

Features, Causes and Prevention of Toxic Anterior Segment Syndrome (TASS) - An Outbreak Investigation

Khawaja Khalid Shoaib

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See end of article for authors affiliations

Correspondence to:
Khawaja Khalid Shoaib
Eye Department
PNS Hafeez, E - 8
Islamabad

Purpose: To analyze features, causes and preventive measures for toxic anterior segment syndrome (TASS) cases, occurring after coaxial phacoemulsification (phaco).

Material and Methods: TASS occurring after uneventful coaxial phaco during May/June 2008 in eye department, Combined Military Hospital Kharian, were analyzed retrospectively in this case series. Clinical features, response to treatment and possible causes were checked during the outbreak (including intracamerally given drugs, irrigating solutions, intraocular lenses and washing/sterilization techniques for instruments) and measures taken to prevent further cases. Follow up continued till Feb 2009.

Results: Nineteen (14.8%) out of 128 phaco cases developed TASS. Out of these nineteen cases, nine (47%) were males and ten (53%) were females. Age ranged from twenty eight years to seventy one years (mean 57 ± 9.7). Follow up ranged from one month to seven months (mean 2.2 ± 2.1). Post operatively, one patient had nausea and vomiting six hours after the operation. On first post operative day, there was corneal edema, anterior chamber inflammation, pupil dilatation, and pigment dusting on the corneal endothelium / anterior surface of intraocular lens in all (100%) cases. At last visit, eight cases (42 %) had corneal haze, seven (37%) had iris atrophy and two (11%) had dilated pupil. Corrected visual acuity became 6/6 in nine cases (47%), rest ranged from 6/6P to hand movement. Different steps were taken to stop TASS and no case occurred in next seven months from July 2008 onwards.

Conclusion: TASS can result in corneal haze or iris depigmentation / atrophy. Even prompt and energetic treatment may leave significant visual morbidity. The exact cause could not be established in this series of cases however more vigilance resulted in cessation of such cases.

Toxic anterior segment syndrome (TASS) is a general term used to describe acute, sterile postoperative inflammation due to a non-infectious substance that accidentally enters the anterior segment at the time of surgery. It has been reported after different types of intraocular surgery e.g. cataract surgery,¹ (including the paediatric),² iris – supported phakic IOL implantation,^{3,4} intravitreal injection of bevacizumab,⁵ post cornea penetrating injury⁶, penetrating keratoplasty (PK)⁷ and vitrectomy with silicone oil injection.⁸ It resembles infectious

endophthalmitis⁹ but improves with steroids. Onset of inflammation in TASS is earlier as compared to infectious uveitis, vitreous cultures are negative and visual recovery is usually better. The present study was carried out to analyze multiple cases of TASS encountered after phacoemulsification (phaco).

MATERIAL AND METHODS

TASS cases were encountered in eye department Combined Military Hospital Kharian during May /

June 2008 and follow up of these cases continued till Feb 2009 (Table 1). Clinical features, response to treatment and possible causes were checked during the outbreak. Data was then retrospectively studied. Single surgeon was performing coaxial phaco and following the same technique for two and a half years prior to development of these cases.

In each case, pre operatively, infection of adnexa was ruled out and anterior segment / optic disc assessment was done. Next, 5% povidone iodine solution was instilled in conjunctival sac, kept for 3 minutes and was then washed with approximately 100 cc of intravenous drip solution of normal saline or ringer lactate. Then finally, the surgeon flushed the conjunctival sac with 10 cc of balanced electrolyte / salt solution (BES / BSS) after applying adhesive tape (Opsite) and eye speculum. The routine included a clear corneal incision of 2.65 mm or 3.2 mm incision enlarged to 5.5 mm, use of sodium hyaluronate (Visco Supreme- USA) and phaco tip of 0.9 mm or 1.0 mm (19 G / 20 G) depending upon whether a rigid or foldable intraocular lens (IOL) had to be implanted. BES/BSS was used in all the cases. Intraocular lenses (IOLs) were implanted in all the cases. These included foldable acrylic (C Flex, Rayner - UK and Idea - Switzerland) and rigid PMMA (DGR - USA). A single suture was applied in a few cases in which rigid IOL was implanted and where wound leakage was suspected. Though phaco hand piece and sleeve were not autoclaved for every new case, after each operation it was a routine to change the phaco tip and sleeve.

