Results of therapeutic keratoplasty using porcine keratoxenoimplant in severe destructive inflammations of the human cornea

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Introduction. *One of key methods of surgical treatment for patients with severe destructive inflammatory process (SDIP) of the cornea is keratoplasty. Being performed as an urgent intervention in SDIP of the cornea, keratoplasty is the only method to preserve the eye as an organ and, in some cases, to create prospects for optic surgery. The problem of donor material shortage is of a special relevance since the legal base providing donor material harvesting is incomplete and as a result of increased military, traffic and home traumatism. The acute shortage of donor material for keratoplasty (KP) forces searching new graft materials. One of such material is a porcine cornea which has many similarities with a human cornea in regard to its structure and biomechanical parameters.*

Material and Methods. *We retrospectively analyzed the outcomes of 32 patients with severe destructive corneal inflammatory diseases of various etiologies, who underwent therapeutic keratoplasty using cryolyophilized keratoxenoimplant of the porcine cornea at Corneal Pathology Department of the Filatov Institute from January 2013 to December 2015.*

Results. *As a result of treatment, the eye as an organ was preserved. Not transparent keratoxenoimplant survival was observed in late postoperative period. Of 37 patients, undergone lamellar or penetrating keratoplasty, keratoxenoimplant survival was semitransparent in 9 cases (33.3%) and opaque in 18 cases (66.7%). Biological dressing survived opaque in two cases; and in three cases it resolved within 2-8 weeks after operation. At late follow-up period after keratoxenotransplantation partial lysis of xenograft was noted in 7 eyes (21.9%); of them, repeat keratoplasty using donor human cornea was performed in 5 cases, single-stage glaucoma surgery was in one case, and single-stage cataract extraction in another one. In the late follow-up, glaucoma surgery was performed in 5 eyes (15.6%). As a result of xenotransplantation, visual acuity improved in 5 eyes (15.6%), did not change in 24 eyes (75%), and changed for the worse in 3 eyes (9.6%). In destructive processes of small diameter with paracentral and peripheral location, we could preserve and improve visual functions. Prospects for optic surgery performance were kept in 20 patients (62.5%).*

Conclusion. *Thus, under the urgent condition when donor human cornea is not available, keratoxenoimplant can be used for therapeutic keratoplasty in order to manage the inflammatory process and to preserve the eye.*

Key words: destructive inflammatory corneal disease, therapeutic keratoplasty, keratoxenoimplant

Introduction

Corneal diseases are one of the leading causes of blindness and impaired vision. Based on the data from World Health Organization (WHO), corneal pathology is among three first causes of visual impairment [1, 2]. The most common causes of corneal damage are keratitis and corneal ulcers associated with severe inflammation [3, 4, 5].

Non-surgical treatment for corneal ulcers does not always have a medical effect for a variety of reasons: pathogen virulence; secondary changes in the corneal tissue, caused by polymorphonuclear leukocyte infiltration of the cornea; proteolytic enzyme activation; and violation of regeneration and reparative processes which are complicated by tissue destruction and lead to corneal perforation and loss of the eye [6, 7]. Thus, this corneal pathology requires urgent surgical intervention, especially in progressive lysis of tissues and perforation

threat. One of key methods of surgical treatment for patients with severe destructive inflammatory process (SDIP) of the cornea is keratoplasty. Being performed as an urgent intervention in SDIP of the cornea, keratoplasty is the only method to preserve the eye as an organ and, in some cases, to create prospects for optic surgery [2, 7, 8, 9].

The performance of the surgery depends directly on availability of donor material for keratoplasty. In Ukraine, the problem of donor material shortage is of a special relevance since the legal base providing donor material harvesting is incomplete and in a result of increased military, traffic and home traumatism. The acute shortage of donor material for keratoplasty (KP) forces searching new graft materials. One of such material is a porcine cornea which has many similarities with a human cornea in regard to its structure and biomechanical parameters [2, 10, 11]. Despite the experimental studies performed previously to investigate the possibility to use corneas from pigs for keratoplasty in humans, this issue is still of a great interest [2, 11, 12]. At the present time, the possibilities of using donor materials from the pigs, in particular corneas, are studying a lot [2, 12, 13, 14, 15].

In 2010, a fabrication technology for keratoxenoimplant from the porcine cornea was co-developed by Filatov Institute of eye Diseases and Tissue Therapy and Horbachevsky Ternopil State Medical University (Patent 52278 U, 2010) [16]. While developing the technology of porcine cornea preservation we used many years' experience of clinical application of cryolyophilixed xenogenic skin of pigs in treatment of patients with severe eye burns [17]. The results of experimental study on investigating the characteristics of keratoxenoimplant and eye response to allotransplantation and xenotransplantation grafted to the corneas of Vietnamese pigs and rabbits, respectively, made it possible to proceed to studying the possibility of its clinical use [15, 18, 19]. Clinical data on using keratoxenoimplant for therapeutic tectonic KP in patients with severe consequences of 3-4 grade eye burns have shown the possibility of its using with an organ-preserved effect and followed by keratoprosthesis in some patients. To the best of our knowledge, there are single unconvincing data in regard to the possibility to use keratoxenoimplant for KP in patients complicated by inflammation of other etiology [15, 19].

