Toxic Anterior Segment Syndrome: Is it Possible to Have Corneal Dysfunction Without Changes in Corneal Morphology?

Toksik Anterior Segment Sendromu: Kornea Morfolojisi Bozulmadan Korneal Disfonksiyon Gelişir mi?

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ABSTRACT

Toxic anterior segment syndrome (TASS) is a sterile postoperative inflammatory reaction caused by a noninfectious substance that enters the anterior segment, resulting in a wide range of toxic damage to intraocular tissues. The process typically begins 12 to 48 hours after anterior-segment surgery, but delayed mild cases have been reported. In this paper, a case of mild late-onset TASS that specifically caused corneal edema without changes in corneal morphology is described. While, ideally, corneal morphology should be documented by a corneal confocal microscopy, this case could be documented by a biomicroscopic anterior and posterior segment examination, central corneal thickness (CCT) detection by a corneal B mode ultrasound and a corneal specular microscope without corneal confocal microscopy. For this case, mild corneal edema was observed on postoperative day 32 (the CCT was 701 µm on postoperative day 32, 602 µm on postoperative day 75) without any specular microscopic changes (the preoperative endothelial cell density was 2660 cells/mm^2, and on postoperative day 75, it was 2660 cells/mm^2) and major inflammation in the anterior and posterior segment of the eye, which responded well and promptly to topical steroid treatment. The aim is to contribute to the identification and proper management of similar patients and to discuss whether TASS causes corneal dysfunction without changes in corneal morphology, as the early detection of mild cases is important in preventing potentially severe cases.

Key Words: Toxic anterior segment syndrome, corneal edema, cataract surgery complications.

ÖZ

Toksik anterior segment sendromu (TASS), enfeksiyöz olmayan toksik ajanların ön segmente girmesi sonucu oluşan, göz içi dokularda değişen yaygınlıkta ve şiddette hasara neden olan steril cerrahi sonrası inflamasyondur. Süreç, tipik olarak ön segment cerrahisinden 12-48 saat sonra başlasa da geç başlayan, hafif belirti ve bulgularla seyreden olgular bildirilmiştir. Bu çalışmada, korneada morfolojik değişikliklere neden olmadan özellikle kornea ödemine yol açan hafif ve geç başlangıçlı TASS olgusu sunulmuştur. Kornea konfokal mikroskopi, kornea morfolojisini en iyi değerlendiren yöntem olmasına rağmen bu olgu, biomikroskopik ön ve arka segment muayenesi, B mod ultrason ile merkezi kornea kalınlık (MKK) ölçümü ve kornea speküler mikroskopi yapılarak değerlendirilebilmiştir. Bu olguda, ameliyat sonrası 32. günde speküler mikroskopik değişiklikler (endotel hücre yoğunluğu; ameliyat öncesi: 2660 hücre/mm^2, ameliyat sonrası 75. gün: 2660 hücre/mm^2) ve belirgin göz içi inflamasyon olmaksızın hafif kornea ödemi (MKK; ameliyat sonrası 32. gün: 701 µm, ameliyat sonrası 75. gün: 602 µm) tespit edildi. Topikal steroid tedavisine hızlı ve iyi yanıt gözlendi. Hafif TASS olgularının erken fark edilmesi, daha sonra karşılaşılabilecek ciddi vakaların önlenmesini sağlayabilir. Bu olgu sunumunda, benzer hastaların teşhisine ve doğru tedavisine katkıda bulunmak, TASS olgularında kornea morfolojisi değişmeden kornea fonksiyon bozukluğu oluşumunu tartışmak amaçlanmıştır.

Anahtar Kelimeler: Toksik anterior segment sendromu, kornea ödemi, katarakt cerrahisi komplikasyonları.

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INTRODUCTION

In 1992, Monson et al.[1] accurately referred to a sterile anterior chamber inflammation observed after cataract surgery as toxic anterior segment syndrome (TASS). TASS is a sterile postoperative anterior-segment inflammatory reaction to a toxic substance that may occur after any apparently uncomplicated anterior-segment surgery.[1,2] Patients typically present symptoms within 12 to 48 hours postoperatively. Severe iridocyclitis may be accompanied by fibrin accumulation, hypopyon, diffuse limbus-to-limbus corneal edema and elevated intraocular pressure (IOP).[2] For TASS, a retrospective case series from Aravind Eye Hospital in India recently reported an incidence rate of 0.22%.[3] Cases limited to the corneal endothelium are characteristic of toxic endothelial cell destruction syndrome (TECDS).[4] While typical TASS presents within 12 to 48 hours after surgery, there have been reports of outbreaks of delayed- or late-onset TASS after cataract surgery when specific types of intraocular lenses (IOL) had been implanted.[5-7]

