Toxic anterior segment syndrome caused by autoclave reservoir wall biofilms and their residual toxins

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PURPOSE: To identify etiology of toxic anterior segment syndrome (TASS) after uneventful phacoemulsification.

SETTING: EyeMD Laser and Surgery Center, Oakland, California.

DESIGN: Retrospective case series.

METHODS: Patient charts with TASS were reviewed. Reservoirs of 2 autoclaves associated with these cases were cultured for bacterial contamination. Cultures were performed on 23 other autoclave reservoirs at surgery centers in the local area. The main outcome measures were the incidence of TASS and prevalence of bacterial biofilm contamination of autoclave reservoirs.

RESULTS: From 2010 to 2013, 11 935 consecutive cataract surgeries were performed at 1 center by multiple surgeons with no reported TASS. Between January 1, 2014, and January 15, 2015, 10 cases of TASS occurred out of 3003 cataract surgeries; these patients' charts were reviewed. Cultures of 2 Statim autoclave reservoir walls grew *Bacillus* species, *Williamsia* species, *Mycobacterium mucogenicum*, and *Candida parapsilosis*. Scanning electron microscopy of reservoir wall sections showed prominent biofilm. The 2 autoclaves were replaced in January 2015. Subsequently, 2875 cataract surgeries were performed with no reported TASS ($P < .001$, χ^2 test). Eighteen of 23 additional regional autoclaves were also contaminated with bacterial biofilms.

CONCLUSIONS: Toxic anterior segment syndrome was strongly associated with bacterial biofilm contamination of autoclave reservoirs. An etiological mechanism might involve transport of heat-stable bacterial cell antigens in the steam with deposition on surgical instrumentation. Data suggest widespread prevalence of bacterial biofilms on fluid-reservoir walls, despite adherence to manufacturer guidelines for cleaning and maintenance. Prevention or elimination of autoclave fluid-reservoir biofilms might reduce the risk for postoperative TASS.

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Toxic anterior segment syndrome (TASS) was first described in 1992,[1] and efforts to identify relevant causes have been ongoing. Periodic outbreaks have at times convincingly been attributed to various contaminants known to be toxic to the corneal endothelium and to other intraocular structures. For example, a multistate outbreak in the United States in 2005 involving 112 eyes attributed to a certain brand of balanced salt solution (Endosol, Abbott Medical Optics)[2] terminated abruptly with removal of the product from surgery centers, although the correlation was never proven and no product with known contaminants was identified. Other outbreaks have not been definitively attributed to a specific cause, although suspicions have been directed at many potential causes, including metallic breakdown particles, incompletely cleaned instruments containing organic materials, and intracameral medications.[3–11]

As a result of the serious consequences of TASS and the lack of consistent evidence pointing to specific causes, nationwide efforts are ongoing by many agencies, including the American Society of Cataract

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and Refractive Surgery (ASCRS) and the Centers for Medicare and Medicaid Services (CMS), to mitigate potential sources of contamination. A 2014 policy paper by CMS provides extensive direction regarding the maintenance of clean, sterile, and safe instruments but bypasses the potential contaminating role of autoclave fluid reservoirs.[A] In 2012, the U.S. Food and Drug Administration (FDA) initiated the Proactive TASS Program (PTP) to systematically work through TASS and its potential causes.[12,B,C] Although endotoxins are recognized as suspects, the PTP only identifies ophthalmic viscosurgical devices (OVDs) as the source for such endotoxins. Regarding the autoclaves, the PTP's guidelines direct users to the *Instructions for Use* by each autoclave manufacturer to guide utilization practices.

Our experiences with autoclave contamination in a recent outbreak of diffuse lamellar keratitis (DLK) after laser in situ keratomileusis (LASIK) at a local surgical facility led us to hypothesize that similar factors were involved in the TASS outbreak. We present evidence that 10 cases of TASS observed at a single surgery center over 1 year involved contaminated steam from reservoir-based Statim 2000 and 5000 cassette autoclaves (SciCan Ltd.) used at the center where the cataract surgeries were performed. Although the autoclaves were correctly monitored, maintained, and used according to the manufacturer's recommendations, our results show that the reservoirs had developed biofilms on their reservoir walls containing *Williamsia* species, *Mycobacterium mucogenicum*, *Candida parapsilosis*, and *Bacillus* species, the latter being well known to sporulate in nutrient-poor environments, such as distilled water.[13]

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PATIENTS AND METHODS

Patients

The charts of patients diagnosed with TASS were reviewed, and patient demographic data, preoperative ophthalmic diagnoses, and vision were assessed. Postoperative data were also reviewed including 1-day postoperative data, clinical course, results of vitreous cultures when performed, and final visual acuity. Institutional review board approval for this study was obtained from the Human Research Protection Program, Sutter Health, San Francisco, California, USA.

Autoclave Maintenance, Bacterial Culture, Electron Microscopy

Maintenance protocols and cleaning routines for the autoclaves in use at the facility were reviewed. In addition, 23 other autoclaves were surveyed and their maintenance routines recorded (Table 1 and Figure 1). To obtain the culture from each autoclave, the autoclave fluid reservoir was drained and the reservoir cultured by aggressively rubbing a moist cotton-tipped applicator along the internal vertical wall (Figure 2) and inoculating blood agar plates for incubation at 37°C. Blood agar plates that produced bacterial or fungal growth were sent to Quest Diagnostics, Sacramento, California, or Focus Diagnostics, Cypress, California, for identification.

Regionally, an effort was made to identify surgical centers and ophthalmic offices at which Statim 2000 or 5000 cassette autoclaves were also in use. These autoclaves were similarly tested for autoclave reservoir bacterial biofilms as described above.

For biofilm imaging, the Statim 2000 cassette autoclave implicated in TASS cases 3, 6, 8, and 10 (Autoclave A) was decommissioned and the reservoir removed from the unit. The interior reservoir wall was sampled by removing a section of vertical sidewall (Figure 3) and submitting it for analysis by scanning electron microscopy (SEM) at the Robert D. Ogg Electron Microscope Laboratory, University of California, Berkeley.

Statistical Analysis

Chi-square analysis was used to assess incidence of TASS before and after autoclave replacement relative to surgeries without TASS. A P value less than 0.05 was considered significant.

RESULTS

Between January 1, 2014, and December 31, 2014, 10 cases of TASS were identified by several surgeons using a local ambulatory surgery center (ASC). Table 2 summarizes each case. In the previous 3 years, which included 11 935 cataract surgeries, no cases of TASS were identified at the same center. Five of the 10 eyes had vitreous biopsies and intravitreal antibiotic