Toxic anterior segment syndrome (TASS): studying an outbreak

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Abstract

Introduction: An effect associated with cataract surgery known as Toxic Anterior Segment Syndrome (TASS) has been reported in recent years. It is an inflammatory non-infectious process which appears within the first few hours after surgery and generally resolves well with topical steroids if the course of treatment is started promptly. In this paper we describe the syndrome and analyze the possible causes for the TASS outbreak that occurred in our hospital and affected 5 patients.

Methods: As the syndrome may be due to multiple causes, the members of a research team created at the hospital reviewed all the procedures involved. The washing and sterilization methods applied to the materials were analyzed, as well as the drugs and substances used which might have caused the outbreak. We verified the substances prepared by the Pharmacy Department, specially the irrigating solution which was used in all the cases.

Results: According to the results obtained in the biochemical, microbiological, pH, osmolarity, and endotoxins assays, the solutions prepared by the Pharmacy Department were all correct.

Discussion: Since the results obtained in the analyses of the substances used were correct and no adverse effect was observed after the re-administration of the substances, we may conclude that the outbreak would be related to the washing process performed previously to the sterilization of the instrumentation used in the surgery, mainly because the recommendation to use distilled and sterile water for this purpose was not followed and, on the contrary, tap water continued to be used.

Key words: Toxic anterior segment syndrome. Cataract surgery. Balanced salt solution. Complications of cataract surgery. Endophtalmitis. Cleaning of intraocular surgical instruments.

Síndrome tóxico del segmento anterior: investigación de un brote

Introducción: En los últimos años se ha descrito una complicación asociada a la cirugía de cataratas, el síndrome tóxico del segmento anterior. Es un proceso inflamatorio que aparece en las primeras horas tras la cirugía, de carácter no infeccioso y que generalmente se resuelve bien con corticoides tópicos si el tratamiento se instaura con prontitud. En el presente trabajo se describe este síndrome y se analizan las posibles causas de un brote que tuvo lugar en nuestro centro y que afectó a 5 pacientes.

Métodos: Se creó un grupo de investigación en el centro que revisó todos los procedimientos implicados, puesto que las causas del síndrome pueden ser múltiples. Se analizaron desde los métodos de lavado y esterilización de material hasta los medicamentos y sustancias utilizadas que pudieron ser causa del brote. Entre estos últimos, se revisaron las sustancias elaboradas en el servicio de farmacia, en especial la solución salina irrigadora, utilizada en todos los casos.

Resultados: Los resultados bioquímicos, microbiológicos, de pH, osmolaridad y de endotoxinas indicaron que las soluciones elaboradas en el servicio de farmacia eran correctas.

Discusión: Dado que los resultados de los análisis de las sustancias empleadas eran correctos, corroborados con su reintroducción sin efecto adverso alguno, se llegó a la conclusión de que el brote más bien estaría relacionado con el proceso de lavado previo a la esterilización del instrumental utilizado en la cirugía, ya que no se estaban siguiendo las recomendaciones de uso de agua destilada y estéril para este fin, sino que, por el contrario, se estaba utilizando agua corriente de la red.

Palabras clave: Síndrome tóxico del segmento anterior. Cirugía de cataratas. Solución BSS. Complicaciones de la cirugía de cataratas. Endoftalmitis. Lavado de instrumental quirúrgico intraocular.

A communication about the outbreak was presented in the Conference of the Spanish Ophthalmology Society: J. Andonegui, L. Jiménez, D. Aliseda, F. Lameiro. Description of an outbreak of toxic anterior segment síndrome after vitreous surgery. 83rd Conference of the Spanish Ophthalmology Society. Las Palmas de Gran Canaria, September 26-27, 2007.

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INTRODUCTION

Ophthalmologic surgery of cataracts is, at the moment, a fast, relatively simple process and in the majority of cases, it is performed succesfully.[1,2] However, in the last few years, an adverse effect has been associated with this type of surgery, the toxic anterior segment syndrome (TASS).[3-7] It is an inflammatory process that begins in the first 12-48 h after cataract surgery or anterior segment eye surgery, which is limited to the anterior segment of the eye, cultures and Gram stains are negative and respond well to treatment with steroids.[2]

The structure that is most affected is usually the corneal endothelium and the clinical characteristics that it presents are: diffuse corneal oedema from limbus to limbus; broad endothelium damage; inflammation of the anterior segment; fibrin deposits, increase in white blood cells; including hypopyon (pus in the anterior chamber between the cornea and the iris); dilated and irregular pupils that later close and hardly dilate, and damage of the trabecular meshwork with an almost constant increase in the intraocular pressure. The most frequent symptoms include blurred vision with or without ocular pain.[2,3,8-11]

The incidence of TASS is considered to be from 0.1% to 2%.[7,12] Fortunately, the serious cases with after effects are not frequent and the mild cases improve in a few weeks and usually go unnoticed.

