Toxic anterior segment syndrome

Síndrome tóxica do segmento anterior

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ABSTRACT

Toxic anterior segment syndrome is acute inflammatory reaction caused by a noninfectious substance that enters the anterior segment, resulting in extracellular damage with necrosis and apoptosis during an immune response. We have the report of a case of toxic anterior segment syndrome (TASS), in which the authors seek to emphasize the most common causes of the appearance of these syndrome. They point out the care that must be taken in the process of sterilization of surgical material, in addition to reviewing the best conduct when faced with these cases. In conclusion, it was noted that the main focus should be on prevention, as treatment only seeks to suppress the secondary inflammatory response. Treatment in cases of toxic anterior segment syndrome (TASS) consists of intense instillation of topical steroids with strict follow-up and control of late complications such as glaucoma.

Keywords: *Anterior eye segment/drug effects; Anterior eye segment/pathology; Ophthalmic solutions/adverse effects; Syndrome; Case reports*

RESUMO

A síndrome tóxica do segmento anterior (STSA) é uma severa reação inflamatória aguda causada por agente não infeccioso que entra no segmento anterior, resultando em lesão celular tóxica com necrose e apoptose mediado por resposta imunológica. Neste relato de caso de STSA são enfatizadas as causas mais comuns para o aparecimento da síndrome, apontam para os cuidados que devem ser tomados no processo de esterilização do material cirúrgico além de revisar a melhor conduta diante desses casos. Em conclusão notou-se que o foco principal deve ser a prevenção, pois o tratamento busca apenas suprimir a resposta inflamatória secundária. O tratamento nos casos de STSA consiste em intensa instilação de esteróides tópicos com seguimento rigoroso e controle de complicações tardias como o glaucoma.

Descritores: Segmento anterior do olho/efeito de drogas e patologia; Soluções oftálmicas/efeitos adversos; Síndrome; Relato de caso

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Introduction

Cataract extraction with lens implant is currently the most common surgical procedure in the United States[1]. Due to its small surgical trauma, phacoemulsification has great success rates, with minimal postoperative inflammation and short-term visual recovery. In recent years, the toxic anterior segment syndrome (TASS) has been described as a sterile endophthalmitis affecting the anterior chamber. The syndrome is related to toxic substances injected into or around the eye or even used topically during the procedure[2].

Toxic anterior segment syndrome is a severe acute inflammatory reaction caused by non-infectious agents that enter the anterior segment resulting in toxic cell damage with necrosis and apoptosis mediated by an immune response[2]. The process typically begins 12 to 48 hours after anterior segment surgery and often improves with steroid use. Gram staining and a negative culture exclude infectious endophthalmitis, which is the primary differential diagnosis[3].

The aim of this report is to describe the investigation conducted during the postoperative period of a routine cataract surgery performed in a public federal hospital without operative complications, which progressed with intense inflammatory reaction, swelling of the cornea and depigmentation of the iris. The authors emphasise the most common causes of TASS, pointing to the necessary precautions in terms of sterilisation of surgical materials and the need to review the best treatment for these cases.

Case report

White, female, 76 year-old patient with hypertension and cardiac arrhythmia, using amiodarone and having used hydroxychloroquine for 17 years without a confirmed diagnosis of rheumatoid arthritis or systemic lupus erythematosus. She sought ophthalmic care due to senile cataract with reduced vision and blurring. On ophthalmic examination (biomicroscopy) senile cataract (grade II) was found in both eyes (BE); no abnormalities were seen in the anterior chamber (AC); intraocular pressure by applanation tonometry was 15 mmHg in BE; corrected visual acuity was 20/40 J2 in the right eye (RE) and 20/30 J2 in the left eye (LE); fundoscopy showed macular epiretinal membrane (macular pucker) in the RE, a normal posterior pole in the LE, and a periphery without significant changes in BE; potential acuity (PAM) was 20/20 with lens exchange in the RE and 20/20 in the LE.

After the initial consultation, phacoemulsification with intraocular lens (IOL) implantation in the RE was indicated. During surgery, no abnormalities were observed, and the steps and time of surgery occurred as expected. One day after surgery a severe inflammatory reaction was observed in the anterior chamber of the RE, with corneal de-epithelisation, intense corneal oedema (limbus to limbus), and Descemet membrane folds (Figure 1). The patient complained of severe pain. Eye pressure on bidigital palpation was normal, similar to the contralateral eye. The patient was treated with topical steroids (prednisone), lubricants and hyperosmolar solution (polydimethylsiloxane).

