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Pathological Findings in Lens Capsule and Silicone Intraocular Lens Extracted From Eye With Chronic Infectious Endophthalmitis

Shizuya Saika,* Yoshiji Kawashima,*
Takeshi Miyamoto,* Yuka Okada,* Sai-ichi Tanaka,*
Yoshitaka Ohnishi,* Akira Ooshima† and Akio Yamanaka‡

*Departments of *Ophthalmology and †Pathology, Wakayama Medical College, Wakayama, Japan; and ‡Department of Ophthalmology, Kobe Kaisei Hospital, Kobe, Japan*

Abstract: The lens capsule and silicone intraocular lens (IOL) extracted from the eye of a patient with chronic infectious endophthalmitis was examined histopathologically to evaluate the pathology of a capsule and IOL surfaces in the presence of bacterial infection. A 69-year-old man developed an infection in his right eye 4 months after phacoemulsification and aspiration of a cataract and implantation of a silicone IOL. During vitrectomy, the capsule and IOL were extracted and processed for light or scanning electron microscopy. Cryosections of the capsule were subjected to Gram staining and immunohistochemical tests for extracellular matrix components. The lens capsule contained an accumulation of extracellular matrix, including collagen types and fibronectin. A colony of Gram-positive rod bacteria was detected inside the capsular bag. Scanning electron microscopy failed to detect any microorganisms on the IOL surface. Histological examination of cryosections of the extracted capsule confirmed the presence of infection during surgery even though preoperative cultures of intraocular fluid were negative. Immediate antibacterial treatment could be initiated. **Jpn J Ophthalmol 1998;42:456–460**

Key Words: Cataract surgery, extracellular matrix, Gram staining, immunohistochemistry, infectious endophthalmitis, pathology, silicone intraocular lens.

Introduction

Infectious endophthalmitis is one of the complications of intraocular surgery.[1–4] Although various microorganisms may cause this complication, chronic endophthalmitis is most often induced by low-virulence anaerobic bacteria, such as *Propionibacterium acnes*.[1–4] These bacteria reportedly grow in the space between an intraocular lens (IOL) and the lens capsule. Although systemic administration of antibiotics does not eradicate the infection, vitreous surgery, combined with the removal of the IOL and the capsule, is effective. We present here a case of chronic endophthalmitis that occurred after phacoemulsification and aspiration (PEA) of the cataractous crystalline lens, and implantation of a silicone IOL. The eye was treated by vitreous surgery and extraction of the lens capsule and IOL. The extracted lens capsule and silicone IOL were examined by light and scanning electron microscopy (SEM) for evidence of bacterial infection. Cryosections of the capsule were processed for Gram staining or for immunohistochemical staining of extracellular matrix components to detect any infections microorganism(s), and to determine the presence and distribution of such components at the focus of infection.

Case

A 69-year-old man underwent PEA and implantation of a silicone IOL (AMO, PhacoFlex II, SI-30NB, Allergan, San Leandro, CA, USA) in his right eye on August 22, 1996 in another eye clinic. The day before surgery, ofloxacin was instilled topically,

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Address correspondence and reprint requests to: Shizuya SAIKA, MD, Department of Ophthalmology, Wakayama Medical College, 7-Bancho 27, Wakayama 640, Japan

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4 times per day. Corrected postoperative visual acuity on the day after lens implantation was 20/20. Inflammation in the anterior chamber gradually subsided through October 1996. However, beginning in December 1996, the number of inflammatory cells in the anterior chamber increased, leading the patient to consult us on January 31, 1997. Prior to this consultation, levofloxacin orally and topical instillation of sulbenicillin sodium and cefmenoxime had been prescribed for the patient for about 1 month. Corrected visual acuity in the right eye was 20/60 at consultation. He did not complain of ocular pain. Slit-lamp examination revealed marked inflammation in the anterior chamber and corneal stromal edema associated with ciliary injection and marked foldings of Descemet's membrane, which prevented detailed examination of the ocular fundus. Fine whitish precipitates were observed on the corneal endothelium. No hypopyon was seen. Intraocular pressure was 12 mmHg. No abnormal shadow was detected in the vitreous cavity by B-mode echographic examination. On the day of initial consultation, the patient underwent three-port vitreous surgery and extraction of the IOL and capsule. Microbiological culture of the aqueous humor under both aerobic and anaerobic conditions failed to detect any bacteria. The patient received 7-day administration of an intravenous antibiotic and 28-day oral ofloxacin. The eye gradually recovered, and the patient's corrected visual acuity in this eye was 20/20 on February 9, 1997.