At the end of surgery, every case was given 0.1 ml of 0.5% intracameral moxifloxacin (Vigamox- Alcon). Phaco machine used during this period and afterwards was Pulsar II (Optikon-Italy). In all TASS cases, extensive (1 - 2 hourly) topical steroid eye drops were used. Initially Prednisolone / Dexamethasone (Predforte / Tobradex) and later Flourometholone (FML Forte) eye drops were used to avoid rise in intraocular pressure. Visual acuity, state of cornea, intraocular inflammation, condition of iris / pupil and intraocular pressure were recorded on each visit. Severe cases had follow up visit after every 1 - 2 weeks while mild / moderate cases were reviewed on monthly basis.

RESULTS

There were nine (47%) male and ten (53%) female patients (Table 1). Age ranged from twenty eight years to seventy one years (mean 57 ± 9.7). Follow up ranged

from one month to seven months (mean 2.2 ± 2.1). Post operatively, one patient (case No. 8) had nausea and vomiting six / seven hours after the operation. He reported the incidence next day because he went home after surgery. On first post operative day, there was corneal edema, anterior chamber inflammation (average ++, 10 - 20 cells per field), pupil dilatation, and pigment dusting on the corneal endothelium and anterior surface of intraocular lens in all (100%) cases. Despite treatment, the damage was severe in one case (case No.3). In this case, corneal edema was gradually replaced with broad white lines / tracks of fibrosis. Pupil was widely dilated, there was severe diffuse iris atrophy (especially at mid peripheral iris, where a whitish band of atrophy replaced the normal iris architecture) and ectropion uveae (posterior pigmented epithelium pulled to anterior iris surface around the papillary margin). In another case, damage was slightly less severe (case No.8). In this case corneal edema was generalized and vision after eight months was counting fingers at 2 meters. In this case intraocular pressure remained high even after eight months of treatment with dorzolamide timolol combination (Cosopt) and Latanoprost. He was probably a steroid responder as steroids were continued for this duration. In five other cases, iris had slightly washed out appearance with loss of fine crypts on the surface. Thus the total number of patients, who had iris atrophy, was seven (37%). There was pigment dispersion from anterior surface of iris resulting in pigment dusting on the corneal endothelium and anterior surface of intraocular lens in all these cases having iris atrophy. It gradually decreased in intensity with time. Faint generalized corneal haze caused deterioration of corrected vision in six cases (32%). In two other cases (11%) corneal haze involved half / two thirds of cornea with the center at the limbal incision wound and sparing the part farthest from the entry wound. Thus the total number of cases having corneal haze at the last visit, was eight (42%). Pupil dilatation persisted in two cases (11%). Corrected visual acuity became 6/6 in nine cases (47%). One case had decreased corrected vision due to unrelated diabetic retinopathy while rest of the cases had decreased corrected vision ranging from 6/6P to hand movement. Apart from the two cases in which detailed retinal examination was not possible due to corneal haze and one having diabetic retinopathy, no macular problems were encountered in any case. Different steps were taken to stop TASS (Table 2) and no case occurred in next seven months from July 2008 onwards.

Table 1: Clinical features of TASS patients

| Sex | Age | Features at Presentation | Features at Last Visit | VA | FU |
|-----|-----|--------------------------|------------------------|-------|----|
| M | 56 | CE+, PD+, AC++ | N | 6/6 | 1 |
| F | 66 | CE+, PD+, AC+ | N | 6/6 | 2 |
| M | 28 | CE++, PD+++, AC++ | CH+++, PD+++, IA+++ | HM | 7 |
| M | 52 | CE+++, PD+, AC++ | CH+ | 6/12P | 2 |
| M | 48 | CE++, PD++, AC++ | CH+ | 6/12 | 1 |
| F | 67 | CE+, PD+, AC++ | N | 6/6 | 1 |
| F | 57 | CE, PD, AC++ | CH+ | 6/9 | 2 |
| M | 58 | CE+++, PD++, AC+++ | CH++, PD+, IA++, ↑ IOP | CF 2m | 7 |
| F | 47 | CE+, PD+, AC+ | DR | 6/24 | 3 |
| F | 63 | CE+, PD+, AC+ | N | 6/6 | 1 |
| M | 49 | CE++, PD+, AC+++ | CH+, IA+ | 6/18 | 3 |
| F | 56 | CE+, PD+, AC+ | N | 6/6 | 1 |
| F | 61 | CE+, PD+, AC+ | N | 6/6 | 2 |
| F | 68 | CE++, PD++, AC++ | CH+, IA+ | 6/12 | 1 |
| M | 63 | CE+, PD+, AC+ | N | 6/6 | 1 |
| F | 58 | CE+, PD++, AC++ | CH+, IA+ | 6/12 | 2 |
| M | 59 | CE+, PD+, AC++ | IA+ | 6/6 P | 1 |
| F | 71 | CE+, PD++, AC++ | IA+ | 6/6 | 1 |
| M | 62 | CE+, PD+, AC+ | N | 6/6 | 1 |

