Sympathetic ophthalmitis following vitreoretinal surgery: Does antecedent trauma make a difference?

Ekta Rishi, Pukhraj Rishi, Bindu Appukuttan, Jaydeep Walinjkar, Jyotirmay Biswas, Tarun Sharma

Background: Sympathetic ophthalmitis (SO) has been reported following vitrectomy; however, there is a lack of data on the role of antecedent penetrating ocular trauma impacting the disease manifestation in eyes developing SO following vitrectomy. Aim: To report differences in the presentation and outcomes of SO in eyes with or without a history of antecedent penetrating trauma; SO being diagnosed after vitreoretinal (VR) surgery. Design: Comparative case series. Methods: Seventeen consecutive patients presenting with SO following VR surgery, diagnosed between 1995 and 2011 were included. Eyes with and without prior penetrating injury were included in Group I (n = 7) and Group II (n = 10), respectively. All Group I patients had received systemic steroids prior to presentation. Demographic and clinical parameters were evaluated. Results: Differences were observed between Group I and Group II mainly with regards to time interval between VR surgery and diagnosis of SO (1.5 months vs. 8 months, P = 0.10), presence of neurosensory detachments (100% vs. 30%, P = 0.01), and the inciting eye vision at presentation (nil light perception in 28.5% vs. 80%, P = 0.049). Other differences observed though not statistically significant were optic disc and retinal vessel involvement (42% vs. 70%, P = 0.28), Dalen-Fuchs nodules (localized vs. diffuse) and leaks on fundus fluorescein angiography (pin-point vs. pin-point leak). Conclusion: SO in patients with antecedent penetrating ocular trauma present early with the central serous chorioretinopathy-like picture. Prior use of systemic steroids might have a bearing on the differences in presentation and the visual acuities between the two groups.

Key words: Corticosteroids, immunosuppression, inflammation, sympathetic ophthalmitis, trauma, vitreoretinal surgery

Sympathetic ophthalmitis (SO) is a bilateral diffuse uveitis occurring as a consequence of ocular trauma or surgery in one eye. The eye sustaining the injury or undergoing surgery is called the “inciting” or the “exciting” eye while the contralateral normal eye is called the “sympathizing” eye. Mackenzie[1] in 1840 and Fuchs[2] in 1905 provided the earliest description of SO. The possibility of an autoimmune inflammatory response against uveal antigens as the etiology was proposed by Elschnig[3] in 1910. Prior penetrating injury has been the most common precipitating factor for SO. However, recent studies have reported increase in the incidence following surgical procedures.[4-10] The etiologic shift from accidental trauma to surgical trauma can probably be explained by the improved access to emergency surgical care following accidental ocular trauma. Gass[11] has reported SO following vitrectomy and Lewis et al.[12] have reported cases of SO after trauma and vitrectomy. However, there is a lack of data on the role of antecedent penetrating ocular trauma impacting the disease manifestation in eyes developing SO following vitrectomy. In this study of 17 patients with SO following vitreoretinal (VR) surgery, we analyze the impact of antecedent penetrating ocular trauma in disease manifestation and treatment outcomes.

Methods

Review of the medical records of 17 patients presenting with clinical features of SO, between 1995 and 2011 was done. Only those patients with a history of VR surgery prior to the episode of SO were included. SO was diagnosed if features of posterior segment involvement in the form of either classic chorioretinal lesions or exudative retinal detachment (RD) or optic disc edema and sunset glow fundus were present, with or without bilateral anterior uveitis.[4] The minimal diagnostic criteria was the presence of multiple pin-point areas of hyperfluorescence with or without late dye pooling and disc leakage on fundus fluorescein angiography (FFA) and/or the presence of diffuse choroidal thickening of the posterior pole on ultrasound B scan (USG). The patients were divided into two groups; those with prior penetrating injury constituting Group I and those without, constituting Group II.