While, ideally, corneal morphology should be documented by a corneal confocal microscopy; biomicroscopic anterior and posterior segment examinations, central corneal thickness (CCT) detection by a corneal B mode ultrasound and corneal specular microscopy might aid physicians in documenting corneal function and morphology. We describe a case that presented symptoms similar to TASS. However, the time of onset, severity and limitation of findings predominantly to the cornea led us to conclude that the eye was experiencing mild late-onset TASS. To the best of the authors' knowledge, mild late-onset TASS particularly caused corneal edema without changed corneal morphology and occurring in one eye after sequential bilateral cataract surgery has not been reported previously.

CASE REPORT

A 75-year-old man presented decreased vision in both eyes. Previously, a pterygium excision had been performed in both eyes. The patient had no systemic disease. The cataracts had a moderate level of nuclear sclerotic opacity. Preoperatively, his corrected distance visual acuity (CDVA) was 0.2 [-4.50] in the right eye and 0.4 [-2.00] in the left eye, his endothelial cell density (ECD) was 2741 cells/mm^2 in the right eye and 2660 cells/mm^2 in the left eye and his intraocular pressure (IOP) was 14 mm Hg in the right eye and 15 mm Hg in the left eye. After uncomplicated phacoemulsification cataract surgery on the right eye, he underwent a similar surgery on the left eye after an interval of two days. The right eye was operated on during the fourth of five operative cases for cataracts, and the left eye was operated on during the third of four operative cases for cataracts.

SURGICAL TECHNIQUE

On the day of operation, four eyes of four patients underwent elective phacoemulsification cataract surgery and IOL implantation. Only one eye developed TASS. Before surgery, the pupil was dilated using tropicamide 1% (Tropamid®, Bilim Ilac, Istanbul, Turkey), phenylephrine hydrochloride 2.5% (Mydfrin®, Alcon Laboratories, Inc., Fort Worth, TX, USA) and cyclopentolate 1% (Sikloplejin, Abdi Ibrahim, Istanbul, Turkey).

Following an antisepsis of the lids, eyelashes and conjunctiva, which was achieved using povidone-iodine 5%, the phacoemulsification and hydrophobic acrylic IOL implantation procedure was performed under intracameral anaesthesia using preservative-free lidocaine 1%. The procedure ended with an intracameral injection of cefuroxime axetil 1mg/0.1 cc. No tight patches or topical ophthalmic ointments were used; however, light patching was applied for the first three hours after surgery, and hourly applications of topical ophthalmic solutions dexamethasone 0.1% (Maxidex®, Alcon Laboratories, Inc., Fort Worth, TX, USA) and tobramycin 0.3% (Tobrex®, Alcon Laboratories, Inc., Fort Worth, TX, USA) began on the day of the surgery.

POSTOPERATIVE

On postoperative day 1 for each eye, the right eye had grade 2+ white blood cells in the anterior chamber and a CDVA of 0.7; similarly, the left eye had grade 2+ white blood cells in the anterior chamber and a CDVA of 0.8. The dosage of the topical drugs was reduced successively four times each day. On postoperative day 6 for the right eye and 8 for the left eye, the anterior chamber inflammation improved, and the patient was instructed to taper his drugs gradually over the next three weeks.

On postoperative day 32 for the left eye, the patient presented symptoms of mild left-eye discomfort and reduced vision and stated that he had gradually tapered the dosage of his eye drops and finally had ceased them two days before, as instructed. An examination of the left eye revealed corneal edema, an anterior chamber flare of 2+ and anterior chamber cells of 2+ without hypopyon, fibrin or vitreous inflammation. The CDVA was 0.5, the ECD was undetectable, the central corneal thickness was (CCT) 701 µm and the IOP was 16 mm Hg. No retinal pathological findings were detected using a fundus examination or optical coherence tomography (OCT) imaging (Figure 1). A topical dexamethasone 0.1% ophthalmic solution each hour was again recommended because it had controlled the anterior chamber inflammation until recently, and the vitreous did not present signs of inflammation. At the same time, there were no complaints for the right eye, which had a CDVA of 0.9 (+0.75, -0.75x108), an ECD of 2572 cells/mm^2, a CCT of 592 µm and an IOP of 15 mm Hg.