M = Male, F = Female, CE = Corneal edema, PD = Pupil Dilatation, AC = Anterior chamber cells: + = Mild (< 10 per field), ++ = Moderate (10-20 per field), +++ = Marked (> 20 per field), VA = Visual acuity at last visit, CH = Corneal haze, IA = Iris atrophy with pigment dusting, FU = Follow up in months, N = Normal, DR = Diabetic retinopathy, IOP = Intraocular pressure, + = Mild, ++ = Moderate, +++ = Marked.

Table 2: Suspected causes of TASS and actions taken to prevent further cases.

| Suspected Causes of TASS | Action Taken |
|---|--------------|
| 10% Povidone iodine (PI) solution used instead of 5% for conjunctiva | 5% ensured |
| Povidone iodine scrub was used instead of the solution | No scrub |
| Antiseptic / povidone iodine for instruments prior to autoclaving | Discontinued |
| Residual washing powder (Surf) on instruments after washing | ↑ Rinsing |
| Clear corneal incisions allowing povidone iodine to gain entry in eye | PI Stopped |

DISCUSSION

Presenting clinical features in an outbreak of TASS involving 112 cases included blurred vision (60%), anterior segment inflammation (49%), and cell deposition (56%).¹⁰ Main features reported in another series were, severe iridocyclitis, atrophic iris changes, cystoid macular edema, anterior capsule phimosis, and posterior capsule opacification.¹¹ TASS following cataract surgery with intraocular lens implantation is associated with a low corneal endothelial cell density.¹²

Different causes of TASS have been considered. In one series, increased levels of endotoxins were found in the BSS which was withdrawn, resulting in termination of the outbreak¹⁰. In another cluster, no specific cause of the outbreak could be identified, however no additional cases were reported after changes were made to the materials and equipment used for surgery.¹³ TASS encountered after penetrating keratoplasty was most likely due to accumulation of cleaning substances or heat – stable endotoxins on the surface of the routinely used guided trephine system.⁷ Another outbreak investigation suspected washing process performed previous to the sterilization of the instrumentation used in the surgery, was to be blamed. Tap water had been used instead of the recommended distilled and sterile water.¹⁴ Review of a series concluded sterilization responsible for the syndrome, because after ethylene oxide gas sterilization was replaced with autoclaving, no such incidents occurred.^{2,15} Similarly impurities in autoclave steam moisture have also been associated with TASS.¹⁶ Another series suspected residual povidone iodine on instruments among other causes of the syndrome.⁶ Different other substances presumed to cause TASS include antiseptic solution used to soak surgical instruments before subsequent surgery,^{17,18} trypan blue¹⁹ that was administered intracamerally to improve visualization of the capsule, preservatives in ophthalmic solutions, ophthalmic viscosurgical devices (e.g. Multivisc BD),³ intraocular lenses,²⁰ ointment in the anterior chamber following cataract surgery,²¹ preservatives²² (benzylchonium chloride), iris-supported phakic intraocular lens,²³ intracameral cefuroxime (Axetin), enzymatic detergents used in cleaning surgical instruments,²⁴ talc from surgical gloves and silicone oil⁸ etc. Other factors thought to cause TASS are inadequate flushing of phaco and irrigation / aspiration handpieces, detergents at the wrong concentration, ultrasonic bath, antibiotic agents in balanced salt solution, preserved epinephrine,

inappropriate agents for skin prep.²⁵

Recently a good trend of adequate handpiece flushing, deionized/distilled final rinse, reduction in the use of preserved epinephrine and reduction in the use of enzymatic detergents has been observed. However, increase in a few unfavourable practices e.g. handling of intraocular lenses or instrument tips with gloved hands, poor instrument maintenance, and ultrasound bath use without adequate routine cleaning, needs attention.²⁶ Penetrating keratoplasty may be required if corneal transparency is not restored. Descemet-stripping automated endothelial keratoplasty has also been found effective in eyes with TASS – associated corneal edema.²⁷

