsistent results.

There are only a few reports in the literature on the use of amniotic membrane (AM) transplantation to treat restrictive strabismus. Yamada et al. published a case report on the successful treatment of restrictive strabismus occurring after retinal detachment surgery, Sheha et al. described wrapping the extraocular muscles (EOM) with AM in a case of consecutive exotropia, and Kersey and Vivian used AM in conjunction with mitomycin C in two patients with complex strabismus surgery [10–12]. Strube et al. reported a case series describing the use of AM transplant to repair restrictive strabismus occurring after a variety of anterior segment, oculoplastic and retinal surgeries [13].

In our study, we used AM to decrease scar formation in strabismus cases with ocular restrictions that had developed after a prior ophthalmic surgical procedure.

Patients and methods

Patients with restrictive strabismus resulting from previous strabismus surgery were identified in the general strabismus clinic over a 6-year period. Patients were questioned about the type of deviations and previous surgeries. Objective clinical findings (visual acuity, angle of deviation and degree of duction deficit) were recorded in both the pre- and postoperative periods. Krimsky test or alternate prism and cover test were used to the measure the angle of deviation according to visual acuity and patient cooperation. The degree of duction deficit was graded on a scale of −4 to 0. No movement beyond the midline is grade −4. Grade −3 indicates 25 % movement. Grade −2 indicates 50 % movement, and grade −1 indicates 75 % movement. In grade 0 there is no duction deficit. In order to detect the restrictions, intraoperative forced duction tests were performed several times during the surgery. Analysis of passive forced duction was done using the following scale: grade 0, no restriction; grade 1, minimal restriction terminally; grade 2, the globe could move past the midline; grade 3, the globe could not be moved past the midline; grade 4, the globe could not be moved.

Strabismus surgery, which includes an excision of adhesions and scar tissue, a repositioning of the EOM (according to the degree of deviations) and placement of AM between the EOM and tenon tissue was performed. Fresh AM was obtained from elective Cesarean sections of seronegative patients. After dissection from chorionic tissue, it was washed by sterile serum physiologic solution, which included gentamicin 50 μg/ml. Washed tissue was kept in the same solution for 30 min before it was prepared for the surgery. Two pieces or sheets of appropriately sized fresh AM (approximately 8 × 6 mm) covering the bare sclera and tenon's capsule were used for each muscle. The first sheet (stromal side facing the sclera) was placed under the EOM, and the second one (stromal side facing towards tenon's capsule) was placed over the EOM. The stromal side of the AM facing toward the tenon's capsule and sclera was placed in order to decrease postoperative scar formation. AM transplant was sutured to the posterior and anterior edges of the bare sclera with 8–0 polyglactin 910 sutures. This technique provided more stability to the graft. Also conjunctival recession with covering of the bare sclera by AM (stromal side facing down) was performed in patients with characteristic signs of indentation. The AM used to cover the bare sclera after conjunctival recession was sutured separately to the episcleral bed and conjunctival edge with polyglactin 910 suture. All surgeries were performed under general anesthesia by the same surgeon (BT). Informed consent was obtained from patients or patients' guardians before the operations. The ethical committee of our research and education hospital approved the study.

Results

The clinical characteristics, orthoptic measurements and surgical outcomes of these patients are summarized in Table 1. There were 9 women and 5 men. The mean age of the patients was 17.2 years. The mean preoperative duction deficit of the patients was 1.7; the mean postoperative duction deficit was 0.2 (Table 2). The mean follow-up period was 18 months (range 6–32 months). The mechanism of restrictive strabismus was due to varying degrees of scar tissue formation, conjunctival contracture (patient 2, 3, 6, 7, 9, 10, 11), fat adherence (patient 11), slipped muscle (patient 5, 13, 14) and tight rectus muscle (patient 2, 3, 12). Forced duction testing was positive preoperatively and negative at the end of the surgery in 12 (86 %) cases. Postoperatively all patients improved in deviation and duction. The mean preoperative deviation of the patients was 34.3 PD, and the mean post-operative deviation was 4.6 PD. Total improvement in the duction deficit with less than 8 PD deviation was achieved in 12 (86 %) of the patients. Patient 9 with congenital fibrosis had a bilateral abduction deficit (−2), and patient 11 with residual esotropia had adduction deficit (−1) OS. There were no complications due to the use of the AM transplant. All patients had successful outcomes after AM transplantation with complete reepithelization of the conjunctival defect. No scarring resulting in secondary restriction was identified in the area of AM transplantation.