The purpose of the present study was to analyze the outcomes of therapeutic keratoplasty, using keratoxenoimplants fabricated from cryolyophilized porcine cornea, in patients with severe destructive corneal inflammatory diseases.

Materials and methods

We retrospectively analyzed the outcomes of 32 patients with severe destructive corneal inflammatory diseases of various etiologies who underwent therapeutic keratoplasty at Corneal Pathology Department of the Filatov Institute from January 2013 to December 2015. The study involved 17 men and 15 women aged 19 to 86 (M=53.4±SD13.5). Etiology of destructive inflammations was as follows: bacterial in 12/32 eyes, herpetic in 7/32, combined (bacteria + fungal) in 3/32, autoimmune in 6/32, fungal in 2/32, rosacea in 1/32, and subtotal acute keratoconus in 1/32 eye.

Clinical forms of corneal damage included corneal ulcers in 27/32 eyes, abscess in 4/32 eyes (with phacocele in one eye), and subtotal acute keratoconus in 1/32 eye. Purulent exudates were noted in the anterior chamber in 11/32 eyes. Inflammation disease was complicated by perforation in 17/32 eyes, by descemetocele in 2/32 eyes, and by endophthalmitis in 4/32 eyes. Secondary hypertension (T+, T++) and secondary glaucoma were diagnosed in 8/32 and in 1/32 (case 3) patients, respectively.

Microbiological investigation of conjunctival cavity fluid and corneal surface scraping revealed the microflora growth in 14/32 eyes (43.8%). Among them, Staphylococcus epidermidis revealed in 3 eyes, Staphylococcus haemolyticus in 1 eye, Escherichia coli in 2 eyes, Pseudomonas aeruginosa in 2 eyes, Pseudomonas aeruginosa + Candida albicans in 1 eye, Enrerococcus + yeast-like fungi in 1 eye, Staphylococcus epidermidis + yeast-like fungi in 1 eye, and mold fungi in 2 eyes. In the rest 18/32 eyes (56.2%), microbiological investigation revealed no microflora growth.

The localization of severe destructive corneal inflammatory diseases was central/paracentral and peripheral in 25 and 7 cases, respectively.

All patients underwent a general clinical examination including taking the history from a patient, biomicroscopy of the cornea using fluorescence test, visometry, visual field examination, electrophysiologic examination (examination of the electrical sensitivity and lability of the optic nerve), and posterior segment ultrasonic scanning.

All patients were obtained informed consent for surgical intervention.

Keratoxenoimplants

Keratoplasty was performed using keratoxenoimplants fabricated in Ternopol Institute of Biomedical Institutions according the technology developed (Patent 52278 U, 2010) [16].

Keratoxenoimplant fabrication technique consisted in removal of the cornea with scleral rim from a healthy special condition-raised and freshly slaughtered pig, afterwards, cryoprotector treatment of the cornea and liquid nitrogen cryopreservation at -1960C with following vacuum drying. Then, keratoxenoimplant was quality inspected, product packed and sterilized using a radiation-based technique.

Histology and morphology tests have revealed that such way of corneal preservation allows maintaining the hystomorphological structure of the cornea [14, 15].

Cryolyophilized keratoxenoimplant was registered by the Ministry of Health of Ukraine as a medical device (Order No.495 of the State Inspectorate for Quality Control of Medicines of the Ministry of Healthcare of Ukraine, 09.12.2011, №495; Certificate of Registration No. 9967/2010) and is allowed to be used in the medical practice.

Keratoxenoimplant preparation for surgery

1.5 to 2 hours before surgery under the standard operating conditions and meeting aseptic and antiseptic regulations, keratoxenoimplant was taken out from the plastic package and placed into the sterile isotonic normal saline at 18-20^{0}C for 90-120 minutes. After soaking process was completed, keratoxenoimplant was prepared to a recipient by implant size and shape forming.

Keratoplasty

Depending on the area, depth and location of the inflammatory process in the cornea, we performed lamellar KP in 17/32 patients, penetrating KP in 10/32 (classic and step-by-step KPs in 4 and 6 cases, respectively), "biological dressing" by Puchkovskaya in 5/32 cases.

While performing penetrating KP, pre-soaked keratoxenoimplant was placed in the vacuum trephine bed of a required diameter and graft disc 0.25-05 mm bigger than trephine opening in the recipient's cornea was cut. On completion all necessary reconstructive procedures in the anterior chamber, the graft was placed in the trephine opening and sutured.

While performing step penetrating KP by a trephine of a larger diameter corresponding to corneal damage area, we cut the cornea at the depth of 85-90% of the corneal thickness and removed layer-by-layer affected lamellae of the cornea. Afterwards, using a trephine of a smaller diameter, corresponding to the destructive inflammation area, in the deep corneal lamellae, we performed penetrating excision of affected tissue. Through the full-thickness hole in the anterior lamellae of the cornea, we performed all necessary reconstructive interventions in the anterior chamber, which were focused on the recovery of the anatomical structure of the eyeball: division of anterior and posterior synechiae, excision of retrocorneal and pupillary membranes, removal (if indicated) of opaque lens, iridectomy and etc. The full-thickness graft with a diameter 0.25 larger than the lamellar bed was cut out from keratoxenoimplant and placed in the lamellar bed prepared and secured with 10/00 nylon sutures.