Collected data included age, sex, presenting complaints, history of antecedent penetrating ocular trauma or any other ocular surgery, timing of the surgical procedures performed, the time interval between the VR surgery(ies) and the onset of symptoms, and the duration of follow-up and the final visual outcome. The clinical parameters recorded included the best corrected visual acuity measured by Snellen's chart.

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at each visit, anterior and posterior segment manifestations with FFA and ultrasound B-scan features. Therapeutic response to steroids (oral, intravenous, and topical) and immunosuppressants (azathioprine and cyclosporine) and complications during the course of the treatment were also noted. The final visual outcome between the two groups was compared using nonparametric statistical tests. Statistical software (SPSS for Windows, version 13.0 SPSS Science, Chicago, IL, USA) was used for statistical analysis. The statistical significance was assumed at $P \leq 0.05$.

**Results**

Seven patients were included in Group I, whereas 10 patients were included in Group II. Demographic features of 7 patients in Group I are shown in Table 1. Demographic characteristics of 10 patients in Group II are shown in Table 2. Overall, the mean age at presentation was $37 \pm 14.96$ years (range 18–65 years); the mean age at presentation in Group I being 30.28 years (range 18–44 years) and that in Group II being 39.4 years (range 20–65 years). Vitrectomy was performed using
20 g instrumentation in all the patients in the study. Indications for VR surgery are depicted in Fig. 1. Presenting symptoms and their timing of presentation are shown in Table 3. In Group I, 4 (57.1%) eyes underwent repeated surgeries within 2–4 weeks and all of them presented with SO within 1–1.5 months of the last surgery.

All except 1 patient (Case 13) presented in the acute phase of the disease. Clinical presentation in sympathizing eyes (SEs) is shown in Table 4. Patients in Group I predominantly presented with neurosensory detachment [Figs. 2a and 3a] resembling “central serous retinopathy-like picture” (n = 4) along with mild anterior uveitis. Massive exudative RD was seen in the other patients (n = 3). Dalen-Fuch’s nodules were smaller, less numerous, and mostly limited to the posterior pole (n = 1). On disease resolution, atrophic retinal pigment epithelial (RPE) changes were observed more at the macula [Fig. 2b]. However, patients in Group II presented with more significant anterior uveitis along with the posterior segment findings (n = 9). Classical granulomatous uveitis with large mutton fat keratic precipitates were seen in 2 patients. However, iris nodules were not seen in any of the patients. Posterior segment manifestations included disc hyperemia/edema (n = 9), peripapillary choroidal nodules (n = 7), and retinal vascular caliber changes (n = 5) [Figs. 4a and 5a]. Dalen-Fuchs nodules were numerous, coalescent, and present diffusely over the posterior pole and extending to the periphery as well (n = 3).

On disease resolution, RPE atrophy was classically seen in the peripapillary area [Fig. 5b]. Thus, the Group I eyes differed from Group II eyes mainly with respect to the presence of neurosensory detachments (100% vs. 30%, P = 0.01). Other differences noted though not statistically significant were disc and vessel involvement (42% vs. 70%, P = 0.28), Dalen-Fuchs nodules (localized vs. diffuse) and the areas of RPE atrophy on resolution (macular vs. peripapillary).

Though in small numbers, distinct fluorescein angiographic features were noted between the two groups. SEs in Group I revealed RPE leakages (n = 7). The RPE leaks were larger [Figs. 2c and 3b], associated with late pooling of dye (n = 5) [Figs. 2d and 3c, d], and usually confined to the posterior pole (except in 3 patients where the leaks were present beyond the equator). Retinal vessel changes and peripapillary hyperfluorescence were conspicuously absent. In contrast, Group II SEs predominantly showed early hypofluorescence and late hyperfluorescence in the area corresponding to the peripapillary choroidal nodules (n = 7) [Figs. 4b-d and 5c, d], disc leakage in eyes with disc edema/hyperemia (n = 9), segmental staining of the retinal veins and arterioles (n = 2) [Fig. 5c, d], retinal venous beading and tortuosity (n = 6), and RPE leaks that were pin-point, multiple, and scattered all over the postpole extending beyond arcades up to the equator. Pooling of dye was seen in a limited number of patients (n = 2).

