

Recurrent Salzmann's Nodular Degeneration

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Background: We report a patient with Salzmann's nodular degeneration in whom the disease occurred without a history of keratitis and recurred twice after keratectomy.

Case: A unilateral case of symptomatic Salzmann's nodular degeneration developed after cataract surgery in a 75-year-old woman.

Observations: We performed superficial keratectomy and amniotic membrane transplantation two times, but both times the lesions recurred 1 month postoperatively. After we performed the third superficial keratectomy above the level of Bowman's layer, there was no recurrence by the last follow-up 6 months postoperatively.

Conclusions: Salzmann's nodular degeneration can be diagnosed by clinical characteristics, even if there is no history of keratitis. Because it can recur after surgical removal of the lesion, patients with this disease need to be followed-up periodically. **Jpn J Ophthalmol 2003;47:401-404** © 2003 Japanese Ophthalmological Society

Key Words: Keratectomy, recurrence of disease, Salzmann's nodular degeneration.

Introduction

Salzmann's nodular degeneration is a nodular degeneration of the cornea. In this disease, single or multiple white, gray, or blue elevated nodules are distributed in the central or peripheral cornea. Salzmann's nodular degeneration usually develops in cornea with a history of phlyctenulosis and trachoma, vernal keratoconjunctivitis, measles, scarlet fever, or various other viral diseases.^{1,2} The degeneration is usually bilateral, occurs more often in women, and develops more frequently as patients age.²

We report a case of unilateral Salzmann's nodular degeneration, which occurred without a known causative disease of the cornea, and recurred twice despite removal.

Case Report

A 75-year-old woman was admitted to our hospital with complaints of experiencing pain and foreign-body

sensation in her left eye for several months. Cataract surgery on her left eye had been carried out 1 year previously, and no specific corneal or systemic disease had been found at the time of surgery. In our initial examination, corrected visual acuity was 20/25 OD and 20/60 OS. Slit-lamp examination showed mild lens opacity OD and a posterior chamber intraocular lens OS. A white elevated nodule <1 mm in size was detected in the upper temporal cornea of her left eye, 3-4 mm distant from the corneal center, accompanied by peripheral vascularization and corneal erosion that was stained by fluorescent dye (Figure 1A). We thought the lesion was infectious, and started to treat it with quinolone and tobramycin eyedrops.

On the 6th month after the initial visit, the size and density of the lesion had not improved and vascular ingrowth had progressed. The patient was treated additionally with acyclovir ointment and artificial tear eyedrops. On the 15th month after the initial visit, pain and foreign body sensation in the left eye were aggravated, and the size of the lesion and the vascular invasion had increased (Figure 1B). We diagnosed the case clinically as Salzmann's nodular degeneration, and performed superficial keratectomy and amniotic membrane transplantation around the nodule and the vascularized area

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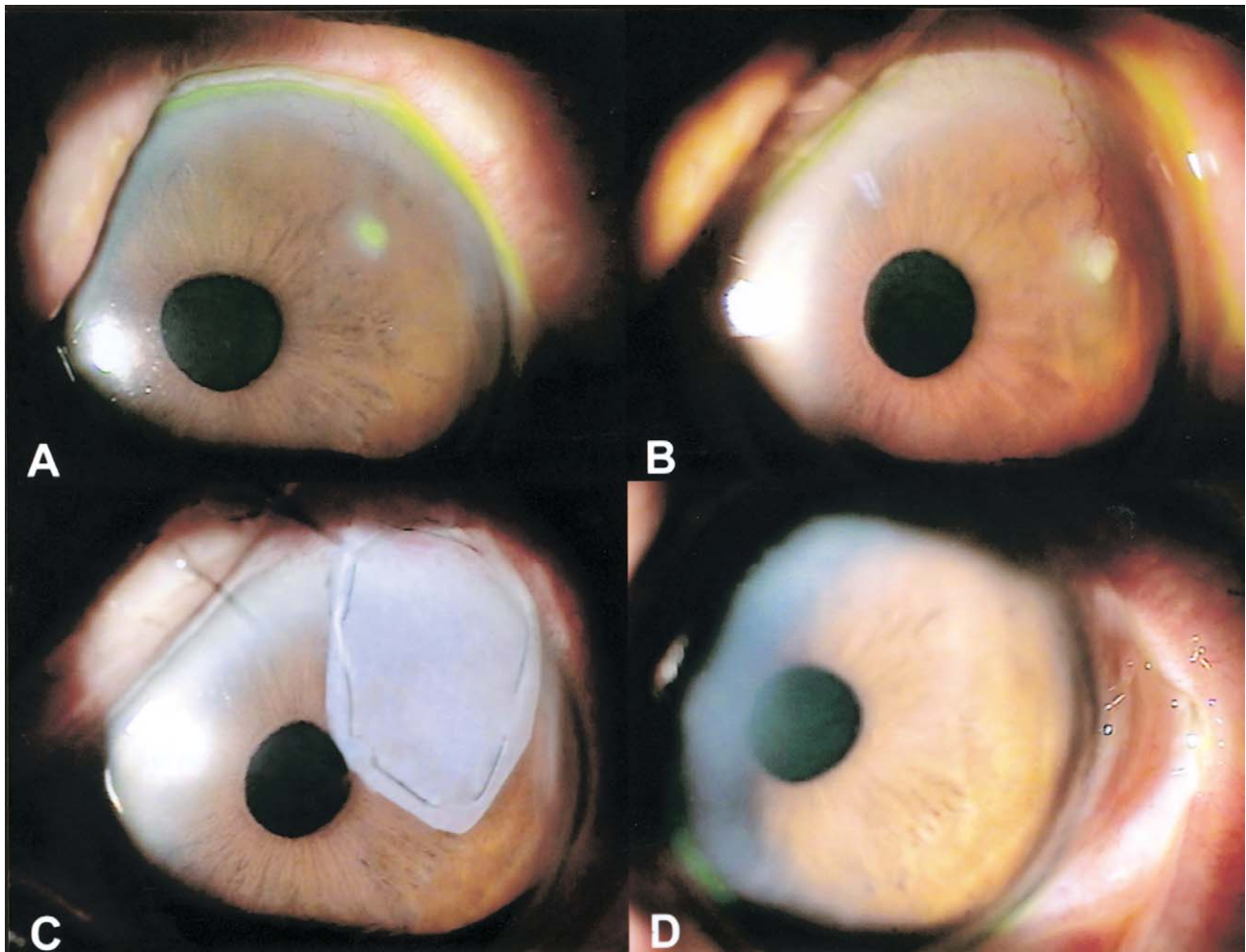