To perform lamellar kerapoplasty and to obtain a lamellar graft, keratoxenoimplant was fixed on a special stencil and dissected to the depth required (1/2 or 2/3 the thickness, as usual). Afterwards, a disc was cut from the anterior keratoxenoimplant layers using a trephine of a necessary diameter. The graft consisting of anterior and inner layers of keratoxenoimplant was placed onto the pre-prepared bed and secured with 10/00 nylon sutures.

Lamellar and full-thickness grafts were sutured with interrupted and combined (interrupted + uninterrupted) sutures in 23 (85.2%) and 4 (14.8%) cases, respectively.

While preparing for "biological dressing" of the cornea by Puchkovskaya, keratoxenoimplant was fixed on a special stencil and dissected to the depth of 1/2 or 2/3 its thickness. On a scleral rim, we marked scleral lingulae (2 to 4) at 12, 3, 6, and 9 o'clock, respectively, 2 to 2.5 mm width and 1.5 to 2 mm length to be sutured to the sclera of the recipient's eye. Redundant tissue of the sclera was cut off with scissors.

The patients who preoperatively were diagnosed secondary hypertension underwent basal iridectomy during xenografting. Patient T. (case 3) with secondary glaucoma was performed simultaneously lammelar xenografting and sinus trabeculectomy.

Blepharorrhaphy was performed in two cases; one of them was simultaneous with keratoxenoimplant "biological dressing" of the cornea (Patient N., case 30). In the second one (Patient M-k, case 17), blepharorrhaphy with xenograft covering with the conjunctiva was performed at 13 days after lamellar xenografting due to partial lysis of the graft.

Diameter of lamellar and full-thickness xenograft was 3.5 to 10.0 mm (M=6.35±SD1.83) and 4.5 to 9.0 mm (M=8.25±SD1.46), respectively.

Postoperatively, all patients received local and systemic anti-inflammatory therapy including antibiotics when indicated, antifungal, anti-viral, hypotensive and other medication. Beginning at 5 postop day, patients undergone lamellar and penetrating xenokeratoplasty with graft diameter ≥ 8.0 mm received in a consistent manner 0.05 mg dexamethasone 5 times per day, tapering every five/seven days, or 4 mg intravenous infusion No10-15. After xenograft was epithelialized, patients received locally 0.1% dexamethasone 4 to 6 times a day in a tapering regimen for 6 months.

Inflammatory reaction in the postoperative period was assessed as follows: moderate (+) when it was expressed by moderate hyperemia of the conjunctiva, vasodilation of the limbus and the cornea that surrounded recipient's graft, moderate swelling of the graft; apparent (++) when it was characterized by apparent hyperemia of the conjunctiva, vasodilation of the limbus and the cornea that surrounded recipient's graft, vascularization of limiting graft rim and accompanied by apparent swelling of the graft, through which anterior chamber structure was slightly visualized, and partial lysis of the graft; pronounced (+++), when it was characterized by pronounced hyperemia of the conjunctiva, vasodilation of the limbus and the cornea that surrounded recipient's graft, vascularization and swelling of the graft through which anterior chamber structure was not visualized, and graft lysis in the postoperative period.

Outcomes of therapeutic KP with keratoxenoimplant were assessed at early (1 to 30 days) and remote (3, 6, 12 months) terms after operation.

Surgical success was defined as inflammatory disease management and preservation of the eye.

Results and Discussion

The course of the post-operative period varied in different patients and depended on the severity of the baseline condition of the eye, type of keratoplasty and graft diameter (Table 1)

Therapeutic lamellar keratoplasty outcomes

The most favorable course of the post-operative period was observed in 12/32 patients who underwent lamellar xenokeratoplasty with graft diameter 3.5 to 6.5 mm (M=5.42±SD1.08). The localization of lytic lesion in the cornea was central/paracentral and peripheral in 26/32 (81.2%) and 6/32 (18.8%) cases, respectively. The former patients had moderate inflammatory reaction (+) observed at 4 to 5 days after surgery. Epithelialization of the graft surface was slow down and completed at 6

Table 1. Characteristics of clinical cases

No	Patient	Sex	Age	Diagn.	Etiol.	Complic.	IOP	Conc. syst. path.	KP	Implant diameter	Inflamm.	Early biological outcomes	Late biological outcomes	Repeat op.	Pre Vis	Post Vis
1	P-r	f	73	U *	B	Perf.	(-)	-	LKP	5.0	+	ST	ST	-	0.2	0.3
2	K-k	f	61	U *	A	Perf.	(-)	RhA	LKP	6.5	+	ST	ST	-	0.5	0.5
3	T-ts	m	27	U	B	Perf.	Вт. гл.	-	LKP + G	9.0	++	O	O + L	-	Pr.f. certa	Pr.f. certa
4	N-o	f	54	U	Herp	Perf.	(-)	-	LKP	6.0	+	ST	ST	-	0.02	0.02
5	Ia-i	m	81	U	B	-	(-)	-	LKP	6.5	+	ST	ST	-	0.01	0.01
6	L-k	m	54	U *	Herp	DC + Perf.	(-)	-	LKP	6.0	+	ST	ST	-	0.02	0.06
7	R-va	f	47	U	B	-	N	-	LKP	8.5	++	O	O + L	-	Pr.f. certa	Pr.f. certa
8	K-ts	m	62	U	F	Perf.	(-)	R	LKP	5.5	+	ST	ST	-	0.05	0.05
9	B-ia	f	57	U	A	Perf.	(-)	RhA	LKP	3.5	+	ST	ST	-	0.06	0.2
10	Kh-o	m	61	U	Herp	Perf.	(-)	-	LKP	6.0	++	ST	O + L	PKP + G	0.02	0.02
11	K-r	f	58	U *	A	Perf.	(-)	RhA	LKP	3.5	+	ST	ST	-	0.07	0.07
12	M-v	f	32	U	Mix B + F	DC	(+)	-	LKP	8.5	++	O	O	-	Pr.f. certa	Pr.f. certa
13	M-v	m	86	U *	B	Perf.	(-)	-	LKP	5.5	+	ST	ST	-	0.02	0.02
14	L-ko	m	54	U	Herp	-	N	-	LKP	4.5	+	ST	ST	-	0.1	0.35
15	O-k	f	32	U	Herp	Perf.	(-)	-	LKP	6.5	++	ST	O + L	AMT	0.,03	0.03
16	Tr-v	m	47	A	B	End.	(+)	-	LKP	10.0	++	O	O	G	Pr.f. certa	Pr.f. certa
17	M-k	f	36	U	B	DC	(+)	-	LKP	7.0	++	O + L	O	Conjunctival dressing + Blrph	Pr.f. certa	Pr.f. certa