TASS is causes by problems of toxicity, and not sterility. Generally, any substance found in the anterior chamber of the eye can be toxic.

It must be differentiated from infectious endophthalmitis for a correct diagnosis to later carry out a correct therapeutic approach.[2-4,7,8,13]

If TASS is suspected, topical steroid treatment should be started immediately (for example: prednisolone acetate 1%) every hour, and if not, damage may end up being permanent. Endophthalmitis cannot be discarded until the response to topical steroids is clear as it is the definitive diagnosis test.[2,3,7,13]

The objective of this study is to determine the possible causes of an outbreak of TASS that took place in our centre, the possible implication of the pharmacy department, as well as the revision of the syndrome, given its emergent character.

METHODS

In March of 2007, the ophthalmology department reported 5 cases of TASS that took place in patients that underwent vitreoretinal surgery in 2 consecutive surgical sessions (2 and 3 cases, respectively), and performed by different ophthalmologists.

A research group was created, consisting of personnel from the quality control management department and the departments of preventive medicine, hospital hygiene, ophthalmology, surgery, the sterilization unit, and the pharmacy, that analysed all of the factors that could cause TASS. The material washing and sterilisation methods were studied along with the medications and solutions used, and the personnel involved in all of the processes.

Regarding the pharmacy, the substances elaborated on site: BSS irrigation solution (balanced saline solution) and intracameral cefuroxime. As a precaution, commercial BSS solution was acquired and the batches of cephuroxime used were changed.

Ophthalmic solutions should be sterile, painless (a factor that is usually associated with its pH) and neutral (isotonic with tears).[14,15] Because of this, the following analysis were repeated: pH (Beckman pH-meter, model 50-pH Meter), osmolarity (Osmo Station™, model OM-6050); and microbiological cultures were taken (in agar-blood plates during 5 days) of the batch of BSS solution used, as well as of all of the batches available. The same parameters were analysed in the commercial BSS solution as well as in the intracameral cefuroxime.

The concentration of endotoxins in the substances was also determined using the horseshoe crab (*Limulus polyphemus)* amoebocyte lysate gelification method. Standard maximum concentrations of endotoxins were not found as described by the BSS solution. In fact, in an outbreak that took place in the United States at the end of 2005, the same problem was found.[16] According to the Royal Spanish Pharmacopea, the preparations for irrigations should not contain more than 0.5 IU of endotoxins per millilitre.[17] Regarding the cefuroxime, the maximum concentration for intravenous administration was used as no endotoxin limits are available, according to Spanish Pharmacopea, 0.1 IU/mg.

Disposable surgical instruments were used when possible. However, resterilised material had to be used in all cases, making it necessary to analyse washing and sterilising methods. The material was meticulously washed, first manually and then in a sonographic washing machine, always using water from the network. The material was dried with filtered medicinal air before being sterilised using the Sterrad® method (mixture of hydrogen peroxide and plasma gas).

The sterilising equipment was revised and found to be working correctly. The surgical instrumentation was also revised, all of stainless steel or titanium which should avoid the accumulation or generation of any residues from rusting in the sterilisation process.

The research group asked the pharmacy department to analyse the water that was found at that moment in the sonographic washing machine and from that taken directly from the network for endotoxins.

RESULTS

At first, it was thought that our patients presented an infectious endophthalmitis, and a vitrectomy was performed urgently on the first patients taking microbiological cultures and treatment was given with intra-vitreous antibiotics. After receiving negative results of the microbiological cultures of the first patients and evaluating the clinical signs that they presented, a conclusion was reached that these were in fact 5 cases of TASS. They were treated

with topical corticosteroids, which satisfactorily resolved the cases between 4-7 days. One patient suffered a retinal detachment (Table 1).

The analysis of the substances showed the following results:

A. Analysis of the BSS solution elaborated in the pharmacy and also of the commercial solution (Table 2).
B. Analysis of intracameral cefuroxime 10 mg/mL in saline.

– pH: 7.58
– Osmolarity: 330 mOsm/L.
– Microbiological results: negative culture.
– Analysis of endotoxins: <0.1 IU/mg.

C. Analysis of the water used to wash instruments before sterilization: no conclusions could be reached given that there were no references or recommendations of endotoxins in the water destined for this use. The values that were obtained were between 10 and 20 IU/mL. As a reference, the maximum limit of endotoxins in water for injectables is 0.25 IU/mL.