Figure 1. (A) Unilateral Salzmann's nodular degeneration in a 75-year-old woman. A fluorescent dye-stained white elevated lesion with peripheral vascularization is seen in the upper temporal mid-peripheral cornea. (B) Fifteen months after initial visit; no improvement of lesion, which had increased in size and vascularization. (C) First postoperative state after superficial keratectomy and amniotic membrane transplantation. (D) Six months after third superficial keratectomy; lesion had disappeared.

(Figure 1C). During superficial keratectomy, we tried to remove the lesion completely at the level of the superficial stroma using a beaver blade. In histopathologic examination, electron microscopy showed irregular disruption of the collagenous stroma by invaginated epithelial cells and activated fibroblasts. Bowman's membrane was missing in this zone, and basement membrane-like materials were scattered within the collagenous stroma (Figures 2A, 2B). The patient used quinolone and 0.1% fluorometholone eyedrops 4 times a day for 1 month postoperatively and after that, artificial tear drops frequently.

One month after superficial keratectomy, the previous corneal lesion had almost disappeared, but two new, white, relatively flat nodules were noted simultaneously at the temporal peripheral cornea. Six months after keratectomy, the nodules had increased in size and vessels

invaded the lesion. The patient again complained of persistent pain and foreign-body sensation.

Seven months after the first keratectomy, we repeated superficial keratectomy and amniotic membrane transplantation, but one nodule recurred again 1 month after the second operation. Under slit-lamp microscopy, we removed this nodule above the level of Bowman's membrane carefully with a no. 15 blade. At the last follow-up, 6 months after the third operation, the symptoms of the patient were improved and the corneal nodular lesion had disappeared completely (Figure 1D).

Discussion

Salzmann's nodular degeneration is a rare disease first reported by Salzmann¹ in 1925 as a nodular degeneration