Pathological Examination

The Capsule

The extracted lens capsule was embedded in OCT compound (Miles Laboratories, Elkhart, IN, USA). Cryosections were fixed in cold acetone and processed for hematoxylin and eosin (HE) staining, Gram staining, and immunohistochemical staining for types I and IV collagen and for cellular fibronectin. For immunohistochemistry, cryosections were allowed to react with several monoclonal antibodies: mouse monoclonal immunoglobulin gamma G (IgG) anticollagen type I antibody [donated by the Depart-

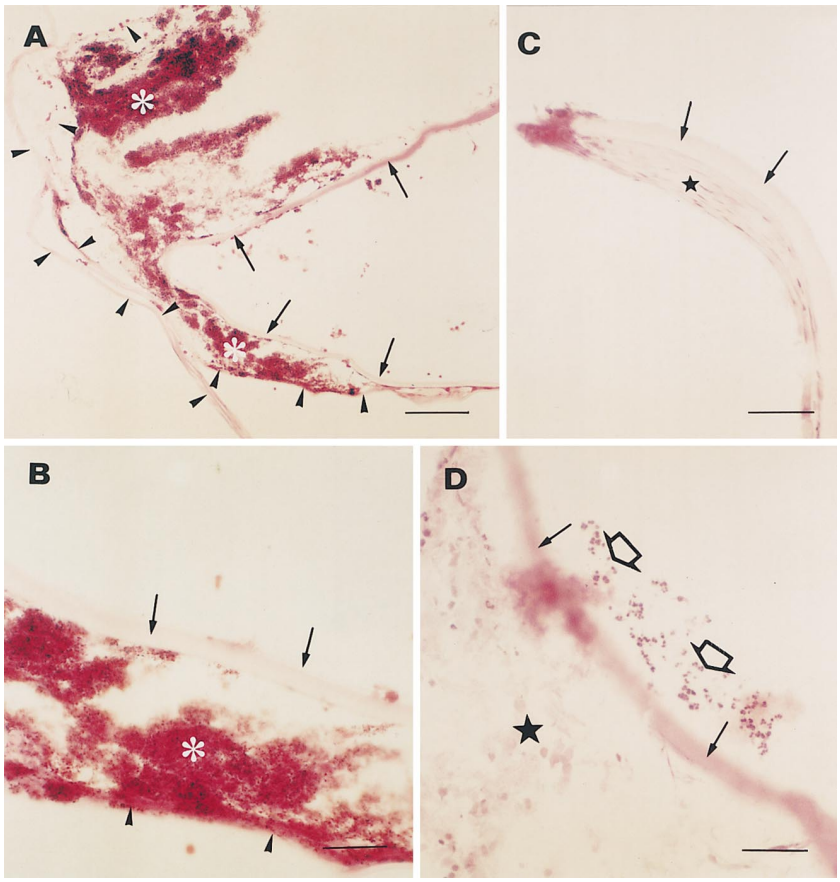

Figure 1. Light microscopic findings in capsule extracted during vitreous surgery. (**A**) Infectious focus of Gram-positive bacteria (white asterisks) was observed between anterior (arrows) and posterior (arrowheads) capsules. (**B**) High-power photomicrograph of infectious focus inside capsular bag. Gram-positive rod bacteria (white asterisk) were found growing between anterior (arrows) and posterior (arrowheads) capsules. (**C**) Slender cells, presumably lens epithelial cells (star), proliferated at edge of anterior capsule (arrows). (**D**) Polymorphonuclear leukocytes (open arrows) were found to infiltrate outside anterior capsule (thin arrow). Infectious focus (star) was seen inside anterior capsule [A, B, Gram staining; C, D, Hematoxylin and eosin staining, Bar: 100 μm (A), 25 μm (B–D)].

