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Recurrent Salzmann's corneal degeneration

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Abstract. Three keratoplasties were carried out on two patients because of nodular degeneration of the cornea. Progress after keratoplasty could be followed up in one eye for 17 months and in the other two eyes, for 2.5 and 9 years, respectively. The implant with the short follow-up of only 17 months remained glass-clear; nothing abnormal was discovered during the checkups. In the case of the other patient in whom a longer follow-up period was possible, the following findings were evident: (1) a remarkably late epithelial immune response in one eye (after 18 months) with subsequent incomplete reepithelisation and formation of fine, superficial, cloudy opacity (observation period 2.5 years); (2) formation of dense but flat, superficial areas of opacity in the cornea of the other eye (observation period 9 years). These areas may be regarded as a precursor of Salzmann's corneal degeneration. No difference could be found between the histological findings in the explants and those in a degenerative pannus or an older scar caused by inflammation of the Bowman membrane.

Introduction

In 1925, Salzmann presented 25 cases of nodular corneal alteration; first called dystrophy, it was later assigned to the degnerative afflictions of the cornea [9]. Seventy-four cases with this condition have been published so far. The following factors are regarded as typical of the disorder:

- A history of superficial keratitis
- Lustrous nodules of the corneal surface, which are blue-white in color, slightly elevated and may be found both at the limbus and the corneal periphery
- Slow progression without reactive inflammation of the eye
- A preference for the female sex
- Unilateral in 80% of all cases
- nonspecific histological findings.

The diagnosis is based on the clinical findings. On the whole, former studies have concentrated on the histological alteration of corneal explants and biopsy specimens from the superficially excised nodules [3, 5–9, 11]. On the other hand, very little is known about the course or development of Salzmann's corneal degeneration over many years after keratoplasty. Following the clinical observation of two patients, one over a period of 9 years running, it occurred to us that a late manifestation of opacity of the donor cornea could be seen as a recurrence of the primary disease, although the complete picture of Salzmann's corneal degeneration did not develop. Houber [5] and Vannas [11] merely report that a relapse of the primary disease in the graft is possible. In addition, the development of Salzmann's corneal degeneration over many years after keratoplasty is unknown, even with regard to alteration of the surface of the donor cornea or a possible immune reaction. It seems valuable to us, therefore, to discuss two patients whose case histories we were able to follow for several years after keratoplasty. We discovered impairment of epithelialization, a late epithelial immune reaction, and opacity of the Bowman membrane, which we regard as a recurrence of the primary disease.

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Case reports

Case 1

A woman suffering from severe myopia was 65 years old (born 1914) when she first came to the University Eye Clinic. The only remarkable finding in her history was recurring keratitis (scrophulosa), which occurred between the ages of 2 and 15.

Initial findings in 1979. Dryness of the eye, blepharitis, photophobia, epiphora, nodular corneal alteration (Fig. 1), strabismus convergens sinister; visual acuity RE cc 0.05, LE 1/35 (strabismic amblyopia). The ocular fundus could not be reliably assessed due both to cataract and to advanced corneal opacity. It was verified by ultrasound, however, that the retina was not detached on either side. The axial length was 29.25 mm on the right, and 30.00 mm on the left. Therapeutic contact lenses improved neither the symptoms nor functional impairment.

Operative measures in the left eye. In 1979, the m. internus was repositioned, and the m. externus resected; in September 1979, perforating keratoplasty was carried out: the diameter of both the recipient and donor cornea was 7 mm; during the course of trepanation, intermediary injury of the iris occurred.

Development after keratoplasty. The graft remained clear at first. Due to the cataract, visual acuity did not improve, however. A moderte blepharitis persisted. The intraocular