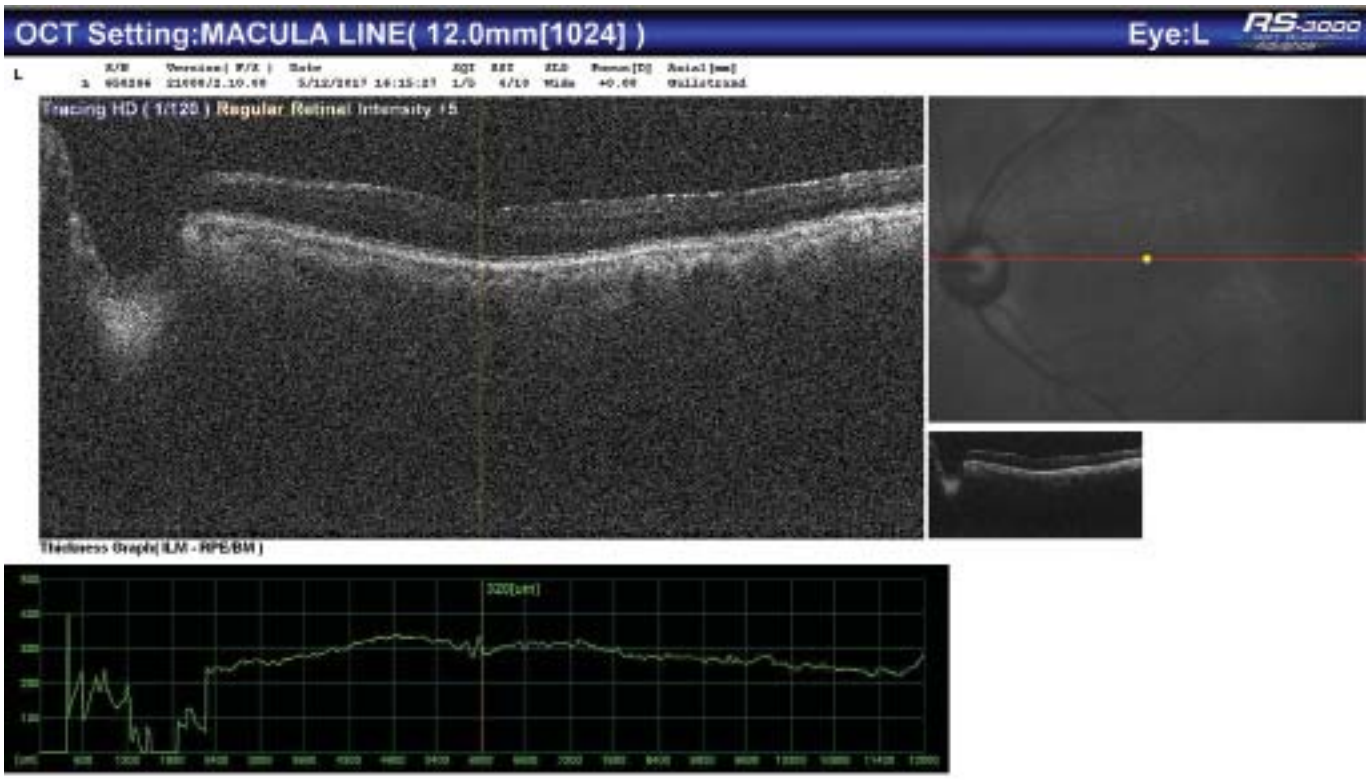

Figure 1. *Optical coherence tomography of the left eye. There were no pathological findings. The image was blurry, indicating corneal edema.*

On postoperative day 35 for the left eye, the inflammation of the anterior chamber had improved; however, the corneal edema, although reduced, was still present. The CDVA was 0.5, and the CCT was 652 µm. On postoperative day 75 for the left eye, the corneal edema and the anterior-segment inflammation were completely resolved. The CDVA was 0.9 (+0.75, -1.25 70), the ECD was 2660 cells/mm^2, the CCT was 602 µm and the IOP was 16 mm Hg.