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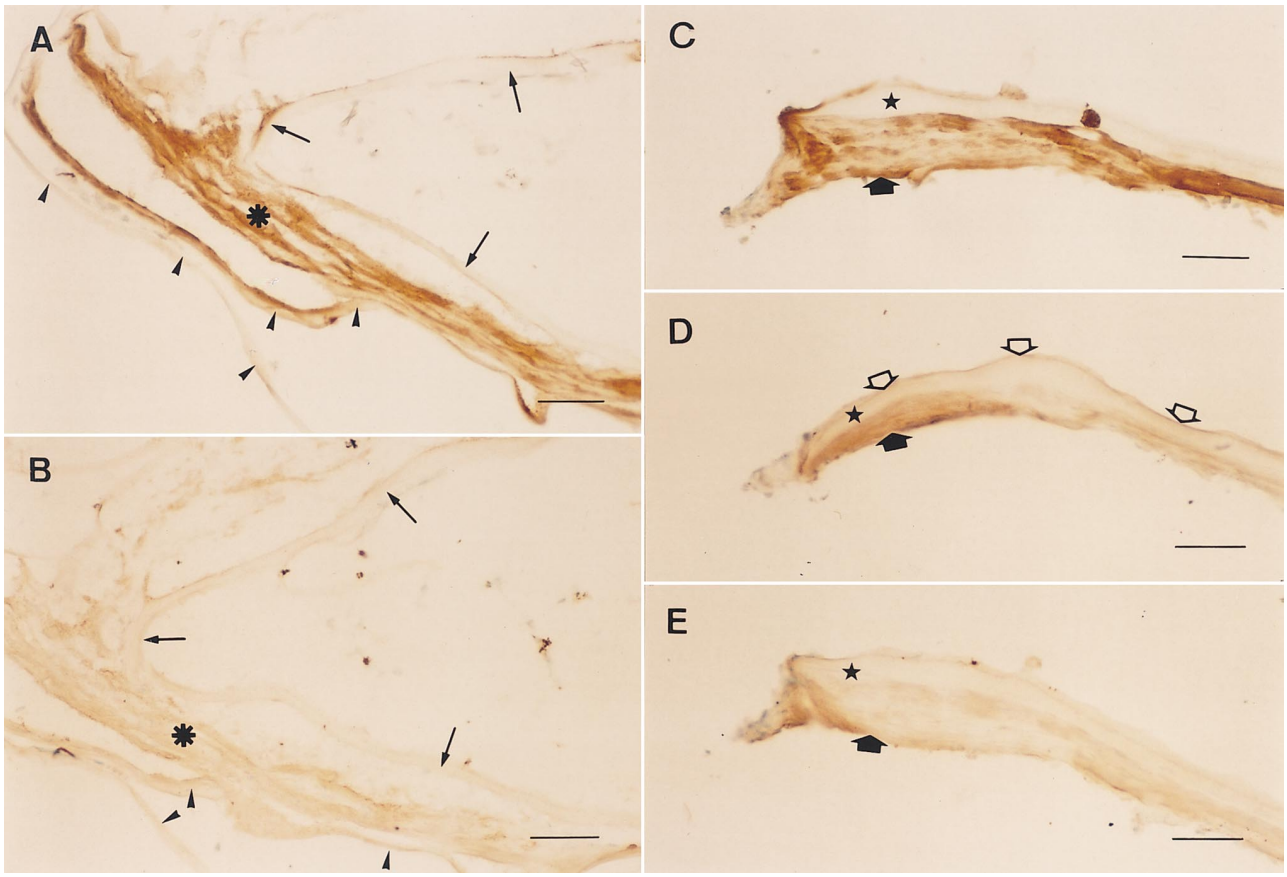