During subsequent visits iris atrophy and intense depigmentation and keratic precipitates were observed (Figure 2). The inflammatory reaction responded to steroid use and the corneal oedema remained restricted to the central area (Figure 3). Intraocular pressure remained normal at 14 mmHg in BE. Visual acuity with best correction was 20/40 with lens exchange in the RE after two months, and specular microscopy showed severe polymegathism and very low endothelial cell counts for the patient's age. Examination of the LE showed mild pleomorphism and cell counts within the normal range (Figures 4a and b). No inflammation was seen at the posterior pole upon examination with mydriasis (Figures 5a and b).

After discontinuation of the steroid eye drops, a relapse of the inflammatory reaction was observed, with anterior synechiae (Figure 6), severe corneal oedema and elevation of the intraocular pressure (IOP) to 50 mmHg in the RE. For this reason, prednisone eye drops were reinitiated and the hypotensive agents Trusopt (dorzolamide, MSD) and Combigan (brimonidine 0.2% and timolol 5%, Allergan) were prescribed. Currently the IOP is controlled (15mmHg) with medication, no inflammation is seen in the anterior chamber with prednisone 4 times a day, synechiae occupy approximately 3/4 of the corneoscleral angle and the corneal oedema persists, preserving only the inferior region of the cornea .

Figure 1: Figure 1: Biomicroscopy of the anterior segment of the right eye 24 hours after surgery, showing intense oedema, corneal de-epithelisation, and Descemet membrane folds

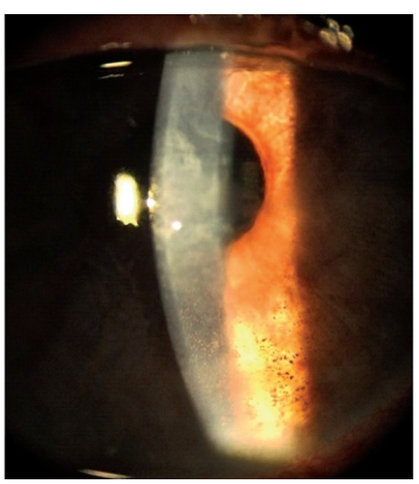

Figure 2: Biomicroscopy of the anterior segment during a follow-up visit. Note the intense iris depigmentation and keratic precipitates.

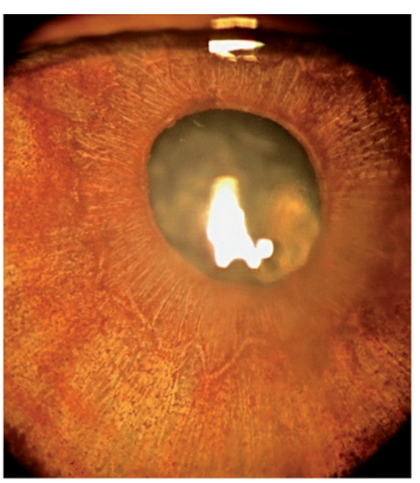

Figure 3: Biomicroscopy showing improvement in inflammation and persistent corneal oedema in the central region

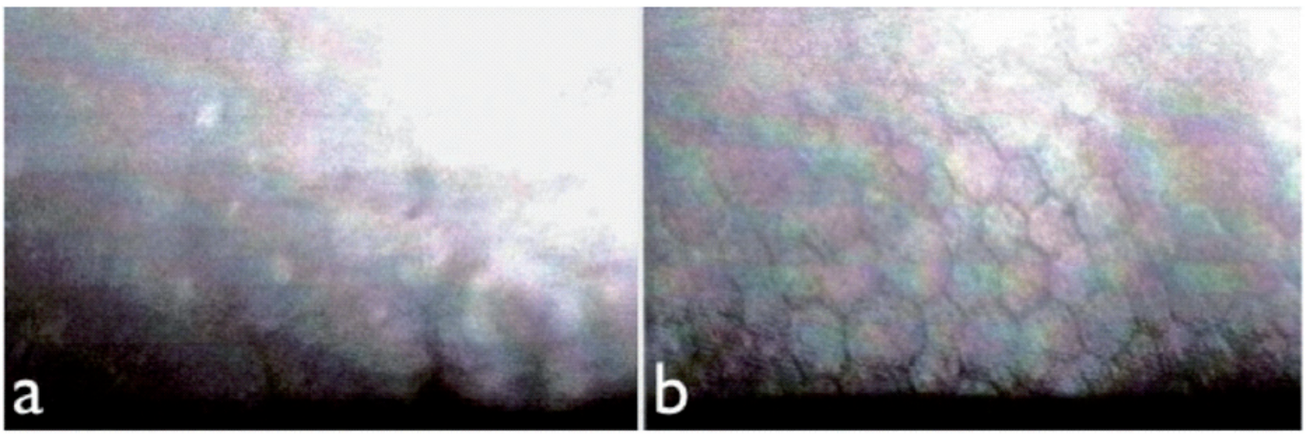

Figure 4: Corneal specular microscopy showing an important reduction in endothelial cells counts and polymegathism in the right eye (a), and normal cell counts with mild pleomorphism in the left eye (b)