Discussion

Despite the best preoperative evaluation and surgical techniques, reoperation will continue to be a part of strabismus management. Strabismus reoperations aim to achieve stable alignment, full ocular rotation with no incomitance and

Table 1 Clinical characteristics and surgical details of patients

No.	Sex	Age	Visual Acuity	Incomitance	Previous surgery	Pathology	Diagnosis	Surgical procedure	Preop deviation	Postop deviation	Preop duction deficit	Postop duction deficit
1	F	8	R 0.4 L 0.9	Limited R adduction	R MR 5 mm recession R LR 5 mm resection	Scar tissue	Consecutive exotropia	R MR 5 mm advancement	30 PD XT	6 PD XT	R-1 adduction	0
2	F	25	R 0.6 L 0.8	Limited R abduction	R LR recession 9 mm R MR resection 5 mm	Scar tissue Tight muscle (MR) Conj contracture	Consecutive esotropia	R MR 5 mm recession + conj recession 6 mm	25 PD ET	6 PD ET	R-2 abduction	0
3	F	8	R 1.0 L 0.1	Limited L adduction	L MR recession 5 mm L LR resection 8 mm	Scar tissue Tight muscle (LR) Conj contracture	Consecutive exotropia	L LR recession 8 mm + Conj recession 4 mm	30 PD XT	4 PD XT	L-1 adduction	0
4	F	25	R 1.0 L 1.0	Limited B adduction	B LR recession 8 mm R MR resection 5 mm B IO disinsertion	Scar tissue	Residual exotropia	R MR 3 mm rerecession L MR 6 mm resection	40 PD XT	2 PD XT	B-1 adduction	0
5	F	32	R 0.9 L 0.9	Limited R adduction	R LR recession 9 mm R MR resection 6 mm	Slipped MR 5 mm	Consecutive exotropia	R MR pseudotendon resection 5 mm and advancement 5 mm	45 PD XT	6 PD XT	R-2 adduction	0
6	M	13	R 0.8 L 0.8	Limited R abduction	B MR recession 6 mm	Scar tissue Conj contracture	Residual esotropia	R MR rerecession 3 mm RLR resection 5 mm + R conj recession 3 mm	40 PD ET	4 PD ET	R-1 abduction	0
7	F	18	R 1.0 L 0.9	Limited L abduction	L LR resection 5 mm L MR recession 5 mm	Scar tissue Conj contracture	Residual esotropia	L MR rerecession 3 mm + conj recession 4 mm	20 PD ET	2 PD ET	L-1 abduction	0
8	M	9	R 0.9 L 0.05	Limited L adduction	L MR recession 5.5 mm L LR resection 6 mm	Scar tissue	Consecutive exotropia	L MR advancement 5 mm	35 PD XT	4 PD XT	L-1 adduction	0
9	F	18	R 1.0 L 0.8	Limited B abduction	L MR recession 5 mm	Scar tissue Conj contracture	Congenital fibrosis + residual esotropia	L MR rerecession 3 mm + conj recession 6 mm, R MR recession 8 mm + conj recession 6 mm	75 PD ET	25 PD ET	B-4 abduction	B-2 abduction
10	F	20	R 0.5 L 1.0	Limited R adduction	R MR recession 6 mm, R LR resection 8 mm, R IO myectomy	Stretched scar tissue Conj contracture	Consecutive exotropia	R MR pseudotendon resection 3 mm and R MR advancement 5 mm, + conj recession 7 mm	45 PD XT	0 PD	R-2 adduction	0