Figure 2. Immunolocalization of collagen I (**A**) and cellular fibronectin (**B**) in capsular bag. Marked immunoreactivity (asterisk) for collagen type I or cellular fibronectin was observed between anterior (thin arrows) and posterior (arrowheads) capsules, where infectious focus had been detected. (**C**–**E**) Immunolocalization of collagen type I (**C**), collagen type IV (**D**), and cellular fibronectin (**E**) in extracellular matrix. Accumulation (thick arrows) was on inner surface of edge of anterior capsule (star). Marked immunoreactivity for each component was seen. Anterior portion of anterior capsule (open arrows) (**D**) was also immunoreactive for these components. [Indirect immunostaining, Bar: 25 μm (**A**, **B**), 50 μm (**C**–**E**)].

ment of Pathology, Wakayama Medical College, Japan, ×100 in phosphate-buffered saline (PBS)]; mouse monoclonal IgG antitype IV collagen antibody (donated by the Department of Pathology, Wakayama Medical College, Japan, ×100 in PBS); and mouse monoclonal immunoglobulin gamma M (IgM) anticellular fibronectin antibody (Sigma, St. Louis, MO, USA, ×100 in PBS). Specimens were then washed in PBS, and treated with peroxidase-conjugated secondary antibodies (Cappel, Organon-Teknika, Durham, NC, USA, ×100 in PBS). The color of the antibody complexes was then developed with 3,3′-diaminobenzidine in Tris-HCl buffer (pH 7.6) containing 0.01% hydrogen peroxide. Specimens were counterstained with methyl green, dehydrated through a graded ethanol series, mounted in Canada balsam and observed under light microscopy.

SEM of IOL

The extracted silicone IOL was fixed in 2.0% glutaraldehyde in 0.1 mol/L phosphate buffer, dehydrated first in a graded ethanol series and then in a critical point dryer, and coated with gold by ion spatter (Hitachi HCP-2, Tokyo). The specimen was observed under a SEM (T-220, Nihon Denshi, Tokyo).

Results

Light Microscopy with HE Staining or Gram Staining

In the lens capsular bag, slender cells, presumed to be lens epithelial cells, were found proliferated on the capsule (Figures 1A–C). A focus of infection by Gram-positive rod bacteria was observed inside the

capsular bag (Figures 1A–B). Polymorphonuclear leukocytes were seen outside the capsular bag adjacent to the focus of infection; only a few leukocytes were seen inside the capsular bag (Figure 1D).

Immunohistochemistry

Immunoreactivity for collagen types I (Figure 2A) and IV (not shown) and for cellular fibronectin (Figure 2B) was detected in extracellular matrix that had accumulated in the capsular bag around the IOL. Marked immunoreactivity was observed at the focus of the bacterial infection (Figures 2A, B). An accumulation of extracellular matrix on the inner surface of the anterior capsule exhibited marked immunoreactivity for collagen types I and IV and for cellular fibronectin (Figures 2C–E). Immunoreactivity for these matrix components was also seen in the anterior portion of the anterior capsule (Figure 2D).

SEM of IOL

We observed a few cellular deposits on the IOL, including macrophages (not shown) and foreign-body giant cells, some with erythrocytes adhering to their surface, and the presence of acellular fibrous materials (Figures 3A–D). Typical bacterial adherence was not seen.

Discussion

We have described light microscopic findings on the lens capsule and scanning electron microscopic findings on the silicone IOL extracted from an eye of a patient with chronic infectious endophthalmitis.