Medical management, duration of treatment, follow-up, and recurrence of inflammation are shown in Table 5. Oral

**Table 3: Differences in presenting symptoms and timing of presentation in the two groups**

| Symptoms (%) | Group I (n=7) | Group II (n=10) |
|--------------|--------------|-----------------|
| Diminution of vision | 5 (71.4) | 9 (90) |
| Headache | 0 | 4 (40) |
| Eye pain and redness | 0 | 3 (30) |
| Metamorphopia | 3 (42) | 0 |
| Floaters | 3 (42) | 0 |

**Table 4: Clinical presentation in SEs in the two groups**

| Clinical features | Group I (n=7) (%) | Group II (n=10) (%) |
|------------------|------------------|------------------|
| Anterior segment findings | | |
| Absent/mild anterior nongranulomatous uveitis | 5 (71) | 4 (40) |
| Anterior nongranulomatous uveitis | 1 (14) | 4 (40) |
| Granulomatous uveitis | 1 (14) | 2 (20) |
| Posterior segment findings | | |
| Vitritis | 4 (57) | 6 (60) |
| Neurosensory detachment | 7 (100) | 3 (30) |
| Disc involvement | 4 (57) | 7 (70) |
| Subretinal infiltrates | 2 (28.5) | 4 (40) |
| Fundus fluorescein angiography | | |
| FFA performed | 6 (85.74) | 7 (70) |
| Pin-point hyperfluorescence | 6 (100) | 5 (71.4) |
| Disc leakage | 3 (50) | 6 (85.74) |
| Retinal vessel wall staining | 2 (28.5) | 3 (42.8) |
| Ultrasound | | |
| Ultrasound B scan performed | 6 (85.74) | 9 (90) |
| Exudative RD | 6 (100) | 5 (71.4) |
| Increased choroidal thickness | 3 (50) | 7 (77.7) |

SEs: Sympathizing eyes, RD: Retinal detachment, FFA: Fluorescein angiography

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**Figure 1:** Bar diagram depicts the indications for vitreoretinal surgeries in 17 eyes that developed sympathetic ophthalmits following surgery.
and topical corticosteroids were the mainstay of treatment. Treatment with oral steroids was initiated with a dose of 1.5–2 mg/kg, tapered and followed-up with a maintenance dose of 5–10 mg/day. Multiple drug combinations were found necessary to control the inflammation in patients with inciting eyes (IEs) having ≤ PL vision in Group II and in all patients (except 1 who presented in the resolving stage of the disease) in Group I. Eyes with recurrent inflammation were managed with repeat cycles of immunosuppressive and systemic steroid therapy. No light perception (NLP) was noted in 2 (28.5%) and 8 (80%) of the IEs in Group I and II, respectively (P = 0.049). The final visual acuity in the SE was observed to be better in Group I, though not statistically significant (100% vs. 70%, P = 0.33) [Fig. 6].

Two SEs (Case numbers 16, 17) in Group II showed visual deterioration due to secondary glaucoma and optic atrophy, respectively.

With respect to the IEs, 5 (71.4%) eyes in Group I showed deterioration of visual acuity while 1 eye remained same and 1 improved. Two eyes that worsened were prephthisical at presentation, 1 had secondary glaucoma with optic atrophy, 1 had second insult to IE in the form of another penetrating trauma and 1 developed recurrent rhegmatogenous RD. The final visual acuity in the IEs in Group II eyes remained the same in 6 (60%) eyes, worsened in 3 (30%) eyes, and improved in 1 (10%) eye. Among the 3 eyes that worsened, 1 developed secondary angle closure glaucoma eventually resulting in optic atrophy. The other 2 eyes were prephthisical at presentation and became phthisical with time. Treatment-related complications have been listed in Table 6.

