RESULTS OF PENETRATING KERATOPLASTY IN SYPHILITIC INTERSTITIAL KERATITIS

GOEGEBUER A., ***, AJAY LOHIYA**, ***, CLAERHOUT I.*, KESTELYN PH.**

ABSTRACT

Purpose: To compare the results in our patient series after penetrating keratoplasty (PKP) for syphilitic interstitial keratitis (IK) with those described in the literature.
Methods: Retrospective case series in which visual acuity (VA), graft clarity, rejection episodes, intraocular pressure and endothelial cell density (ECD) were examined postoperatively.
Results: Postoperative VA improved in all cases. There was no evidence of wound dehiscense or occurrence of retrocorneal membrane formation in any case. Postoperative inflammation was not more severe in our patients with syphilitic IK compared to patients undergoing PKP for other reasons. A normal decline in ECD proved that there was no subclinical inflammation as well.
Conclusion: PKP for syphilitic IK has a good prognosis in our case series as far as graft survival is concerned. Improvement in VA was present in all cases, though sometimes limited. In our case series, we experienced less postoperative complications than described in the older literature, which is probably due to better microsurgical techniques used nowadays.

RÉSUMÉ

But: Comparer les résultats obtenus chez nos patients après une kératoplastie transfixiante pour kératite interstitielle (KI) syphilitique avec ceux décrits dans la litérature.
Méthode: Analyse rétrospective des cas, avec acuité visuelle, clarté du greffon, épisodes de rejet, pression intraoculaire et comptage postopératoire des cellules endothéliales.
Résultats: L'acuité visuelle s'est améliorée dans tous les cas. Il n'y avait pas de signes de déhiscence du greffon, ni d' occurrence d'une membrane rétrocornéenne. L'inflammation postopératoire n'était pas plus prononcée chez nos patients avec une kératite interstitielle comparée aux patients opérés pour d'autres raisons. Un déclin normal du comptage des cellules endothéliales prouvait qu'il n'y avait pas d'inflammation infraclinique.
Conclusion: Une kératoplastie transfixiante pour KI syphilitique a un bon pronostic en ce qui concerne la clarté du greffon. Tous les patients bénéficiaient d' une amélioration de l'acuité visuelle, bien que parfois limitée. Nous rencontrions moins de complications postopératives chez nos patients que dans les séries décrites dans la litérature ancienne, ce qui est probablement du a l'évolution des techniques microchirurgicales.

KEY-WORDS

Penetrating keratoplasty, syphilitic interstitial keratitis, postoperative inflammation, endothelial cell density

MOTS-CLES

Kératoplastie transfixiante, kératite interstitielle syphilitique, inflammation postopératoire, comptage des cellules endothéliales.

.....

* *Department of Ophthalmology, Ghent University Hospital, Belgium*
** *Department of Ophthalmology, LTMMC & LTMGH, Sion, Mumbai, India*
*** *Both authors contributed equally*

received: 16.07.03
accepted: 16.09.03

INTRODUCTION

Although syphilis has become rare, it still is an existing cause of ocular disease.

Syphilis is a multi-system, multi-symptom disorder, caused by a spirochete, *Treponema pallidum*, that occurs primarily through sexual transmission, but can also be spread through blood transfusion or direct contact with an infected lesion. Transplacental transmission leads to congenital syphilis. Clinically, if untreated, acquired syphilis may follow three classic stages: primary, secondary and tertiary syphilis. In cases of congenital syphilis, patients may manifest Hutchinson's triad: interstitial keratitis, deafness and teeth malformation.

In acquired syphilis, various inflammatory ocular complications may occur in the secondary or third stages: episcleritis, uveitis, glaucoma, neuroretinitis, chorioretinitis, ischemic vasculopathy, infectious optic neuropathy, optic atrophy and pupil abnormalities.

Interstitial keratitis (IK) is a typical manifestation of congenital syphilis (4), but may rarely occur in acquired syphilis. The active keratitis begins with a corneal infiltrate, uveitis and Descemet's membrane alterations. This progresses to heavy superficial and deep vascularisation, leading to the so called 'salmon patches'. Clearing is associated with corneal thinning and ghost vessel formation. Chronic ocular signs of congenital syphilis include stromal scarring, ghost vessels and residual deep vascularisation, cornea guttata, scrolls in Descemet's membrane, glaucoma, band keratopathy, corneal thinning, lipid keratopathy and Salzmann's degeneration. Other late sequelae of congenital syphilis include cataract, pigmentary retinopathy (salt and pepper fundus) and optic atrophy (7).