No	Patient	Sex	Age	Diagn.	Etiol.	Complic.	IOP	Conc. syst. path.	KP	Implant diameter	Inflamm.	Early biological outcomes	Late biological outcomes	Repeat op.	Pre Vis	Post Vis
18	Ch-n	m	75	U	B	Perf.	(-)	-	SPKP	8.5/4.0	++	O + L	O	LKP	Pr.f. certa	Pr.f. certa
19	V-t	m	52	U	Herp	-	N	-	SPKP	8.0/5.0	++	O	O	-	Pr.f. certa	Pr.f. certa
20	N-v	m	61	U	A	-	N	RhA	SPKP	10.0/5.0	++	O	O + L	-	0.03	0,02
21	K-sh	f	31	U	B	Perf. + lens	(- -)	-	PKP	9.0	+++	O	O	-	Pr.f. incerta	Pr.f. incerta
22	B-va	f	33	U *	A	Perf.	(-)	RhA	SPKP	8.0/4.0	++	ST	O + L	PKP	0,02	0,02
23	K-t	f	65	A	Mix B + F	End.	(+)	-	PKP	9.0	+++	O	O	G	Pr.f. certa	Pr.f. certa
24	Z-ba	m	19	U	A	Perf.	(-)	-	SPKP	8.0/4.0	++	ST	O	-	0.04	0.03
25	K-n	m	53	A	F	End.	(++)	-	PKP	9.0	+++	O	O	G	Pr.f. certa	Pr.f. certa
26	T-ov	m	72	U	B	Perf.	(-)	RhA	PKP	4.5	+	ST	O	-	0.01	0.01
27	L-ko	f	82	U*	F	-	N	-	SPKP	8.5/4.5	+++	ST	O + L	-	0.02	0.02
28	L-i	m	30	U	B	-	(+)	-	BD	-	+++	BD L	-	LKP	Pr.f. certa	Pr.f. certa
29	S-d	m	39	U	Herp	Staph.	(+)	-	BD	-	++	-	BD L (2 months)	-	Pr.f. incerta	Pr.f. incerta
30	N-t	m	62	U	B	End. post radiation	(+)	Eyelid skin radiation, neoplasm	BD + Blrph	-	++	BD L	-	-	Pr.f. certa	Pr.f. certa
31	G-a	f	57	OKC	-	N	(-)	-	BD	-	+++	BD L	Vasc. leukoma	LKP	0.02	0.01
32	Ch-sh	f	58	A	Mix. B + F	Perf.	(-)	-	BD	-	+++	BD	BD (м) adhesion	G, PKP + CE	Pr.f. certa	0.01

Abbr. sex: m - male, f - female; diagnosis: U - ulcer, A -abscess, AKC – acute keratoconus; etiology: B -bacterial, Herp - herpetic, A - autoimmune, F – fungal, Mix - mixed, * - peripheral location; Complications: Perf.- perforation, DC – descemetocele, End.- endophthalmitis, Staph.- staphyloma; IOP–intraocular pressure: N-norm, (-), (- -) - hypotension, (+), (++) – increased; Concomitant systemic pathology: RhA- rheumatoid arthritis,R- rosacea; keratoplasty -: LKP – lamellar keratoplasty, PKP – penetrating keratoplasty, SPKP- step penetrating keratoplasty, BD- biological dressing; Inflammation -: (+) - moderate, (++) - apparent, (+++) - pronounced; Early biological outcomes: ST – semitransparent implant, O – opaque implant, L – lysis of implant; Late biological outcomes: ST – semitransparent implant, O – opaque implant, L – lysis of implant; Repeat operations: G – glaucoma surgery, PKP – penetrating keratoplasty, LKP – lamellar keratoplasty, CE – cataract extraction, AMT – amniotic membrane transplantation, Blrph- blepharorrhaphy.

to 9 days. In all cases, implants at early terms survived semitransparantly (Fig. 1, 2). At the remote time points of follow-up (at 2 months), lamellar grafts were opaque in two cases with perforated ulcers of herpetic etiology.