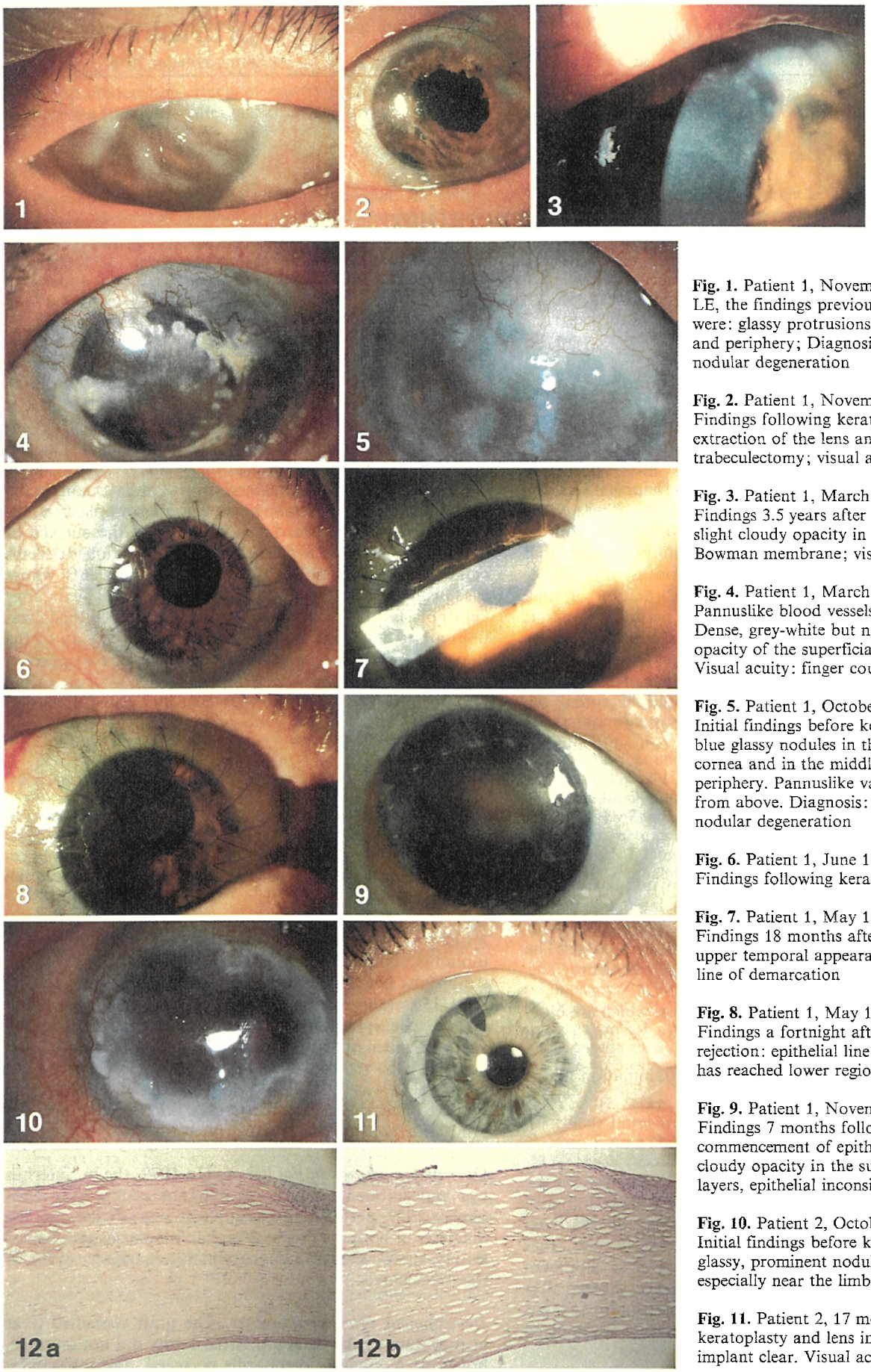

Fig. 1. Patient 1, November 1978. In the LE, the findings previous to keratoplasty were: glassy protrusions in the center and periphery; Diagnosis: Salzmann's nodular degeneration

Fig. 2. Patient 1, November 1980. LE: Findings following keratoplasty, extraction of the lens and trabeculectomy; visual acuity cc 0.4

Fig. 3. Patient 1, March 1983. LE: Findings 3.5 years after keratoplasty: slight cloudy opacity in the level of the Bowman membrane; visual acuity cc 0.1

Fig. 4. Patient 1, March 1987. LE: Pannuslike blood vessels from above. Dense, grey-white but non-prominent opacity of the superficial corneal layers. Visual acuity: finger counting

Fig. 5. Patient 1, October 1986, RE: Initial findings before keratoplasty with blue glassy nodules in the center of the cornea and in the middle of the periphery. Pannuslike vascularization from above. Diagnosis: Salzmann's nodular degeneration

Fig. 6. Patient 1, June 1987. RE: Findings following keratoplasty

Fig. 7. Patient 1, May 1988. RE: Findings 18 months after keratoplasty: upper temporal appearance of epithelial line of demarcation

Fig. 8. Patient 1, May 1988. RE: Findings a fortnight after epithelial rejection: epithelial line of demarcation has reached lower region

Fig. 9. Patient 1, November 1988. RE: Findings 7 months following commencement of epithelial rejection: cloudy opacity in the superficial corneal layers, epithelial inconsistency

Fig. 10. Patient 2, October 1986. LE: Initial findings before keratoplasty with glassy, prominent nodules of the cornea, especially near the limbus

Fig. 11. Patient 2, 17 months after keratoplasty and lens implantation: implant clear. Visual acuity: LE cc 0.5

pressure varied with a maximum of between 30 and 35 mmHg (due to adrenocortical steriod?). In November 1980, intracapsular cataract extraction, combined with a trabeculectomy (Fig. 2), was performed.