In cases of interstitial keratitis, therapeutic decision making is based on syphilitic disease activity. Distinguishing between active and residual corneal disease is crucial when deciding to start a possible penicillin treatment (3). Penetrating keratoplasty (PKP) is usefull in cases of severe corneal opacification in quiet interstitial keratitis (8). Several problems after PKP for syphilitic keratitis are reported in the literature: higher incidence of serious postoperative uveitis (1) and glaucoma (2, 8), wound dehiscence (8) and rarely retained Descemet's membrane (5). We compared our results after PKP for syphilitic IK with those described in literature.

MATERIALS AND METHODS

We retrospectively studied six cases of penetrating keratoplasty, performed on five eyes of four patients with syphilitic interstitial keratitis (one patient had bilateral grafts, and had a regraft in one eye) and reviewed the literature concerning this subject.

The diagnosis of syphilitic interstitial keratitis was based on the characteristic slit lamp findings of interstital keratitis, combined with a positive TPHA serology.

The study group consisted of one male and three females aged between 39 and 71 years, with a mean age of 60 years. The average follow-up period was 42 months, with a range between 31 and 50 months (median: 40 months).

Donor corneal buttons preserved in organ culture at 31°C, with an endothelial cell density of at least 2200 cells/mm^2, were used for grafting. In all cases, the graft size was 7.25 mm for donor and 7.00 mm for recipient cornea. Double continuous (10-0) non absorbable sutures were used in all patients. In two cases, keratoplasty was combined with lens extraction and IOL implantation. Peripheral iridectomy was not done in any of the cases.

Postoperatively, steroid eye drops were administered with tapering dosage for six months. Systemic steroids were not used.

All patients were followed-up weekly for the first 3 weeks, then monthly for 6 months and then 6-monthly for 3 years. On each follow-up visit, following examinations were done: visual acuity testing on Snellen's chart, slit lamp biomicroscopy, intraocular pressure measuring using applanation tonometry and fundus examination.

Endothelial cell counts were done 6 months after surgery and then yearly thereafter with specular microscope and compared to data obtained from a control group. The data from the control group were used to generate the expected loss of ECD over the different time intervals involved.

RESULTS

Patient characteristics at presentation:

Preoperative slit lamp examination showed the presence of leucomatous corneae with ghost vessels in all cases. One patient had miosis and band keratopathy. Another patient had extensive deep corneal vascularisation in both eyes, but also signs of an old uveitis with posterior synechiae and a pigmentary retinopathy.
VDRL serology was positive in one patient, TPHA was positive in all cases.

Postoperative findings:

Three grafts of three patients remained clear on all follow-up visits. The fourth patient developed an irreversible allograft rejection of the graft in her right eye nine months postoperatively. She underwent a regraft in that eye one year later. A PKP was also performed in the left eye eleven months after the regraft in the right eye. Both grafts underwent two reversible allograft rejection episodes during the first postoperative year. On the last follow up visit, 50 months and 39 months postop respectively, both grafts were clear.
In all eyes, the postoperative inflammatory reaction did not exceed that observed after PKP for other corneal pathologies.
Postoperative best corrected visual acuity improved remarkably in all cases. However, only one eye reached a BCVA of 10/10 and three eyes had a BCVA of less than 5/10 (fig. 1).
There was no evidence of wound dehiscence or occurence of retrocorneal membrane formation in any of our cases. Postoperative IOP was normal in all eyes at all visits.

Endothelial cell density (ECD):

We compared the evolution of the endothelial cell density in our patients with data from a control group. The control group consisted of 167 patients, who had had PKP for other corneal pathologies, in which follow-up was uneventful and in which no additional surgical procedures were performed that could affect the ECD (table 1). The percentage loss relative to the initial density of the graft is also given. Data in the control group are given as mean ± the standard deviation. Mean loss of ECD and standard deviation were used to construct 90% reference ranges at each time interval in the control population (mean ± 1.64 times the standard deviation). A decline in ECD outside this 90% reference range was considered significantly stronger than the expected decline. For instance from transplantation to 6 months postoperatively the endothelial cell loss was 17% with a standard deviation of 13. So a decline over the six month period after the transplantation of more than 38% ($17+1.64\times13$ gives 38%) was considered significantly stronger than expected. Similar reference ranges were constructed for all time periods involved.
Postoperative decline in endothelial cell density in our patient group was not significantly stronger than that observed in the control group, except for 1 patient (who had undergone 2 reversible allograft rejection episodes).