Apparent inflammatory reaction (++) was noted in 5 patients with lamellar xenograft 7.0 to 10.0 mm (M=8.6±SD1.08) in diameter; partial lysis of xenograft was in 4 cases, which resulted in opaque survival of xenograft at early postop period; in two of those with partial xenograft lysis, re-operation was required: cryopreserved amniotic membrane transplantation in one case and conjunctival covering of the graft and partial blepharorrhaphy in another.

Thus, at remote terms, in group of patients who underwent lamellar keratoplasty with keratoxenobioimplant, implants survived semitransparent and opaque in 9 (52.9%) and 8 (47.1%) cases, respectively. Patient X. with opaque survival of the xenograft at the remote terms underwent penetrating keratoplasty using donor human cornea with one-stage glaucoma surgery 10 months later.

Therapeutic penetrating keratoplasty outcomes

The patients who underwent penetrating keratoplasty using keratoxenoimplant had apparent inflammatory reaction at 7-14 days post-operatively. The less apparent inflammation (+) in this group of patients was noted in patient T. (case 26), whose full-thickness xenograft diameter was 4.5 mm. The most pronounced inflammatory reaction was observed in patients with xenograft diameter 8.5-10 mm. Epithelialization of the graft surface was slow down in all cases and completed at 14 to 16 days after lstep KP and at 17 to 21 days after classic penetrating KP. Persistent defects of xenograft epithelium remained in two cases at 27 to 30 days after surgery.

At early postop period at 30 days, 4 and 6 xenografts survived semitransparent and opaque, respectively. At early follow-up period, partial lysis was noted in 4 cases; of them, re-operation using donor human cornea was required in two cases. At remote follow-up period (3 to 6 months after surgery), all full-thickness xenografts were opaque. Full-thickness xenografts 8.5 to 10.0 mm in diameter were characterized by apparent vascularization of both the implant itself and implant surrounded recipient's cornea and had no chance to success in following optic keratoplasty (Fig. 3)

At remote follow-up in this group of patients, glaucoma surgery was performed in two cases due to secondary glaucoma.

Outcomes of therapeutic "biological dressing" xenokeratoplasty by Puchkovskaya

In group of patients who underwent "biological dressing" of the cornea by keratoxenoimplant, the course of the postoperative period was defined by etiology of inflammatory process and the area of affected cornea.

Patient L. with extensive purulent ulcer and corneal melting had pronounced inflammatory reaction (+++) observed in the postoperative follow-up, xenograft was lyzed at 10 days, which required lamellar keratoplasty using donor human cornea (Fig. 4).

Patient S. with corneal staphyloma ulcer also had pronounced inflammatory reaction (+++), xenograft was lyzed at 2 months. The area and depth of ulcer did not change significantly.

In Patient N. with purulent ulcer post-radiation endophthalmitis, we observed apparent inflammatory reaction (+++) with swelling of xenoimplant, which can be seen through sutured eyelids. At two and half months, xenograft was lyzed, the eyelids were unsecured. Moderate vascularized opacity with thinning area covered with stromal lamela was formed in a lower half of the cornea (Fig. 5).

Patient G. who underwent "biological dressing" due to subtotal sharp keratoconus postoperatively had pronounced inflammatory reaction (+++) with xenoimplant lysis at 21 days after surgery and vascular ingrowth in the home cornea. At two months was formed vascularized subtotal opacity, which, thereafter, required lamellar keratoplasty using donor human cornea.

Patient Ch., whose wearing soft contact lens led to corneal abscess of combined etiology, also had pronounced inflammatory reaction (+++) with swelling of xenoimplant which later survived to the corneal surface in the ulceration site and remained hard-secured to the cornea for 11 months. Three months after xenokeratoplasty, the patient underwent glaucoma surgery; and 11 months later, xenograft was surgically removed from the corneal surface during lamellar keratoplasty using donor human cornea.

In this group, in the late follow-up, we performed one glaucoma surgery, two lamellar keratoplasties with donor human cornea and one penetrating keratoplasty with opaque lens extraction.

Analysis of outcomes of therapeutic keratoplasty using keratoxenoimplant fabricated of cryolyophilized porcine cornea showed that the eye as an organ was preserved in all cases. Transparent survival of xenograft in the late follow-up was not observed. Of 27 patients, who underwent lamellar and penetrating xenokeratoplasty, semitransparent and opaque survival of xenograft was achieved in 9 (33.3%) and 18 (66.7%) cases, respectively. "Biological dressing" survived opaque in 3 cases and was lyzed in 3 cases at 2 to 8 months after surgery.

At late terms after keratoxenoimplantation, partial lysis of xenoimplant was noted in 7 eyes (21.9%), in 5 of which, we performed repeat keratoplasty using donor human cornea, with one-stage glaucoma surgery in one case and opaque lens extraction in another. Glaucoma surgery in the late postoperative period was performed in 5 eyes (15.6%). As a results of xenotransplantation performed, visual acuity improved in 5 (15.6%) eyes, did not change in 24 (75%) eyes, changed for the worse in 3 (9.6%) eyes. In paracentral and peripheral-located destructive processes of small diameter we managed to preserve and to improve visual functions. Prospects for optic surgery were remained in 20 (62.5%) patients.