Development after keratoplasty, cataract extraction and trabeculectomy. The intraocular pressure was under control and the graft remained clear at first. Visual acuity improved to 0.4 (with +4.0, ( )−2, 0/5°). Four years after keratoplasty had been carried out (9/1983), cloudy opacity formed in the upper third of the implant (Fig. 3). Visual acuity was reduced to 0.1 (with +3.0, ( )−3, 0/15°). The opacity continued to increase. Visual acuity was reduced to finger counting.

Eight years after keratoplasty, the donor cornea displayed opacity of varying density, especially in the upper half, which merged with the opaque recipient cornea, e.g., in the 9, 11, and 3 o'clock positions (Fig. 4). These alterations were located at the level of the Bowman membrane without showing the lustrous nodules typical of Salzmann's corneal degeneration. Due to consolidation of the corneal opacity, photosensitivity increased once more. Visual acuity remained between the level of 0.03 and finger counting.

Operative measures in the right eye. In October 1986, perforating keratoplasty, combined with extracapsular cataract extraction (Figs. 5, and 6) was performed; the explant and implant diameters measured 6.8 and 7.0 mm, respectively). The transplant healed without complication. The best postoperative visual acuity amounted to between 0.4 and 0.5 (with +2.0, 0–4, 0/11°).

Postoperative progress. An epithelial immune reaction located at the upper margin of the implant developed 1.5 years after corneal grafting (April 1988). Within a fortnight it affected two-thirds of the donor cornea (Figs. 7, 8). Subsequently, whorl-shaped epithelial opacity, slight cloudy opacity of the Bowman membrane, pronounced ocular dryness, photophobia and epiphora appeared. Visual acuity was reduced to 0.3–0.2 cc. After epithelial rejection, the corneal epithelium was no longer intact. Whorl- and band-shaped zones with punctiform staining were found especially frequently in the palpebral fissure (Fig. 9).

Case 2

This woman was 65 years old (born 1918) at the time of her first visit to the University of Cologne Eye Clinic. Remarkable in her case history was again merely keratitis of the right eye at the age of 4 years.

Initial findings in October 1986. A nodular thickness of the cornea of the right eye was more apparent in the periphery than in the center. The prominent regions glimmered blue and were of a glassy nature (Fig. 10). In addition, corneal dryness, cataract, axis myopia with a 26.47 mm axis length, and superficial, peripheral vascularization of the cornea were observed. Visual acuity: finger counting, light projection intact. Findings were confined to the right eye only. The left eye was completely normal.

Operative measures in the right eye. In July 1987, perforating keratoplasty, combined with implantation of a posterior chamber lens of 10 dpt, was performed.

Postoperative progress. The transplant healed without complications. A year after keratoplasty linear alterations of the epithelium appeared around the upper margin of the implant. At first, the findings were interpreted as an epithelial immune response. Since the line remained in position, epithelial discorders of other origins must also be considered. The implant remained glass-clear. Further complications have so far not occurred (17 months after keratoplasty). The latest visual acuity (December 1988) follows: +2.0–2.5/10° = 0.5. As astigmatism was not pronounced, sutures were not removed (Fig. 11).

Histology

Procedure

The corneas were mounted with formallin and embedded in paraffin. For the oxytalan reaction [4], we used deparaffinated and hydrogenated (slide) preparations. The sections were oxidized in 10% oxone for 30 to 60 min at room temperature. Following immersion in water, the slides were stained for 8 min using fresh Gomoris aldehyde fuchsine solution. The oxytalan fibers were blue-violet. The nucleus was stained using haemalum.

Findings

The three explants showed several circumscript areas in the level of the Bowman membrane, which displayed new formation of connective tissue. These corresponded to the clinically apparent nodules (Fig. 12). Cell-poor fibrosis, rich in collagen but without blood vessels or inflammatory cells, similar to a degenerative pannus, appeared to be involved here, causing bulging of the thinned-out epithelium. In one preparation the fibrotic area was separated from the corneal stroma by blood vessels, and mononuclear inflammatory cells were found subepithelially.