Table 1 continued

No.	Sex	Age	Visual Acuity	Incomitance	Previous surgery	Pathology	Diagnosis	Surgical procedure	Preop deviation	Postop deviation	Preop duction deficit	Postop duction deficit
11	M	25	R 1.0 L 0.05	Limited L abduction and adduction	L MR recession, L LR resection (the detail of surgery is unknown)	Scar tissue Conj contracture	Residual esotropia	L MR rerecession 3 mm + conj recession 7 mm	25 PD ET	0 PD	L-2 abduction L-1 adduction	L-1 adduction
12	M	4	NA	Limited R abduction	R LR recession 8 mm R MR resection 5 mm	Scar tissue Tight muscle	Consecutive esotropia	R MR recession 5 mm	20 PD ET	0 PD	R-2 abduction	0
13	F	19	R 0.05 L 1.0	Limited R adduction	R MR resection 6 mm R LR recession 9 mm	Slipped MR 4 mm	Residual exotropia	R MR pseudotendon resection 4 mm and advancement 4 mm	30 PD XT	8 PD XT	R-2 adduction	0
14	M	17	R 0.8 L 0.3	Limited L adduction	B MR recession 5.5 mm	Slipped MR 2 mm	Consecutive exotropia	L MR pseudotendon resection 2 mm + L MR advancement 7 mm	20 PD XT	0 PD	L-1 adduction	0

R right, *L* left, *B* bilateral, *MR* medial rectus, *LR* lateral rectus, *IO* inferior oblique, *Conj* conjunctival, *PD* prism diopter, *Preop* preoperative, *Postop* postoperative

good cosmetic results with the minimal surgical intervention [14]. Favorable cosmetics usually require a white, noninflamed eye with normal, symmetric lid fissures. Furthermore, since mechanical and muscle tone imbalance may be greater than expected from the usual strabismus operations, any reoperation introduces a 33 % probability of yet another procedure that may be needed to achieve satisfactory results [14].

In order to reduce postoperative scar formation and improve duction, we used AM in strabismus reoperations in our study. AM's stroma has been found to suppress transforming growth factor β signaling and downregulate fibroblasts, thereby reducing inflammation and scarring [15]. For this reason, in our surgical operations, we placed the stromal side of the amniotic membrane facing toward the tenon's capsule. Our surgical procedure was slightly different from the procedures used in previous studies [3–6]. Two sheets of AM under and over the EOM were sutured to the sclera so that both sheets of AM were stable after the surgery. We believe that, by inhibiting fibrosis and restrictions around the muscle, this was an important factor leading to improvements in duction deficits. Postoperatively duction in all patients had improved in our study. Conjunctival recession was performed in patients with conjunctival contracture, and AM was also used to cover the bare sclera in order to facilitate conjunctivalization. All patients had successful outcomes after the AM transplantation with complete reepithelization of the conjunctival defect. No scarring resulting in secondary restrictions was identified in the area of AM transplantation. Also, no immunological reaction was observed postoperatively.

In reoperation cases, mechanical restrictions to ocular rotations are primarily found at the conjunctiva, extraocular muscles and scar tissue [16]. Intraoperative forced duction testing is very important, and it confirms the surgeons' preoperative diagnosis and demonstrates whether surgery has effectively relieved restrictions. Forced duction testing needs to be repeated several times during the surgical procedure to determine whether a restriction has been adequately relieved [17]. In our study, forced duction testing was positive preoperatively and negative at the end of the surgery in all cases except in patients 9 and 11, who had positive forced duction testing at the end of the surgery. Patient 9 had bilateral abduction deficit postoperatively, which might be attributable to severe congenital fibrosis syndrome. In patient 11, heavy scar tissue due to possible orbital fat tissue herniation resulting from his previous surgery was observed around the medial rectus muscle. The medial rectus muscle was found to be 9 mm from the limbus, and it was recessed 3 mm. Excision of the fibrous scar tissue and placement of AM improved the abduction deficit of this patient, but a residual postoperative adduction deficit remained. Residual adduction deficit