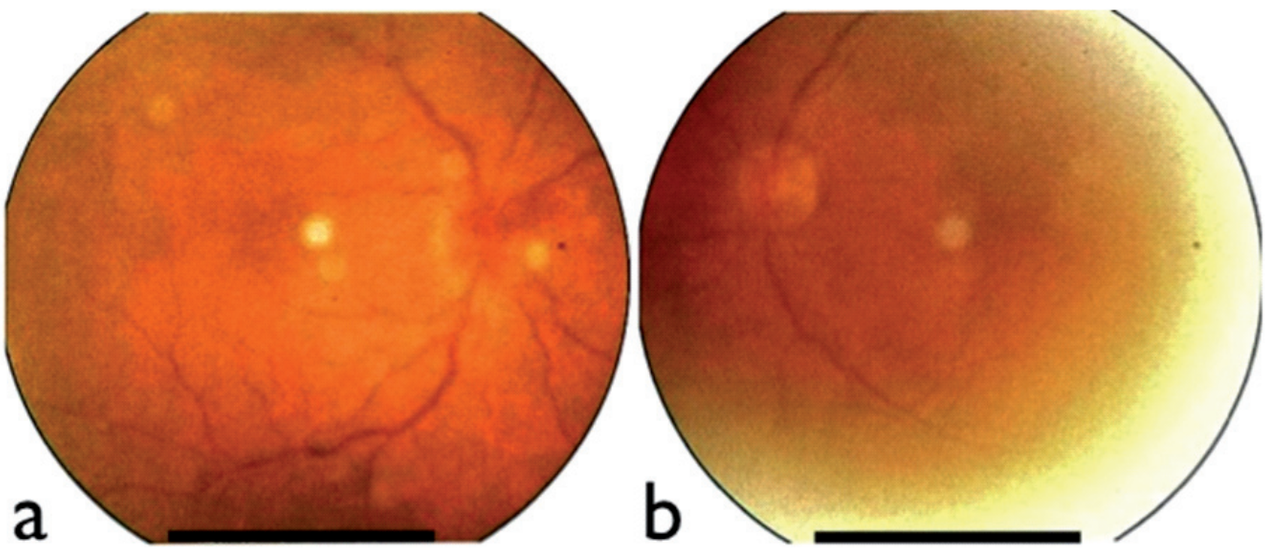

Figure 5: Right (a) and left (b) retinography. Absence of inflammatory signs in the posterior segment of both eyes. Image quality was compromised due to media opacity (corneal oedema in the right eye and cataract in the left eye)

The current visual acuity is count fingers at 2 meters and the therapeutic approach is conservative. However, if any elevation of IOP due to injury to the trabecular meshwork or synechiae is seen after the withdrawal of steroids, the patient will undergo Ahmed valve implant, with possible corneal transplant afterwards.

Discussion

Inflammation after cataract surgery may be related to several factors, such as surgical trauma, residual lens fragments, bacterial infections, toxic reaction to sterile substances, and relapse of uveitis[2]. In 1992, Monson et al.[4] accurately described the toxic anterior segment syndrome (TASS), and similar cases in which the damage was restricted to endothelial cells have been described as the toxic endothelial cell destruction syndrome (TECDS)[5-8].

The toxic anterior segment syndrome most commonly occurs within 24 hours of anterior segment surgery; however, some cases have a late onset. TASS is characterised by postoperative sterile inflammatory reaction caused by a substance that accidentally enters the anterior segment, damaging intraocular tissues. Patients who develop TASS have multiple inflammatory signs and symptoms similar to infectious endophthalmitis, such as eye pain, redness and blurred vision; however, diffuse corneal oedema (limbus to limbus) with destruction of endothelial cells is a characteristic feature of the disease. In severe cases of TASS the formation of fibrin and hypopyon in the anterior chamber may occur. The syndrome can result in permanent damage to the iris, with an irregular and poorly reactive pupil. Although TASS often presents with an early reduction of intraocular pressure (IOP), permanent damage to the trabecular meshwork can lead to secondary ocular hypertension and glaucoma[9].