Pigs are known to be considered today as a potential source of obtaining organs, tissues, and cells for humans [2, 11, 12]. Despite the fact that there are similarities between porcine and human corneas in regard to anatomy and pathophysiology, immunological differences are rather significant [20]. Taking into

account that the cornea is an immune-privileged tissue, which provides it some degree of protection, a xenograft fabricated from the porcine cornea is supposed to behave otherwise than other tissue and organ xenografts [21, 22]. However, immune privilege is known to be lost in the presence of inflammation, infection, trauma, and neovascularization that predisposes to development of tissue antigenic disparity (TSD) [22, 24].

All our patients were high-risk in regard to TSD development: xenokeratoplasty was performed urgently in active inflammation eyes, 71.9% cases (23 eyes) of which had corneal neovascularization.

In spite of available information that immunogenicity of keratoxenoimplant decreases during the fabrication of latter using the technology developed [15, 19], it remains rather high; and none of xenografts in our patients survived transparent. As a result, xenograft survival was semitransparent in 9 (33.3%) and opaque in 67.3% of cases. The best success was achieved after lamellar xenokeratoplasty with keratoxenoimplant 3.5 to 6.5 mm in diameter, which was conditioned by a small diameter of xenograft implanted, the absence of endothelium in lamellar xenograft and farness of the graft from limbus vessels. However, lamellar xenografts of larger diameter (7.0 to 10.0) mm survived opaque that is, likely, associated with a large xenograft diameter and nearness to limbus vessels.

Postoperative course follow-up after penetrating xenokeratoplasty showed that inflammation intensity was lower after step penetrating KP (++) as compared to that after classic penetrating KP (+++); that is likely determined by a small diameter in the anterior corneal layers (4.5 to 5.0 mm) and, as a consequence, (due to the presence of a step) by smaller area of xenograft endothelium contacting to recipient's anterior chamber aqueous humor. Since the step formed from the deep lamellae increases biochemical stability of postoperative scar, the xenograft is well-adapted and the anterior chamber is recovered faster that can also explain the less apparent inflammatory reaction after step penetrating keratoplasty. However, this did not influence significantly on the xenograft survival in the late follow-up.

Obviously, xenocornea preservation methods including cryolyophilization cannot properly negate antigenic specificity of the porcine cornea, which determines the development of tissue antigenic disparity in the postoperative period. Most researchers believe that future belongs to scientific investigations in the field of genetic engineering using the methods of genetic modification of animals, in virtue of which pigs with tissues resistant to graft rejection reaction even in the absence of steroid therapy will be grown [10, 12, 25, 26, 27].

Conclusion

Under the urgent condition when donor human cornea is not available, keratoxenoimplant can be used for therapeutic keratoplasty in order to manage the inflammatory process and to preserve the eye.

Urgent therapeutic keratoplasty (lamellar, penetrating, or step penetrating) with keratoxenoimplant can be performed with a tectonic purpose in the absence of other kind of corneal graft in destructive inflammation processes of different etiology limited to 6.5 mm (semitransparent survival in 33.3%).

In subtotal and total corneal damage with perforation, keratoxenoimplant (penetrating KP, step penetrating KP, or "biological dressing") can be used in the order to preserve the eye and to prepare it for prosthesis.

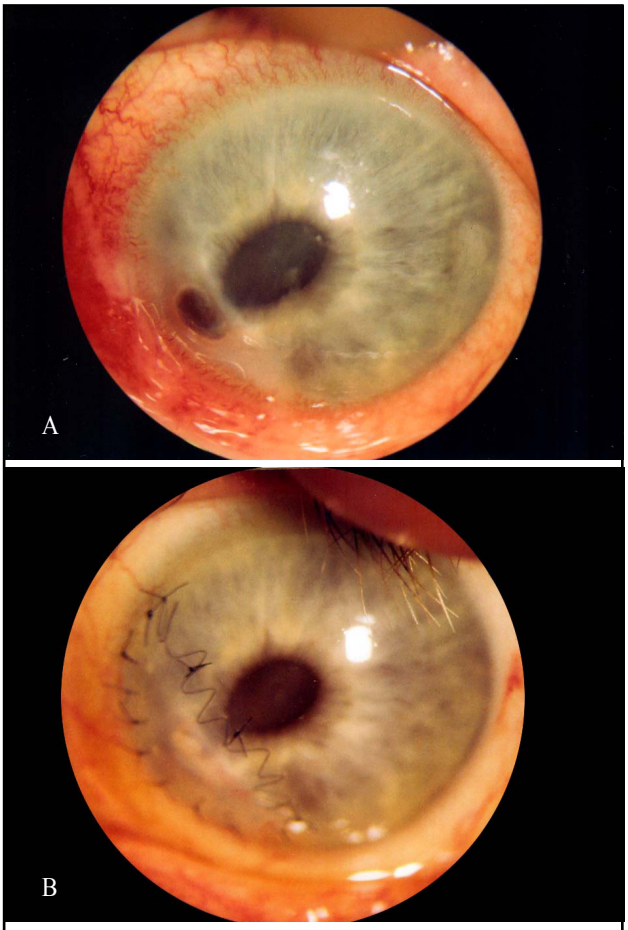

Figure 1. A. Patient P-r (case 1) Peripheral corneal ulcer can be seen; VA - 0.2. B. Patient P-r (case 1) Implant is semitransparent at 28 days after peripheral lamellar keratoplasty; VA – 0.2. 28