DISCUSSION

In this study we have examined the outcome of PKP in syphilitic interstitial keratitis. IK has classically been defined as a non suppurative infiltration of the corneal stroma, with stromal vascularisation. Years after active inflammation, only ghost vessels and corneal scarring remain. Severe IK may leave prominent vessels, a dense scar and corneal thinning (4). Our patients were diagnosed with syphilitic IK based on typical slit lamp findings and positive serology for syphilis. All eyes had healed interstitial keratitis with leucomatous corneae with ghost vessels and in one case extensive deep vascularisation. Signs of old uveitis were present in both eyes of 1 patient.
Serologic testing consisted in VDRL- and TPHA-sceening. VDRL (venereal disease research laboratory) is a non-specific test for *Treponema pallidum* used to assess disease activity and provides an indication of response to treatment, turning negative after succesful treatment. TPHA-testing (treponema pallidum hemagglutination test) is a treponema-specific test, remaining positive for many years to a lifetime in syphilis patients and is used to confirm prior exposure, whether adequately treated or not (6). This explains why all our patients had positive TPHA and only 1 had positive VDRL.

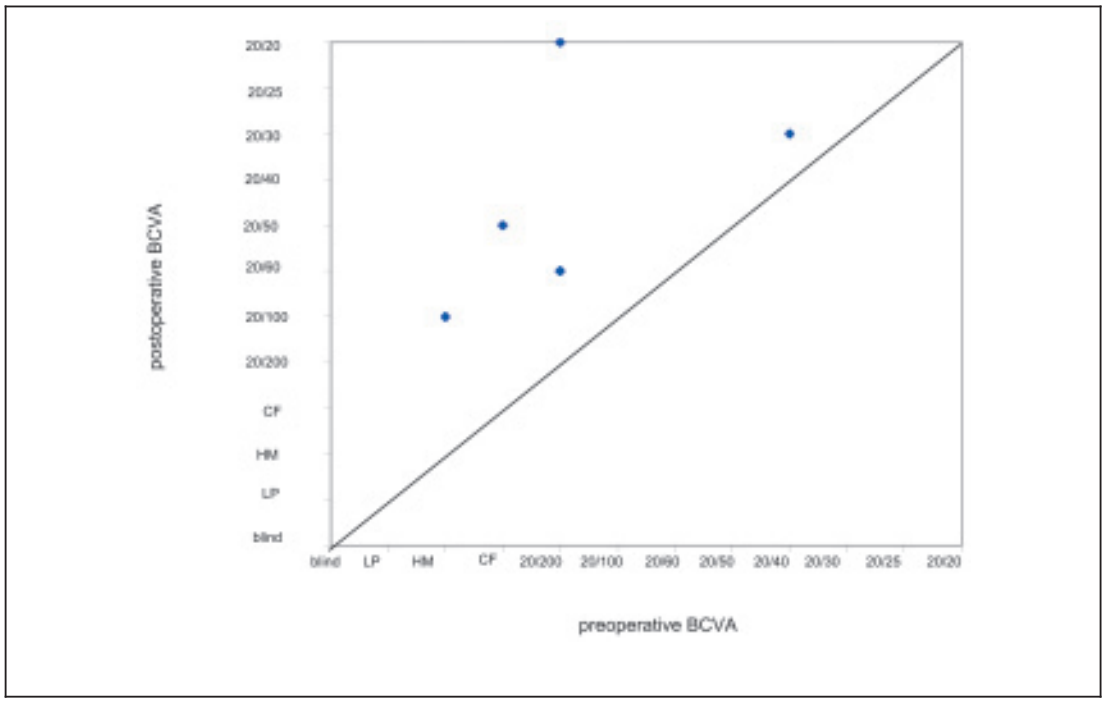

Figure 1. Evolution of pre- and postoperative best corrected visual acuity.

Table 1. *Evolution of endothelial cell density (cells/mm^2)*

CASE	age/sex	Preoperative ECD	6m postop (% loss)	1y postop (% loss)	2y postop (% loss)	3y postop (% loss)	remarks
1	77y, F	3050		2000 (34%)	1720 (44%)	1720 (44%)	
2	65y, F	2950	2200 (25%)	2200 (25%)	2200 (25%)		
3	74y, M	2360	2000 (15%)	1480 (37%)	1200 (49%)	1200 (49%)	
4 OD	45y, F	2625		1600 (39%)	1200 (54%)	1080 (59%)	regraft, 2 reversible rejection episodes at 5 & 12 months
4 OS	45y, F	2200		Oedema	680 (69%)	680 (69%)	2 reversible rejection episodes at 2 & 9 months
Control (n=167)		2575 ± 283	2155 ± 411 (17% ± 13)	1978 ± 469 (25% ± 15)	1723 ± 519 (34% ± 18)	1514 ± 493 (41% ± 17)	
Decline outside 90% reference range			>38%	>50%	>63%	>69%	

