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# Outbreak of Subacute-Onset Toxic Anterior Segment Syndrome Associated with Single-Piece Acrylic Intraocular Lenses

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***Purpose:*** To report the results of a clinical investigation after an outbreak of subacute-onset toxic anterior segment syndrome (TASS) after implantation of single-piece acrylic intraocular lenses (IOLs), which then were recalled voluntarily from the market.

***Design:*** Retrospective, multicenter, observational case series.

***Participants:*** Cases reported to the manufacturer from January 2015 through March 2016 of unusual ocular inflammation after cataract surgery using AcrySof ReSTOR, ReSTOR toric, or AcrySof IQ toric SN6AT6-9 IOLs (Alcon Laboratories, Inc., Fort Worth, TX).

***Methods:*** The independent investigation committee, not Alcon, directly requested the surgeons for data on 304 eyes from 184 facilities.

***Results:*** Consent for data collection was obtained for 201 eyes from 130 facilities. By excluding cases with infectious endophthalmitis and inconclusive cases, the investigation committee identified 147 cases of subacute-onset TASS. AcrySof ReSTOR or ReSTOR toric IOLs and AcrySof IQ toric SN6AT6-9 IOLs were implanted in 94 eyes (63.9%) and 53 eyes (36.1%), respectively. The mean onset time was 13.1±16.4 days after surgery (range, 1−88 days), with 84 eyes (57.1%) demonstrating symptoms within 7 days after surgery. Typical clinical symptoms were mild to moderate exacerbation of inflammation in the anterior chamber after an uneventful clinical course for a few days after surgery. One hundred four eyes (70.7%) were treated with medication alone, and 43 eyes (29.3%) underwent surgery, including irrigation of the anterior chamber, vitrectomy, and removal of the IOL. The mean best-corrected visual acuity (BCVA) at the final visit (−0.012±0.175 logarithm of the minimum angle of resolution [logMAR]) was significantly better than the BCVA at the onset of TASS (0.158±0.351 logMAR) and did not differ from that before inflammation developed (−0.004±0.162 logMAR). Overall treatment outcomes were favorable.

***Conclusions:*** A large-scale outbreak of subacute-onset TASS developed after implantation of a specific model of IOL. *Ophthalmology 2016;■:1−5 © 2016 by the American Academy of Ophthalmology*

Toxic anterior segment syndrome (TASS) is an acute postoperative sterile inflammatory reaction of the anterior segment to toxic substances that is most commonly associated with cataract surgery.[1−4] Typical TASS presents within 12 to 48 hours after surgery,[1] but there have been 2 reports of outbreaks of delayed- or late-onset TASS after cataract surgery with implantation of a particular model of intraocular lenses (IOLs).[5,6] Jehan et al[5] described 10 cases of delayed-onset TASS developing after implantation of hydrophilic acrylic IOLs (MemoryLens; CIBA Vision, Duluth, GA) at a mean of 7.8 days (range, 1−21 days). More recently, 251 cases of late-onset TASS associated with implantation of a 1-piece hydrophobic acrylic IOL (HOYA iSert 251 and 255; HOYA, Tokyo, Japan) were reported that developed at 38.44±32.29 days (range, 0−161 days) after surgery.[6] It has been shown that aluminum contamination was the likely cause of late-onset ocular inflammation in these cases.[6] A similar case was reported in the United Kingdom.[7]

In 2015, the number of cases with unusual inflammatory reaction after cataract surgery in eyes implanted with a specific model of IOL that were reported to Alcon Japan increased significantly. Quintessential clinical symptoms were mild to moderate exacerbation of anterior segment inflammation after an uneventful postoperative course for a few days, and most of the reports described inflammation that seemed noninfectious. These events strongly suggested an association between AcrySof IOLs (Alcon Laboratories, Inc., Fort Worth, TX) and inflammatory complications, leading to voluntary recall of the products in Japan by the manufacturer: AcrySof ReSTOR and ReSTOR toric IOLs in April 2015 and AcrySof IQ toric SN6AT6-9 IOLs in October 2015. The manufacturer's internal investigation found that the surfaces of unused IOLs were contaminated with small amounts of heavy metals and identified several risk factors in the production processes that could have caused such contaminations. The current problem occurred only in Japan because the manufacturing processes of AcrySof lenses shipped to the Japanese market were different from those shipped to other markets to mitigate the issue of severe surface light scattering seen with AcrySof products after surgery.[8−12] In addition, according to the



http://dx.doi.org/10.1016/j.ophtha.2016.12.010
ISSN 0161-6420/16

manufacturer's explanation, some parts of the manufacturing processes for ReSTOR and ReSTOR toric IOLs and IQ toric SN6AT6-9 IOLs differed from those used for other AcrySof products, such as AcrySof IQ monofocal and IQ toric SN6AT3-5 IOLs. To reveal the clinical characteristics of this inflammatory complication associated with AcrySof IOLs, the Japanese Ocular Inflammation Society established a third-party investigation committee, independent from the manufacturer, and collected data for analyses.

## Methods

From January 2015 through March 2016, Alcon Japan received reports from 184 facilities on 304 eyes that demonstrated unusual ocular inflammation after cataract surgery using AcrySof ReSTOR, ReSTOR toric, or AcrySof IQ toric SN6AT6-9 IOLs. The investigation committee, not Alcon Japan, requested data directly from the surgeons. After obtaining consent of the surgeons, a questionnaire was sent asking for clinical data including patient background, surgical procedures, type and serial number of the IOL, intraoperative complications, postoperative medications before the onset of inflammation, time from surgery to first symptom development, clinical findings, intraocular pressure at the onset of inflammation, treatment, best-corrected visual acuity (BCVA) before and after treatment, and results of laboratory culture tests if performed. Best-corrected visual acuity was converted into logarithm of the minimum angle of resolution (logMAR) units for statistical analyses. This study was performed in accordance with the tenets of the Declaration of Helsinki. The study followed Ministerial Ordinance no. 135 of 2004 on Good Vigilance Practice for drugs, quasidrugs, cosmetics, and medical devices stipulated by the Ministry of Health, Labour and Welfare of Japan, for which institutional review board approval and patients' informed consent are not required.