Upon specular microscopic examination, the preoperative ECD was 2660 cells/mm^2, and on postoperative day 75, it was 2660 cells/mm^2. Preoperatively, the coefficient of variation had been 37%, and on postoperative day 75, it was 37%. Preoperatively, the hexagonal cell ratio had been 47%, but on postoperative day 75, it was 45%. Preoperatively, the average cell size had been 375.9, and on postoperative day 75, it was 375.8. In addition, the CCT was 701 µm on postoperative day 32, 652 µm on postoperative day 35 and 602 µm on postoperative day 75 (Figures 2 and 3).

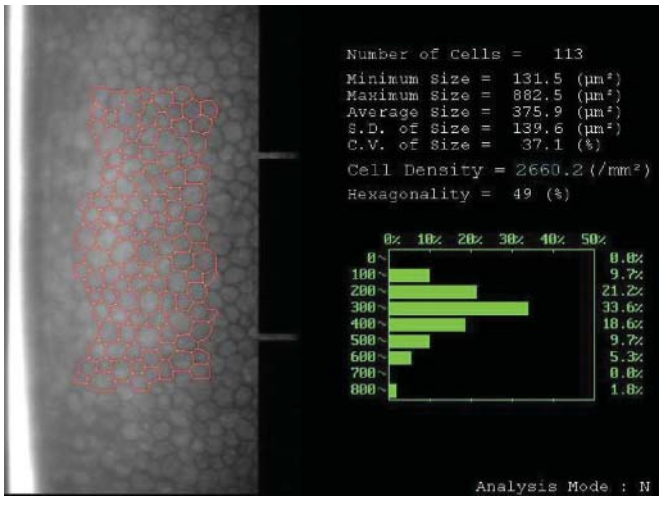

Figure 2. *Preoperative specular microscopic image of the left eye.*

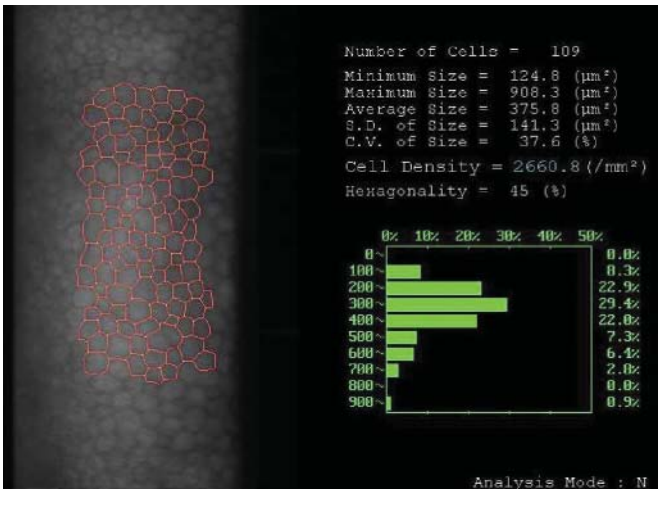

Figure 3. *Specular microscopic image of the left eye on postoperative day 75. Findings were similar to preoperative values.*

DISCUSSION

It is important to differentiate TASS from bacterial endophthalmitis. This differentiation is undemanding, and based on clinical history, symptoms and findings of the patients. Conventional TASS usually presents within 12 to 48 hours after surgery; however, there have been reports of outbreaks of delayed- or late-onset TASS after a cataract surgery to implant a specific type of IOL.[5-7] Endophthalmitis can be classified into two broad categories: acute-onset and delayed-onset. The Endophthalmitis Vitrectomy Study defined acute-onset postoperative endophthalmitis as occurring within six weeks after surgery.[8] In contrast, delayed-onset postoperative endophthalmitis is defined as occurring more than six weeks after surgery.[8] In delayed-onset postoperative endophthalmitis, the clinical picture is a recurrent, often low-grade uveitis that partially responds to topical or systemic steroids. It may occur months or even years after the initial surgical event and presents with mild pain, granulomatous uveitis with or without hypopyon, vitreous activity, capsular thickening or plaque, and in the later stages, visual loss. Propionibacterium acnes has been reported as a common isolated organism in a published series.[9] In the case reported in this study, corneal edema and a very low-grade anterior-chamber reaction were detected, but other ocular structures appeared intact on postoperative day 32. No intracapsular white plaques, hypopyon, granulomatous inflammation or vitreous inflammation was observed, and the eye remitted promptly with a topical dexamethasone 0.1% ophthalmic solution. The case was diagnosed as mild late-onset TASS.