Clinically, it is difficult to differentiate TASS from infectious endophthalmitis, though certain signs and symptoms may help in

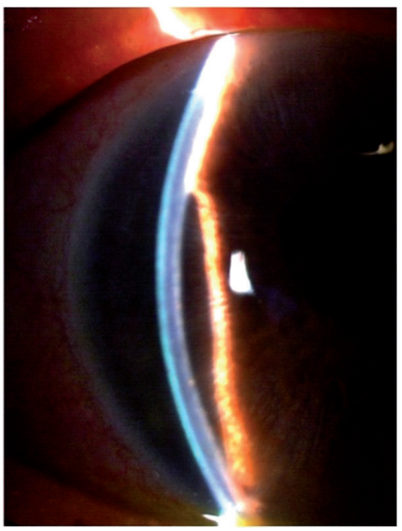

Figure 6: Biomicroscopy showing anterior synechiae.

Figure 7: Example of a suitable container for preparing and diluting the enzymatic detergent.

the differential diagnosis. TASS is limited to the anterior segment and typically begins 24 hours after surgery, while the onset of endophthalmitis occurs 4 to 7 days after surgery and also affects the vitreous cavity and the posterior pole. The favourable response to topical and/or oral steroids associated with diffuse corneal oedema is specific enough for a definitive diagnosis of TASS or to exclude infectious aetiologies.

Vitreous involvement is usually prominent in cases of infectious endophthalmitis. Pain occurs in 75% of patients with endophthalmitis, and other signs of infection, such as eyelid oedema and conjunctival chemosis may suggest endophthalmitis. In such cases, vitreous biopsy with Gram stain and culture can help in the differential diagnosis.

Our case was diagnosed as TASS, and a variety of substances were evaluated as possibly responsible for the toxicity. Many substances can be related to TASS: Chemical irrigation solutions whose chemical composition, pH, or osmolality are incompatible with ocular tissues, drugs containing toxic preservatives (epinephrine, lidocaine and antibiotics), improper use of detergents in the sterilisation of surgical materials, and the use of autoclaves that release impurities or toxic residue (copper, zinc, nickel, and silica)[9,10].

TASS is a problem for ophthalmic surgeons, especially because they work in multidisciplinary team (nurses, technicians, residents, physicians, and pharmacists) and it is often difficult to identify the causative agent of the toxic syndrome.

A possible cause of TASS is related to preservatives used in topical or intraocular drugs. Liu et al.[7] described a series of TASS cases after the inadvertent use of a cream for external eye cleaning containing benzalkonium chloride 0.01%. In most cases the corneal oedema and count-finger visual acuity persisted, requiring corneal transplant[7]. A study with rabbit endothelial cells showed that a maximal concentration of 0.0001% of benzalkonium chloride does not produce structural damage to corneal cells[11].

Intracamerular anaesthetic agents have also been described as capable of causing endothelial damage, oedema and corneal opacities. Kadonosono et al.[12] reported cases of corneal decompensation after the use of lidocaine 2.0% and bupivacaine 0.5% without preservatives. Another study[13,14] compared the safest concentration and type of anaesthetic agent to be used in cataract surgery (phacoemulsification); lidocaine 1% without preservative was found to be the safest drug for this purpose.

The reuse of improperly irrigated and cleansed cannulae containing viscoelastic residue has been related to the onset of toxic inflammation. Kim[15] demonstrated that during sterilisation of the material, denatured viscoelastic proteins may cause inflammation when introduced into the eye.

The use of prophylactic antibiotics at the end of surgery may also be responsible for toxicity reactions, more frequently when these are injected or irrigated in the anterior chamber. Studies have shown concerns about toxic reactions caused by intracamerular or subconjunctival gentamicin and vancomycin, as well as the development of antibiotic resistance[16]. Kramann et al.[17] conducted a study on the prophylaxis of endophthalmitis with intracamerular cefotaxime, showing no significant toxicity on the corneal endothelium three months after surgery. In conclusion, the authors showed that due to the risk of toxicity and the existing rates of infectious complications, antibiotic prophylaxis should not be used routinely.

In 2002, three surgeons in the same centre[18] had TASS cases related to the quality of the water and the steam eliminated by the autoclave during sterilisation. High levels of sulfate, copper, zinc, and nickel were found in water samples.

Finally, after investigating the possible toxic substances related to our case, we came to the conclusion that it was due to inappropriate use of an enzymatic detergent, a toxic chemical substance used for cleaning and removing residue of organic material. This enzymatic detergent, when left inside cannulae or even on the surface of reused materials, can penetrate into the eye leading to an intense inflammatory reaction. Enzymes and other active ingredients in detergents can only be deactivated at a temperature above 140°C, but most autoclaves only reach a maximum temperature of 120°C[9]. The only safe way to remove detergent residue is by using of a sterile water jet; 120 ml of distilled water should be used for each I/A tip, injector or cannula.