In the present study all the cases were done by the same surgical team who had been doing high volume phaco in the preceding two and a half years in the same hospital without any case of TASS. Out of four operation theater assistants, one was replaced during this period however the rest were supposed to continue the routine for washing and sterilization. These TASS cases were randomly encountered during two months. There were twenty cataract instrument sets and ten sets of phaco tips / sleeves.

TASS was a clinical diagnosis. Differential diagnosis considered was infectious endophthalmitis and corneal edema due to mechanical endothelial damage produced by instrumentation (excessive phaco etc). There was no pain in TASS cases. Corneal edema involved all the layers and extended from limbus to limbus, though it varied in intensity from case to case. Vitreous visualization was not possible in severe cases but the rest of the cases had no involvement. Corneal edema of TASS and that of striate keratopathy (resulting from use of excessive phaco especially of hard nuclei) was similar in appearance but iris / pupillary involvement in TASS, made the difference. Moreover, resolution took many weeks in many cases of TASS while it was faster in other cases. In the most affected patient seven months after the operation, cornea was almost opaque and milky white, causing marked deterioration of vision (Hand movement).

Different causes were considered and measures were taken accordingly (Table 2). 5 % povidone iodine solution is useful because when instilled in the conjunctival sac a few minutes before cataract surgery reduces the number of bacteria from 10 to 100 fold^{28,29} but causes problems if it gets into the anterior chamber.³⁰ First possibility considered was that

assistant might not have diluted 10% povidone iodine solution to 5% and rather used the 10% concentration which was being used for the skin. It was ensured that 5% solution was used.

Second possibility was that povidone iodine scrub was used instead of the solution because bottles and labels of the two, manufactured by many companies were found to be similar in appearance. To counter this factor, scrub was removed from operation theater and only solution was used. Even for scrub purposes, surgical team used solution with soap. Even povidone iodine solution of different companies was used to eliminate the possibility of one particular brand causing the problem.

Third potential cause was use of antiseptic solution / povidone iodine solution for disinfection of instruments like two way cannulas before autoclaving and possibility of improper washing resulting in some residual solution. It was addressed with discontinuation of use of any such solution.

Fourth factor suspected was detergent powder (Surf) for cleaning of instruments and possibility of partial rinsing in water resulting in some residual material. It was ensured that proper rinsing with water was carried out.

Fifth aspect examined was the clear corneal incisions (CCI). Though simple to perform, it increases the likelihood of endophthalmitis by approximately 6 times as concluded by European Society of Cataract and Refractive Surgery (ESCRS) study.³¹ Probably because of the fact that it is difficult to make this type of incision water tight, there are more chances that substances can gain entry inside the eye in the immediate post operative period. Povidone iodine solution may be one of these especially in phaco of hard cataracts where excessive manipulations might distort the incision wound. It was especially probable in cases where corneal involvement was centered on limbal wound. However TASS also occurred in a young male (case No. 3) where hardly any phaco power was required. Probably more than one mechanism was involved in the causation of TASS.

Finally practice of intracameral moxifloxacin was evaluated. 0.1 ml of preservative free moxifloxacin (Vigamox – Alcon) delivered intracamerally at the end of phaco was a routine for the last two years. It was thought that assistant might have used drug of any other brand. For a few weeks we stopped instilling povidone iodine solution in the eye and intracameral moxifloxacin.

Though the exact cause of TASS could not be identified in this study, different steps were taken to stop TASS. No case occurred in next seven months from July 2008 onwards. Patients having good visual recovery were lost to follow up earlier while those having marked deterioration of vision reported for maximum duration of follow up.

CONCLUSION

TASS can result in prolonged decrease in corneal transparency or iris depigmentation / atrophy. The exact cause could not be established in this series of cases however more vigilance resulted in cessation of such cases.

Author's Affiliation

Dr. Khawaja Khalid Shoab
Eye Department
PNS Hafeez, E - 8
Islamabad

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