The corneal endothelium maintains corneal clarity through two functions: by acting as a barrier to the aqueous humor and by the activity of the metabolic NA^+ K^+ adenosine triphosphate pump.[10] These functions can be reduced transiently by mild stress without causing decreased endothelial cell density, such as contact lens induced hypoxia and inflammation.[11,12] The type and amount of concomitant, the preoperative ECD and the severity and duration of the inflammation all play roles in the involvement of ocular tissues and the decompensation of the cornea.[3] For specular microscopic findings, the eyes with TASS were characterised by a significantly lower endothelial cell density, a higher mean cell area and a lower mean percentage of hexagonal cells.[13] In contrast, subtle differences were observed between the preoperative and postoperative specular microscopic parameters. In addition, the CCT was 701 µm on postoperative day 32, 652 µm on postoperative day 35 and 602 µm on postoperative day 75. As CCT is an indirect indicator of corneal endothelial function, these findings indicated that the inciting agent in this case particularly affected the cornea functionally but not morphologically.

Many substances can cause TASS if they obtain access to the anterior chamber during surgery or during the immediate postoperative period. Some materials that have been shown to cause TASS include endotoxins; denatured OVDs; preservative and stabilising agents; heavy metals; residues left behind by substances used to clean and sterilise instruments; intraocular medications at toxic doses; irrigating solutions with an incorrect pH, osmolarity or ionic composition; and retained OVD or lens cortical material.[2,14,15] For delayed-onset TASS after MemoryLens (CIBA Vision, Duluth, Georgia, USA) implantation, a possible suspect was reported to be the residual polishing compound aluminum oxide.[5] Late-onset TASS has been associated with HOYA IOLs (iSert 251 and 255; HOYA Co Ltd, Tokyo, Japan), which have been suspected of being contaminated with aluminium.[6] In addition, for a subacute-onset, TASS has been associated with specific IOL models manufactured by Alcon (Alcon Laboratories, Inc., Fort Worth, TX, USA). It was concluded that the observed postoperative inflammatory reactions were influenced by multiple factors.[7]

In our case, the surgeon and operating-room staff were experienced, had attended thousands of eye operations and had never encountered a case of TASS, TECDS or endophthalmitis. All possible explanations for the problem were immediately analysed. It has been several years since any changes were made to the surgical techniques used; the OVDs, irrigation solution or any other materials used; the operating-room staff; or the operating-room protocol for sterilising and preparing surgical instruments for use. For years, the institution has used the same type of hydrophobic IOL from the same manufacturer, and no patient or even the right eye of the case patient had presented TASS. In addition, the IOL manufacturer stated that no TASS had been reported to it in relation to the IOL. Finally, it was concluded that this case had resulted from an inadequate flushing of the cannulated instruments and/or from contact of the IOL with gloved hands. The disposable tubing sets have been exchanged for new sets, and the operating-room protocol for sterilising and preparing surgical instruments was reviewed with the operating-room staff. No case of TASS has been observed since the case reported herein.

Recently, Lee [16] reported a noteworthy case that had some similarities with this case, including TASS that began after reducing the use of the steroid drop, that remitted completely after restarting it, that had a delayed presentation that occurred in one eye after sequential bilateral cataract surgery and that was not preceded or followed by other cases; however, the eye in Lee's case presented both a more prominent anterior-chamber reaction and a higher possibility of endothelial-cell loss compared with the patient's other eye than in this case. As mentioned, in this case, the primary effect was on the cornea, and there was only a slight anterior-chamber reaction. The early detection of mild TASS is thus recommended, as it is important in preventing potentially severe cases. These two cases strengthen the awareness of

TASS by highlighting the mild nature of the condition.

This case report has some limitations. First, we could not document corneal morphology using corneal confocal microscopy. On the other hand, corneal specular microscopy is an adequate tool in identifying subtle as well as macroscopic changes in cornea before and after surgery.[17] Second, slit lamp biomicrocopic anterior segment photos might have been useful to present such a case so further similar studies should use it along with biomicroscopic anterior and posterior segment examinations.

In conclusion, despite the relatively good visual and anatomical outcome of this case, surgical staff must be aware that TASS can have devastating consequences and that mild cases may precede potentially severe outbreaks. Once a case of TASS has been identified, all instruments, drugs and solutions used during the surgery must be thoroughly analysed, and operating-room protocol for sterilising and preparing surgical instruments must be re-examined.

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