The detergent dilution indicated by the manufacturer is 0.5% (5 ml in 1 litre), and the volume of the solution can be adjusted according to the material being used. Our investigation found that the dilution had been done incorrectly, as was the rinsing with a water jet. The material had been placed in a kidney basin (500ml), but 5ml of the detergent were still used. Figure 7 shows a suitable container for diluting and using an enzymatic detergent.

Conclusion

Toxic anterior segment syndrome should be considered as a cause of unexpected inflammatory reaction in patients undergoing cataract surgery. The main focus should be on prevention, as treatment is limited to suppressing the secondary inflammatory response. The treatment of TASS cases consists of intense instillation of topical steroids with strict monitoring and control of late complications such as glaucoma.

References

1. Centers for Disease Control and Prevention (CDC). Toxic anterior segment syndrome after cataract surgery—Maine, 2006. MMWR Morb Mortal Wkly Rep. 2007;56(25):629-30.
2. Mamalis N, Edelhauser HF, Dawson DG, Chew J, LeBoyer RM, Werner L. Toxic anterior segment syndrome. J Cataract Refract Surg. 2006;32(2):324-33.
3. Cutler Peck CM, Brubaker J, Clouser S, Danford C, Edelhauser HE, Mamalis N. Toxic anterior segment syndrome: common causes. J Cataract Refract Surg. 2010;36(7):1073-80.
4. Monson MC, Mamalis N, Olson RJ. Toxic anterior segment inflammation following cataract surgery. J Cataract Refract Surg. 1992;18(2):184-9.
5. Breebaart AC, Nuyts RM, Pels E, Edelhauser HF, Verbraak FD. Toxic endothelial cell destruction of the cornea after routine extracapsular cataract surgery. Arch Ophthalmol. 1990;108(8):1121-5.
6. Nuyts RM, Boot N, van Best JA, Edelhauser HF, Breebaart AC. Long term changes in human corneal endothelium following toxic endothelial cell destruction: a specular microscopic and fluorophotometric study. Br J Ophthalmol. 1996;80(1):15-20.
7. Liu H, Routley I, Teichmann KD. Toxic endothelial cell destruction from intraocular benzalkonium chloride. J Cataract Refract Surg. 2001;27(11):1746-50. Comment in J Cataract Refract Surg. 2003;29(2):233.
8. Pong JC, Tang WW, Lai JS. Toxic endothelial cell destruction syndrome after intraocular lens repositioning with intracameral epinephrine. J Cataract Refract Surg. 2008;34(11):1990-1.
9. Mamalis N. Toxic anterior segment syndrome. J Cataract Refract Surg. 2006;32(2):181-2.
10. Johnston J. Toxic anterior segment syndrome—more than sterility meets the eye. AORN J. 2006;84(6):969-84; quiz 985-6.
11. Green K, Hull DS, Vaughn ED, Malizia AA Jr, Bowman K. Rabbit endothelial response to ophthalmic preservatives. Arch Ophthalmol. 1977;95(12):2218-21.
12. Kadonosono K, Ito N, Yazama F, Nishide T, Sugita M, Sawada H, et al. Effect of intracameral anesthesia on the corneal endothelium. J Cataract Refract Surg. 1998;24(10):1377-81.
13. Kim T, Holley GP, Lee JH, Broocker G, Edelhauser HF. The effects of intraocular lidocaine on the corneal endothelium. Ophthalmology. 1998;105(1):125-30.
14. Anderson NJ, Woods WD, Kim T, Rudnick DE, Edelhauser HF. Intracameral anesthesia: in vitro iris and corneal uptake and washout of 1% lidocaine hydrochloride. Arch Ophthalmol. 1999;117(2):225-32.
15. Kim JH. Intraocular inflammation of denatured viscoelastic substance in cases of cataract extraction and lens implantation. J Cataract Refract Surg. 1987;13(5):537-42.
16. Gills JP. Filters and antibiotics in irrigating solution for cataract surgery. J Cataract Refract Surg. 1991;17(3):385.
17. Kramann C, Pitz S, Schwenn O, Haber M, Hommel G, Pfeiffer N. Effects of intraocular cefotaxime on the human corneal endothelium. J Cataract Refract Surg. 2001;27(2):250-5.
18. Hellinger WC, Hasan SA, Bacalis LP, Thornblom DM, Beckmann SC, Blackmore C, et al. Outbreak of toxic anterior segment syndrome following cataract surgery associated with impurities in autoclave steam moisture. Infect Control Hosp Epidemiol. 2006;27(3):294-8.

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