## Results

Among 304 eyes from 184 facilities reported to Alcon Japan, consent to data collection was obtained from 130 facilities for 201 eyes (Fig 1). Others declined to cooperate for data collection. After sending a questionnaire to these 130 facilities, 15 eyes were withdrawn by the surgeons and there were no responses before the deadline for 5 eyes. As such, clinical data were collected for 181 eyes, which were used for subsequent analyses. Based on the reported clinical course and findings, the investigation committee judged 7 cases to be infectious endophthalmitis, which then were excluded from the analysis. Another 17 eyes were excluded because the condition was inconclusive owing to the paucity of data; for example, the eye was treated with vitrectomy on the day of presentation, and thus it was impossible to diagnose whether the case was infectious or noninfectious. Ten eyes also were excluded because the symptoms were consistent with those of usual postoperative inflammation and not TASS. The remaining 147 eyes were diagnosed with TASS associated with AcrySof IOLs.

Patient characteristics are shown in Table 1. Comorbid ocular conditions included glaucoma in 9 eyes (6.1%), retinal pathologic features in 7 eyes (4.8%), dry eye in 6 eyes (4.1%), corneal disease in 2 eyes (1.4%), allergic conjunctivitis in 2 eyes (1.4%), and uveitis in 1 eye (0.7%). In all cases, phacoemulsification and IOL implantation were carried out. Alcon ReSTOR and ReSTOR toric IOLs were implanted in 94 eyes (63.9%), and AcrySof IQ toric SN6AT6-9 IOLs were used in 53 eyes (36.1%). Four eyes demonstrated intraoperative

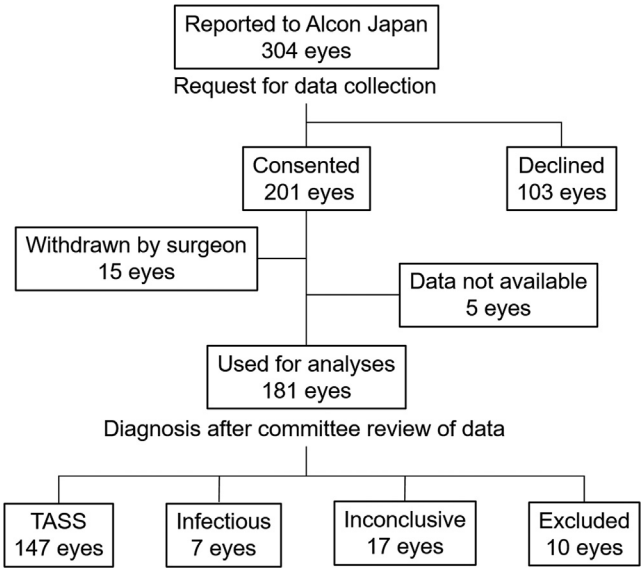


**Figure 1.** Study design algorithm. Among 304 eyes reported to Alcon Japan, consent for data collection was obtained for 201 eyes. After sending a questionnaire, 15 eyes were withdrawn by the surgeon, and there were no responses before the deadline for 5 eyes. Based on the reported clinical data in 181 eyes, the investigation committee diagnosed 147 eyes with toxic anterior segment syndrome (TASS) associated with intraocular lens implantation.

complications related to cataract surgery, including non−self-sealing incision in 2 eyes (1.4%), posterior capsule rupture in 1 eye (0.7%), and damage to the zonular fibers in 1 eye (0.7%).

At the end of surgery, antibiotics were administered to the eye in 125 cases (85.0%) via various routes including eye drops or ointments in 113 eyes, subconjunctival injection in 30 eyes, and intracameral injection in 3 eyes. Subconjunctival injection of steroids was given in 43 eyes (29.3%). After surgery, topical antibiotics, steroids, and nonsteroidal anti-inflammatory drugs were given to 144 eyes (98.0%), 127 eyes (86.4%), and 141 eyes (95.9%), respectively. The mean BCVA before the onset of ocular inflammation was −0.004±0.162 logMAR.

The timing of onset of TASS is shown in Figure 2. The mean onset time was 13.1±16.4 days (range, 1−88 days), with 84 eyes (57.1%) demonstrating symptoms within 7 days after surgery. At the time of onset, 35 patients (23.8%) were not using topical steroids and 12 patients (8.2%) were not receiving topical nonsteroidal anti-inflammatory drugs. The clinical features at the time of onset are listed in Table 2. Many patients showed cells and flare in the anterior chamber, whereas very few showed retinal abnormalities. The mean BCVA at the onset of ocular inflammation was 0.158±0.351 logMAR and was significantly worse than the BCVA before the development of inflammation ($P < 0.001$, paired 2-tailed $t$ test; Fig 3). The mean intraocular pressure was 13.9±4.7 mmHg (range, 6.0−39.0 mmHg). Laboratory culture of the intraocular fluid was performed for 40 eyes (27.2%), and all results were negative.

The treatment procedures used for ocular inflammation are listed in Table 3. Of all patients, 104 eyes (70.7%) were treated with medication alone and 43 eyes (29.3%) underwent surgeries, including irrigation of the anterior chamber, vitrectomy, and removal of the IOL. Many surgeons commented that topical steroids were highly effective in controlling inflammation. The mean BCVA at the final visit was −0.012±0.175 logMAR, which was significantly better than the BCVA at the onset of