DISCUSSION

TASS is a syndrome that has been identified in the last 2 years. The elevated number of cases reported has led to the creation, in the United States, of the TASS Task Force of the American Association of Cataracts and Refractory Surgery (ASCRS).[6] There was an alert in the United States at the end of 2005 associated with the presence of endotoxins in a commercial BSS solution.[4,16] Since then, 90-100 cases have been reported between March and May of 2006[18] in the United States, and cases have also been detected in Canada, such as those reported in the Scarborough Hospital of Toronto, with 5000 annual operations, where they had to shut down an operating room.[5] Another hospital, of Montreal, had 14 cases of TASS in 1 day (March 2006).[7]

Table 1. Clinical and intraoperatory characteristics of the patients

Patient	Age, y	Sex	Preoperatory diagnosis	Operation	Intraocular substances used	Use of resterilised material with plasma gas	Complications
1	75	Female	Epiretinal membrane and cataract	Vitrectomy, phacoemulsification, and IOL implant	BSS, viscoelastic, adrenaline, cefuroxime, trypan blue	Yes	No
2	80	Female	Vitreous haemorrhage	Vitrectomy	BSS	Yes	No
3	70	Male	Epiretinal membrane	Vitrectomy	BSS; trypan blue	Yes	No
4	66	Male	Subluxation of the IOL	Vitrectomy and sutures of iris to IOL	BSS, cefuroxime	Yes	Retinal detachment
5	56	Male	Vitreous haemorrhage	Vitrectomy, phacoemulsification, and IOL implant	BSS; viscoelastic solution, adrenaline, cefuroxime, bevacixumab	Yes	No

BSS indicates balanced saline solution; IOL, intraocular lens.

Table 2. Results of the analysis of the balanced saline solution (BSS)

Parameter	BSS elaborated on site			Commercial BSS (batch 124108)	Standards
	Batch 8F7[a]	Batch 6M7	Batch 15M7		
pH	7.2	7.7	7.81	6.99	4.5-11.5[14] 7.4-9.4 without eye pain[15]
Osmolarity, mOsm/L	289	280	286	300	300 (200-400)[14] 290[15]
Microbiological cultures	Negative	Negative	Negative	Negative	–
Determination of electrolytes	Correct	Correct	Correct	Correct	According to formula
Analysis of endotoxins	<0.5 IU/mL	<0.5 IU/mL	<0.5 IU/mL	<0.5 IU/mL	<0.5 IU/mL[17]

[a]Batch used when the TASS outbreak occurred.

Table 3. Known causes of the toxic anterior segment syndrome[2,11]

Irrigating solutions or viscosurgical devices
Incomplete chemical composition
Inadequate pH (<6.5 or >8.5)
Inadequate osmolarity (<200 or >400 mOsm)
Conservatives or additives (for example: antibiotics, dilating medication)
Contaminants of the ophthalmolgic instruments
Detergent residues (of the sonograph, soaps, or enzymatic cleaners)
Bacterial lipopolysaccharides or other endotoxin residues
Metallic ionic residues (copper, iron)
Denaturalised viscoelastic devices
Ocular medications
Erroneous concentration of medication
Inadequate pH (<6.5 or >8.5)
Inadequate osmolarity (<200 or >400 mOsm)
Vehicles with inadequate pH or osmolarity
Conservatives in the medical solution
Intraocular lenses
Composed to polish and/or shine
Composed for their cleaning and sterilisation

As observed (in Table 3), there are multiple causes, and the most frequently implicated substances are the irrigating and medicating substances, which should be free of any conservatives.[2-4,7-8,16]

At that moment all of the substances used were revised. The elaboration processes for the BSS solution and the intracameral cefuroxime were analysed, although the last one was discarded as it did not coincide in all of the cases that occurred. After confirming that the analyses were correct, the BSS solution that was elaborated onsite was reintroduced, and the same batches of cefuroxime vials were once again used, without any adverse reactions.

However, according to the bibliography found, the majority of TASS cases are related with the cleaning and sterilisation of instruments.[6,19] Inadequate washing leads to an incomplete elimination of residues, such as the viscoelastic, which when combined with detergents or enzymatic cleaners, or those denaturalised in the sterilisation process, may end up causing TASS.[2,19]

The remains of the chemical sterilizers can also cause TASS along with enzymatic detergents and bacterial or endotoxin contamination of the sonographic bath water.[2,6,7,10,19] Although the bacteria are destroyed during the sterilisation process, the lipopolysaccharides that form the endotoxins survive.[2] Also, the inadequate maintenance of the sterilisation systems may cause TASS.[12]

The water used to wash the instruments in the sonographic washer and the posterior rinse was considered as a possible pause. According to the bibliography, this water should be deionised, distilled or sterile[2,8,19] and in abundance.

To conclude, and thanks to the results obtained in the analysis of the substances, the BSS solution can be discarded as a cause, with its reintroduction as the definitive test. It does seem that the most probable cause comes from the use of running water from the network for washing and rinsing the instruments. Although more cases of TASS have not been detected at the moment, no definitive cause has been identified.

The measures taken in the centre from that moment have included the type of water used to treat the material (distilled and sterile) and the acquisition of more instruments to ensure a more exhaustive washing.

The TASS outbreak has made all the personnel involved aware of the syndrome, and prepared for any new TASS outbreaks.

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