Penetrating keratoplasty is a therapeutic option for treating vision-threatening corneal opacification, due to syphilitic IK. However, several problems after PKP for syphilitic IK are reported in literature. Goldman et al. (1) observed a more severe postoperative inflammatory reaction after PKP for IK in congenital syphilis, compared to cases of PKP for other causes. They state that the violent inflammation is frequently associated with the formation of a retrocorneal membrane and graft opacification. Moreover, they observed a weaker anti-inflammatory response to massive steroid (and antibiotic) administration. Rabb and Fine (8) reported a higher incidence of ''homograft reactions'' (=rejection episodes) in their series of 61 PKP's for

syphilitic IK, than observed in keratoplasty for other types of corneal disease. In their series, they found wound dehiscence following suture removal and partial over-riding of the graft to be the most common complications. They suggest that wound healing is retarded due to thinness of the recipient cornea. As glaucoma is more frequent in patients with syphilitic IK (2), there is also an increased risk for postoperative glaucoma after PKP for syphilitic IK (8). A rare complication of PKP for syphilitic IK is splitting of Descemet's membrane with retention of the posterior part at the time of surgery (5).

In our patient series we did not experience the major postoperative complications, described in the older literature: neither wound dehiscence, retrocorneal membrane formation nor retaining of Descemet's membrane. These good results are probably due to better microsurgical techniques used nowadays, since the literature on these complications mainly dates back to the sixties and seventies. There were no cases of postoperative glaucoma.

All grafts were clinically clear at the end of the follow-up period. Postoperative inflammation did not seem to exceed that after PKP for other reasons. However, one patient was subject to several allograft rejection episodes: an irreversible rejection in one eye and two reversible rejection episodes in both the regraft in that eye and the primary graft in the other eye. This patient however, also had a clear history of anterior uveitis with synechiae, seen on preoperative biomicroscopy. Moreover, on close examination, ghost vessels were not always completely empty and may have constituted an additional risk factor for allograft rejection.

Endothelial cell density did not show a greater-than-expected decline when compared to a control group. This proves that these patients are probably not subject to subclinical inflammation postoperatively, since this would certainly affect their ECD even in the absence of clinical rejection episodes.

Visual acuity improved remarkably in all cases. However, final visual acuity was 10/10 in only one eye and was less than 5/10 in 3 eyes. One possible reason for these moderate visual results is some degree of amblyopia, due to the occurrence of IK at an early age. Another possible hypothesis could be the poor optical quality of the surface of the graft, due to limbal stemcell deficiency as a late sequel of IK, a hitherto unreported complication. In conclusion, the results of our study show that prognosis of PKP for syphilitic interstitial keratitis is the same as for PKP for other corneal pathologies, regarding graft clarity, visual acuity and ECD

REFERENCES

(1) GOLDMAN J.N., KENNETH M.D. and GIRARD F. – Causes of opacity after corneal graft in interstitial keratitis. Bull Mem Soc Fr Ophtalmol 1967; 80:126-131.

(2) GRANT W.M. – Late glaucoma after interstitial keratitis. Am J Ophthalmol 1975; 79:87-91.

(3) HARISPRASAD S.M., MOON S.J., ALLEN R.C. and WILHELMUS K.R. – Keratopathy from congenital syphilis. Cornea 2002; 21:608-609.

(4) KNOX CM and HOLSCLAW DS. Interstitial keratitis. Int Ophthalmol Clin 1998; 38:183-195.

(5) KURZ G.H. and D'AMICO R.A. – Retained Descemet's membrane after keratoplasty for old interstitial keratitis. Am J Ophthalmol 1973; 76:51-53

(6) LARSON S.A., STEINER B.M. and RUDOLPH A.H. – Laboratory diagnosis and interpretation of tests for syphilis. Clin Micriobiol Rev 1995; 8:1-21

(7) PROBST L.E., WILKINSON J. and NICHOLS B.D. – Diagnosis of congenital syphilis in adults presenting with interstitial keratitis. Can J Ophthalmol 1994; 29:77-80.

(8) RABB M.F. and FINE M. – Penetrating keratoplasty in interstitial keratitis. Am J Ophthalmol 1969; 67:907-917

Acknowledgements: Ilse Claerhout is a research assistant for the Flemish Fund of Scientific Research-Flanders (FWO-Vlaanderen)[1]

.....

Corresponding author:
Ilse Claerhout
Ghent University Hospital
De Pintelaan 185
9000 Ghent
Belgium
tel.: +32-9-240.43.88
fax: +32-9-240.38.38
ilse.claerhout@UGent.be