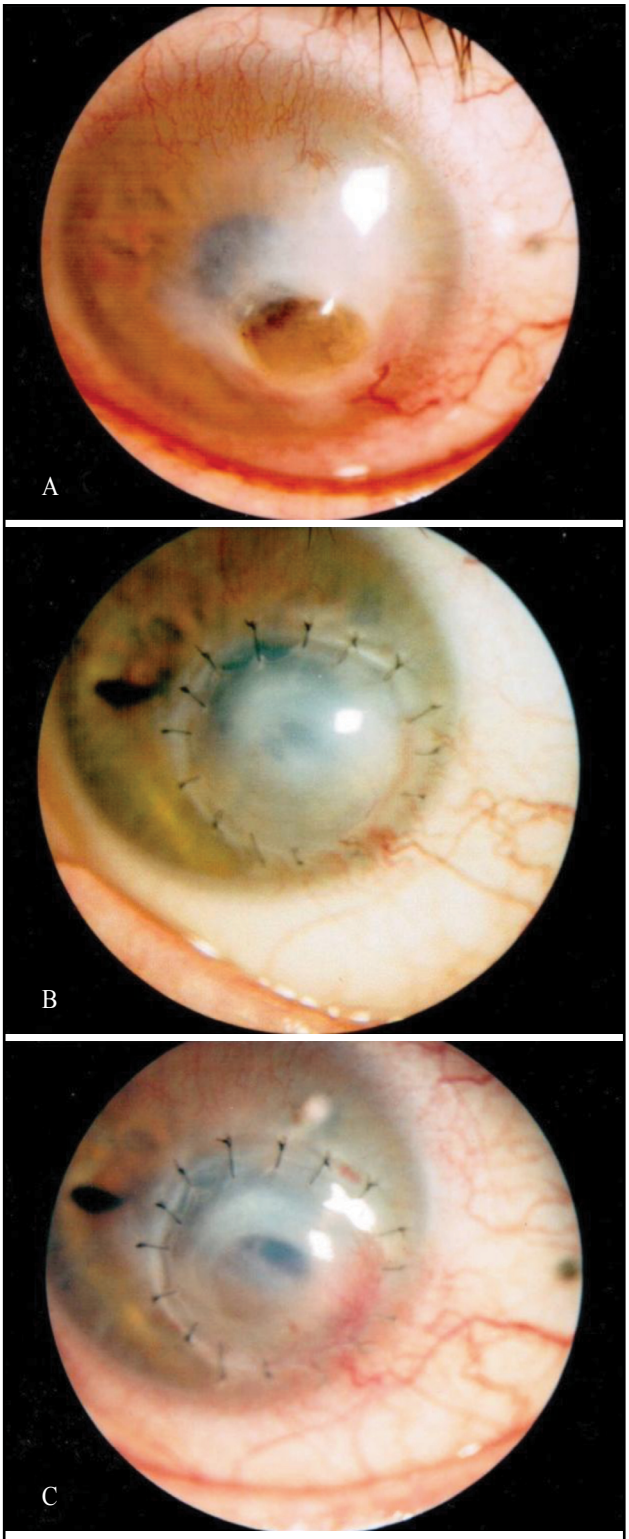

Figure 2. Patient L-k (case 6) Corneal ulcer of herpetic etiology, complicated by descemetocele and microperforation are observed; VA-0.02. B – Implant is semitransparent at 1 month after lamellar keratoplasty; C - Implant is semitransparent at 6 months after lamellar xenokeratoplasty; VA-0.06.