Discussion

The histological findings in the corneal explants are nonspecific. They differ neither from a degenerative pannus cornae nor from an older scar of the Bowman membrane following inflammation or trauma. The diagnosis "Salzmann's degeneration of the cornea" may therefore only be based on the clinical findings and not on the histopathological findings alone. Staining of the oxytalan fibers was used to delimit the newly formed connective tissue from the preexisting corneal stroma. The normal adult corneal stroma does not contain any oxytalan fibers [1, 2]. Signs of inflammation could only be found in one preparation at the edges of the nodules. A connection between Salzmann's nodules and inflammatory cells has occasionally become apparent [5, 8, 11]; they are, however, inconsistent

Fig. 12a, b. Patient 1. Part of the corneal explant from the RE of the first patient: aldehyde fuchsin staining, **a** preceded by oxidation; **b** without oxidation. The newly formed connective tissue (see **a**), blue-violet in colour, is a Salzmann's nodule. The corneal epithelium above is rarefied or completely missing. The anterior corneal stroma contains blood vessels. Apart from that, no further symptoms of inflammation can be found (×25)

and cannot be seen as a means of sufficiently clarifying the etiology of this condition.

It must be considered whether perforating keratoplasty may be given preference over the lamellar operative procedure. On the whole, opacity is confined to the superficial layers of the cornea; a lamellar keratoplasty with no risk of endothelial immune reaction would therefore be preferable. No reliable conclusions as to the incidence of immune response can be drawn from previous studies. There are many different reasons for a graft reaction, which may result in the formation of a retrocorneal membrane as described in the study of Houber [5].

Following are the reasons we chose perforating keratoplasty, which generally also allows better functional results:
– In advanced cases, the alterations caused by Salzmann's degeneration can also affect the middle, and occasionally even deep stroma layers.
– Pannuslike, peripheral superficial blood vessels are consistent with Salzmann's degeneration, but the deep-seated corneal vascularization important for an immune response does not form part of the typical clinical picture.
– Surface complication, which probably play an important part in the genesis of this disorder, occur after both lamellar and perforating keratoplasty.

Two particularities became noticeable in our patients after several years of observation: (1) Superficial opacity of the stroma (relapse of the primary condition?); (2) an epithelial immune response that developed at a later stage.

With regard to the first peculiarity, recurrence of Salzmann's corneal degeneration in the transplant has already been pointed out [5, 11]. As in the case of our patient, Houber [5] and Vannas [11] emphasized that the opacity was neither raised above the surface nor did it show the typical lustrous blue nodules. Since the early forms of Salzmann's corneal degeneration have not been recorded, it is possible that the recurrence of Salzmann's nodules begins with an uncharacteristic flat opacity in the transplant, particularly as these alterations are not typical of any other autonomous disorder. Our patient first showed progressive cloudy opacity of the Bowman membrane 4 years after keratoplasty. Until now, 5 years later, no typical protuberances have developed. We suggest that the opacities described, are the incipient form of Salzmann's degeneration, which may take more than 9 years to develop. However, it cannot yet be excluded that there is an unclassified degenerative process with flat rather than nodular scarring.

Regarding the second point, it is accepted that the clinical appearance of an epithelial immune reaction in a corneal graft consists of a sharply demarcated rejection line that begins in the periphery of the transplant, is confined to the transplant, and migrates across it within days or 2–3 weeks. The epithelial immune reaction ends in reversible changes in the epithelium and usually occurs during the first 2 months after grafting. Since the epithelium of the donor graft may survive longer, a later manifestation is possible [10]. The moving line on the epithelium that we observed in our patient fulfilled the criteria of what is called an epithelial rejection line after corneal transplantation. We therefore interpreted it as an immune reaction against the donor epithelial cells. The corneal epithelium may possibly have a decisive bearing on the pathogenesis of Salzmann's corneal degeneration. Prior to the immune reaction, the epithelial layer was intact and without irregularities. Following the immune response, surface alterations with dryness of the eye and epithelial defects, like those prior to grafting, reappeared and have persisted to date (6 months after the immune response). These facts and the late manifestation of the immune reaction suggest that the recipient cornea is not able to build up an intact corneal surface. It must be taken into account, therefore, that the impaired epithelization of long standing in Salzmann's degeneration plays a part in the pathogenesis of the scar formation in the neighboring Bowman membrane.

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