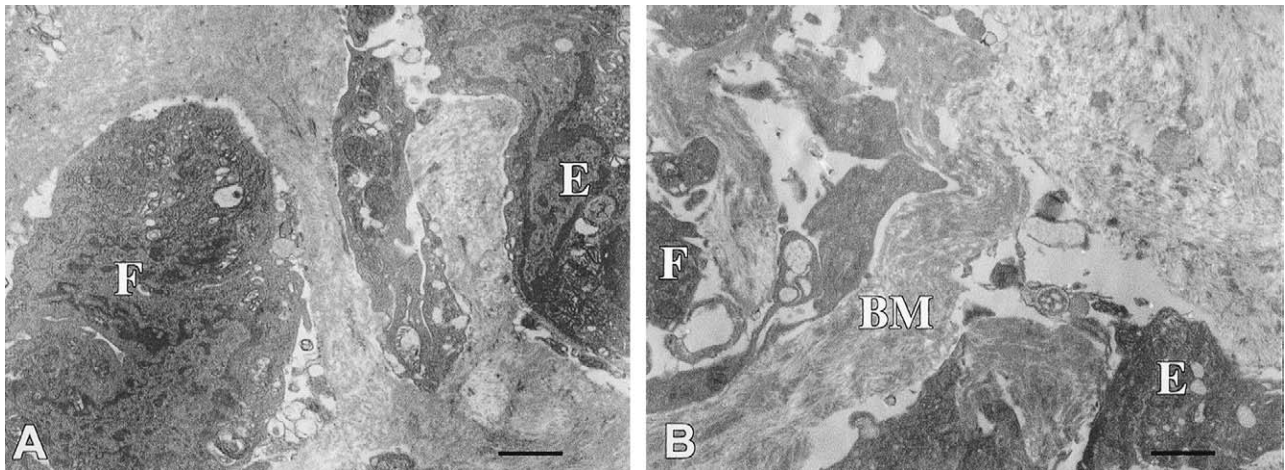


Figure 2. Electron microscopic findings of the nodule. (A) The collagenous stroma of the cornea is disrupted irregularly by invaginated epithelial cells (E) and activated fibroblasts (F) with well-developed and abundant rough endoplasmic reticulum. Bowman's membrane is missing in this zone. Bar = 1 µm. (B) Basement membrane-like materials (BM) are scattered within the collagenous stroma. Bar = 1 µm.

of the cornea that occurred several years after a trachomatous or phlyctenular keratitis. Other than phlyctenulosis and trachoma, Salzmann's nodular degeneration has been reported as a late sequela to vernal keratoconjunctivitis, measles, scarlet fever, or various other viral diseases.^{1,2} There is also the report that it is associated with epithelial basement dystrophy, and the report that it is inherited in a family with autosomal dominant inheritance, or it may appear in eyes with no known history of keratitis.^{3,4}

The nodules usually vary in number from one to nine; white, gray or blue nodules are elevated above the surface of the cornea.² They occur either in scarred cornea or at the edge of transparent cornea, and are distributed in either the central or peripheral cornea.² The underlying cornea may be scarred, vascularized, edematous, or normal, depending on the patient.³ A pigmented line, which ran horizontally along the superior one third of the cornea at the base of some nodules, has been reported.⁴ The degeneration is bilateral in 80% of the cases, occurs more often in women, and develops more frequently as patients age.^{2,3} In our patient, Salzmann's nodular degeneration had developed unilaterally as one nodule accompanied by peripheral vascularization, occurring 1 year after cataract surgery without a known causative corneal disease.

In histopathologic examination, hyaline plaque is precipitated between the corneal epithelium and Bowman's membrane. Corneal epithelium, which has varying thicknesses and in nodular areas often consists of only a single layer of flattened epithelial cells, shows degenerative changes. Bowman's membrane is missing over the

nodule, and in this zone there is excessive secretion of a basement membrane-like material. Hyaline degeneration of collagen, cellular debris, and electron-dense hyaline deposits are seen in the collagen of the nodule.² But the histological findings are nonspecific and are not different from a degenerative pannus or an old scar following inflammation or trauma. The diagnosis may therefore be based only on the clinical findings and not on the histopathological findings alone.⁵ External irritation because of poor epithelial protection can be considered as a causative factor.² In one specimen, B and T lymphocytes and major histocompatibility complex class II antigens were noted. It is also thought that an active immune process may play a role.⁴

Patients are usually asymptomatic, and there is no need for treatment. Treatment is required when there is associated corneal erosion or when patients complain of lacrimation, photophobia, diminished vision, or foreign-body sensation. In the past, cryotherapy was used, but recently the lesion can usually be successfully treated with simple excision of the nodule or superficial keratectomy with a blade.³ Occasionally, excimer laser phototherapeutic keratectomy (PTK) may be another treatment option.³ When superficial keratectomy of a peripheral nodule is performed, refractive change such as a myopic shift, or reduction in hyperopia can result from central corneal steepening. Rarely, lamellar or penetrating keratoplasty is indicated for central or deep stromal invasion and, in one study, when penetrating keratoplasty was performed, recurrences occurred several years later.⁵ In these recurrences in the transplant, the opacity was neither

raised above the surface nor did it show the typical lustrous blue nodules.⁵ Longstanding impaired epithelization in Salzmann's nodular degeneration may play a part in the pathogenesis of the scar formation in the neighboring Bowman's membrane.⁵

In our patient, we performed not only complete removal of the lesion by superficial keratectomy, but also amniotic membrane transplantation for the purpose of preventing inflammation, scar, or vascularization, and for the palliation of symptoms. However the lesion recurred twice. When we performed superficial keratectomy above the level of Bowman's membrane, it had not recurred by the last examination at 6 months postoperatively. Based on this experience, we think that, when treating Salzmann's nodular degeneration, minimizing injury to Bowman's membrane and corneal stroma, and exercising care during surgery can help to prevent recurrence. The

management of Salzmann's nodular degeneration will need further investigation.

In conclusion, Salzmann's nodular degeneration can be diagnosed by clinical characteristics without a history of keratitis and can recur after surgical removal of lesions. Therefore, patients with this disease need to be followed up periodically.

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