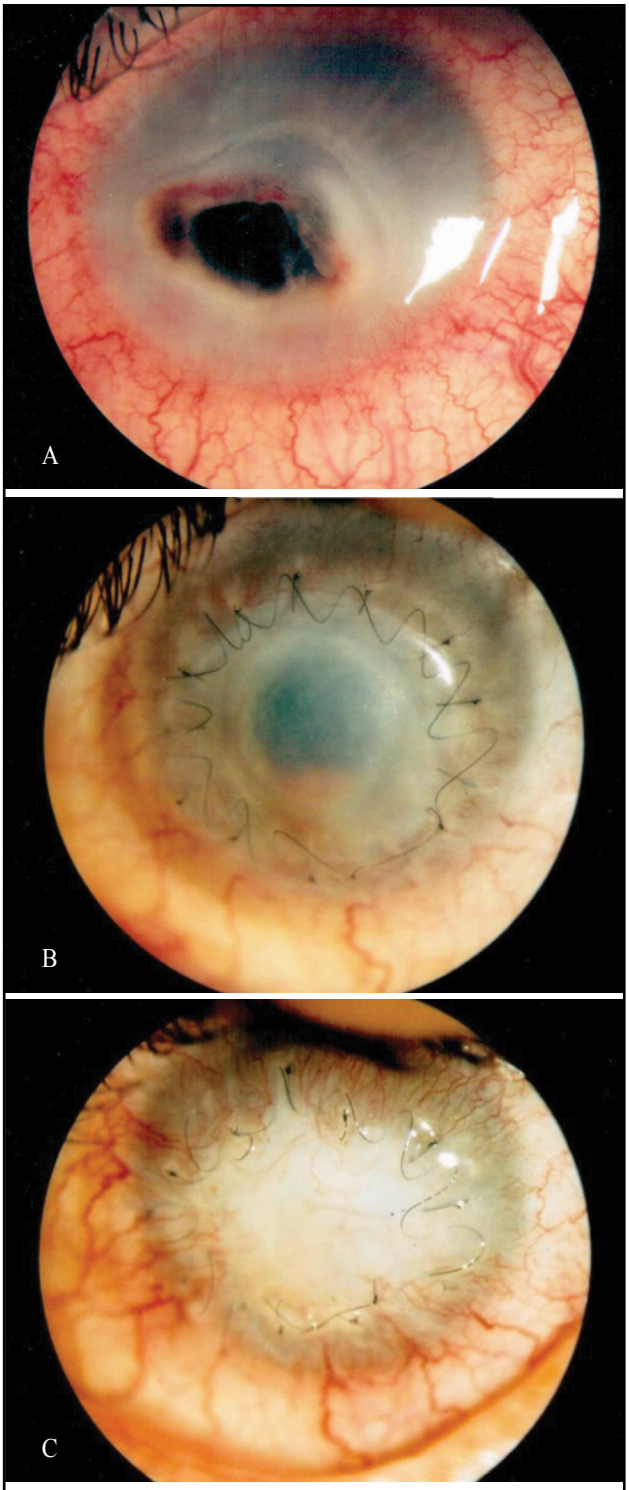

Figure 3. Patient K-sh (case 21) Expanded perforated ulcer of the cornea with phacocele can be seen; VA – pr.incertae; B - Implant is semitransparent at 27 days after penetrating xenokeratoplasty; VA – pr.incertae; C – implant is opaque and vascularized at 6 months after penetrating xenokeratoplasty; VA– pr.incertae

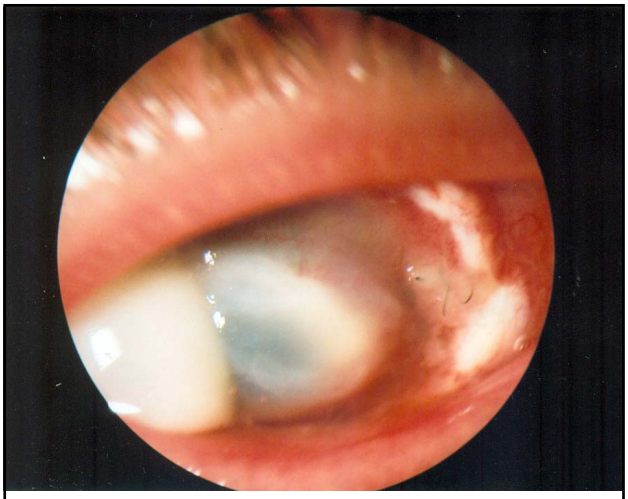

Figure 4. Patient L-i (case 28) Biological dressing is lyzed at 10 days after corneal covering by xenograft due to corneal ulcer; VA – pr.f,certae

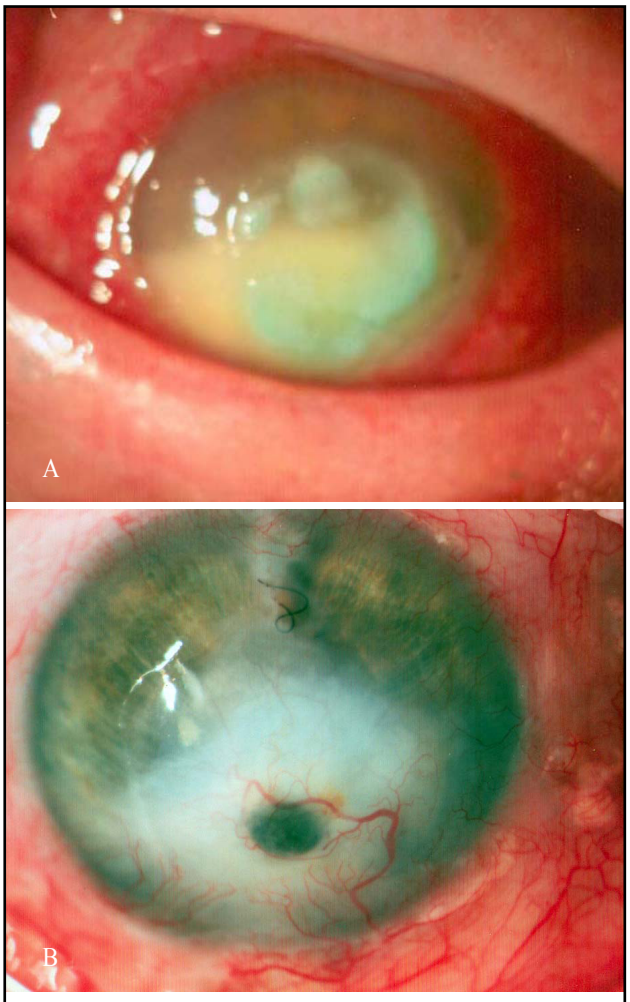

Figure 5. Patient N-t (case 30) A - Corneal hypopyon ulcer and postradiation endophthalmitis are present; VA – pr.f.certae; B – at 6 months after xenograft corneal biological dressing and one-stage blepharorrhaphy, biological dressing is lyzed, in the lower part of the cornea there is apparently vascularized opacity with thinning covered with stromal layer and epithelium

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