The focus of infection by Gram-positive bacteria was detected histologically inside the capsular bag, but culture of the aqueous humor, under both aerobic and anaerobic conditions, failed to isolate any pathogen. The bacteria detected by Gram staining were *Corynebacterium sp*. or *P. acnes*. Although clusters of polymorphonuclear leukocytes were observed outside the capsular bag adjacent to the focus of infection, almost no inflammatory cells were detected inside the capsular bag, suggesting that the infectious focus was not affected by the defense system of leukocytes. Scanning electron microscopy of the extracted silicone IOL showed the adherence of foreign-body giant cells and acellular deposits, as previously reported.[5–9] Outgrowth of lens epithelial cells has been seen in experimental animal cases.[10] No typical lens epithelial cells were detected on the surface of the present IOL, although it had been implanted in the capsular bag and its peripheral optic portion had been covered by the anterior capsule. Almost no bacteria and no polymorphonuclear leukocytes were observed on the surface of this IOL.

An accumulation of extracellular matrix on the inner surface of the lens capsule showed immunoreactivity for collagen types I and IV and for cellular fibronectin, in association with a proliferation of cells presumed to be lens epithelium. These matrix components were considered to be the products of proliferating lens epithelial cells. Accumulation of matrix components, including various types of collagen, has been observed in cases of opacification of the

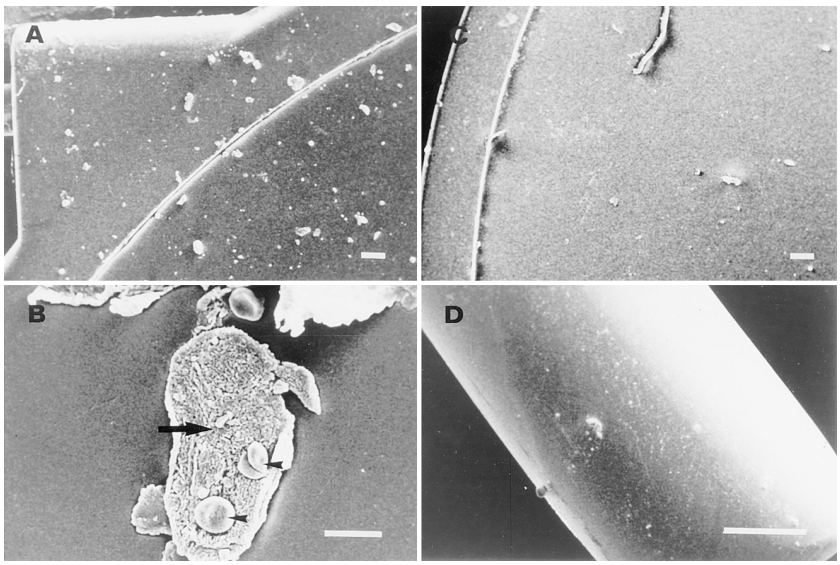

Figure 3. Scanning electron microscopy of explanted silicone intraocular lens (IOL). (**A**) Anterior surface of edge of IOL. Typical cellular adhesion was not seen. (**B**) Foreign-body giant cell (arrow) with arythrocytes (arrowheads) on its surface was seen on anterior surface of IOL. (**C**) Scanning electron micrograph of posterior surface of IOL; no cellular or bacterial adherence was seen. (**D**) Scanning electron micrograph of haptic loop of IOL. No cellular or bacterial adherence was seen. Bar: 100 μm (**A**, **C**), 10 μm (**B**), 50 μm (**D**).

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posterior capsule without infectious complications.[11,12] Immunoreactivity for cellular fibronectin and type I collagen seemed most marked at the focus of infection, a finding that suggests an intracapsular infection may increase opacification of the posterior capsule after the implantation of an IOL.

Although preoperative cultures of the aqueous humor were negative in the present case and the condition was considered either infectious endophthalmitis or noninfectious inflammatory eye disease, Gram staining of the extracted capsule proved highly useful in detecting intraoperative infection. Although culturing the capsular bag may be useful for determining which species had caused the infection, such cultures take about 1 week. The addition of appropriate antibiotics to the intraocular solution used during vitreous surgery after the histological confirmation of the infection could help to prevent further damage of ocular tissue caused by intraoperative infection.

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