Table 2 Forced duction scores and limitation in ductions

No	Forced duction score		Limitation in ductions				
	Preop	Postop	Preop	1 Week	1 Month	3 Month	6 Month
1	−1add	0	−1	0	0	0	0
2	−2abd	0	−2	0	0	0	0
3	−1add	0	−1	0	0	0	0
4	−1add	0	−1	0	0	0	0
5	−2add	0	−2	0	0	0	0
6	−1abd	0	−1	0	0	0	0
7	−1abd	0	−1	0	0	0	0
8	−1add	0	−1	0	0	0	0
9	−3abd	−2	−4	−2	−2	−2	−2
10	−2add	0	−2	0	0	0	0
11	−2abd	0	−2	0	0	0	0
	−1add	−1	−1	−1	−1	−1	−1
12	−2abd	0	−2	0	0	0	0
13	−2add	0	−2	0	0	0	0
14	−1add	0	−1	0	0	0	0

Preop preoperative, *postop* postoperative, *add* adduction, *abd* abduction

might be attributed to previous LR resection performed in another institution.

The conjunctiva may contribute to problems associated with strabismus reoperation by causing restriction and a poor cosmetic outcome. In our study, we observed the characteristic indentation sign of conjunctival restriction in seven cases and performed conjunctival recession. If conjunctival contracture is associated with scar tissue and adhesions, it may limit ocular rotations in the same field (reverse leash). In patient 11 we observed reverse leash due to heavy scar tissue attributed to possible orbital fat tissue herniation resulting from his previous surgery around the muscle. Fibrous scar tissue excision, amniotic membrane placement between muscle and tenon tissue, and conjunctival recession of 7 mm were performed in this patient. Although −2 abduction deficits were relieved, −1 adduction deficit was still observable.

Severe restriction of ocular motility due to fibrosis of perimuscular connective tissue in experimental models of restrictive strabismus is reported in the literature [18]. Mahindrakar et al. [19] reported that all results were stabilized by the first month, which is in accordance with the wound healing period of 4–6 weeks. In our cases limitation of duction was stabilized in the first week. This might be attributed to AM transplantation preventing adhesions by forming a temporary biological barrier between the layers of perimuscular connective tissue.

AM transplantation has been used for multiple purposes in ophthalmic surgery. It is most often used in ocular surface reconstruction [20]. It has been shown to reduce stromal inflammation, fibrosis and immunogenicity in experimental models. In most countries, fresh or cryopreserved AM can be used for ocular surgery. A cost-effective alternative is fresh AM that can be used at no cost to patients. The preparation technique suggested by Kim and Tseng increased the bioavailability of cryopreserved AM [21, 22]. The biological properties of these membranes are similar, except for the viability of the epithelial cells [23]. In a recent experimental controlled strabismus surgery study, AM was used under the superior rectus muscle of pigmented rabbits to prevent fibrosis and adhesion formation. The results show that AM has an antifibrotic effect and an effective role in the prevention of adhesion formation with possible physical barrier action [24]. A case report describing the use of AM to reduce adhesion formation in a patient with consecutive esotropia and limited duction showed possible benefits of this procedure [11].

In the study of Kassem et al. [25], wrapping of extraocular muscles with lyophilized AM resulted in extensive adhesion and inelastic, fibrotic muscles. The cause of fibrosis was not clearly identified in this study, but it was clear that lyophilized AM was ineffective in protecting against its development, although cryopreserved AM was successfully used by the same surgical technique for this purpose [11]. In our series, fresh AM was used to reduce fibrosis and restrictions, and none of the patients suffered from the complication indicated by Kassem et al.

We thought that AM placement between the extraocular muscle and tenon tissue primarily improves the ductions and secondarily decreases the residual angle of deviations by inhibiting postoperative scar formation. One of the potential limitations of the study is the lack of a control group. But considering the unique features of these complicated cases, a study with a comparison group would prove difficult. This could also be the reason why the authors of the previous studies demonstrating the use of

AM in complicated strabismus cases presented case reports or case series instead of control group studies [11–13]. The results of the previous experimental and clinical studies and those of our study suggest that there may be a role for AM in the management of strabismus reoperations [26]. Further controlled clinical studies should be performed to show the benefits of this procedure.

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