Table 5: Medical management: Therapeutic agents, duration of treatment, follow-up and recurrence of inflammation in the two groups

| Treatment details                        | Group I (n=7) (%) | Group II (n=10) (%) |
|-----------------------------------------|-------------------|---------------------|
| Drugs                                    |                   |                     |
| Oral prednisolone (1.5-2 mg/kg/day; tapered) | 7 (100)           | 9 (90)              |
| Intravenous methyl prednisolone (1 mg IV for 3 days, followed by oral steroids) | 6 (85.7)           | 5 (50)              |
| Additional immunosuppressives            |                   |                     |
| Azathioprine (50 mg TID - 1 month; tapered) | 6 (85.7)           | 8 (80)              |
| Cyclosporine (175 mg BID; tapered)       |                   |                     |
| Average duration of treatment (months)   | 7.8               | 9                   |
| Follow-up period                         | Median 24 months  | Median 34 months    |
| Eyes with recurrence of inflammation     | 1 (14.7)          | 4 (40)              |

IV: Intravenous, TID: Three times a day, BID: Twice a day

Discussion

SO following VR surgery has been reported previously.\[7,9-13\] There are some reports of SO developing following VR surgery in the setting of antecedent trauma and few without\[7,10,11,13\] In our series, we tried to study and analyze the presentations and outcomes in both the groups. Patients with antecedent penetrating trauma were seen to present early and had better visual outcomes with treatment.

In patients with multiple surgeries, it was the subsequent (postprimary repair) VR surgery that was seen as the inciting factor in 71.4% patients in Group I and 50% patients in Group II. This aspect has also been reported by Tamai et al.\[13\] This could be explained by the additional insults imposed by the multiple surgeries. Thus, any kind of “recurrent” surgical manipulation in the IE can act as a trigger for SO.\[6,11\] We found an earlier presentation (median 1.5 months) in Group I in comparison to Group II, though not statistically significant. Galor et al.\[14\] also found that trauma-inflicted patients presented earlier than surgically induced SO patients.
However, patients in Group II had varied presentation with a median of 8 months (range 20 days to 12 years) similar to the study by Pollack et al.\[7\]. Both groups were similar with respect to the presenting visual acuity in the SEs but differed in the presenting vision among IEs (\(P = 0.029\)), which was significantly better in Group I. This may be due to longstanding posterior segment disease in Group II and also since 4 eyes were prephthisical. Better visual acuity in Group I patients could also be explained by the earlier presentation. 40% patients presented with NLP in the IEs in Group II. The clinical features in eyes from Group II involved mainly the optic disc, peripapillary area, and the retinal vessels, whereas neurosensory detachments at the macula were conspicuous in Group I eyes. This is in contrast with the findings by Pollack et al.\[7\] where anterior segment involvement was seen in 75% patients. Predominant involvement of the posterior segment has also been observed in a study on the Asian-Indian population by Gupta et al.\[15\]. Isolated neurosensory detachment in Group I may easily be confused with central serous chorioretinopathy. A plausible explanation for this presentation is that these patients were treated with oral steroids at/before the presentation, which could have suppressed the inflammatory changes in the posterior segment leading to a limited disease manifestation. It is imperative to consider this differential in such eyes as patients with penetrating ocular injury are frequently treated with systemic steroids and the possibility of central serous retinopathy (CSR) masquerading as SO or vice versa cannot be ruled out. Differentiating between the two is even more essential from the treatment point of view as SO requires initiation of steroid therapy, whereas CSR warrants its discontinuation.

All patients in Group I (except 1) required additional immunosuppression with oral steroids, whereas IEs with \(\leq PL\) vision (\(n = 8\)) in Group II required additional immunosuppression. This may imply that badly damaged and phthisical IEs require more aggressive management. Our treatment regime was comparable to that used by Su and Chee.\[6\] However, despite different treatment regimens the visual outcomes were good in the SEs in about 88% of the patients. The effect of the surgical outcome of cataract extraction in SEs has been reported earlier.\[14,17\] In our study too, we found that patients who underwent cataract extraction or any other ocular surgery, in the sympathizing or the IEs, in the quiescent phase of the disease under steroid cover did reasonably well. However, surgeries on the IEs during the active phase of the disease were associated with recurrences of SO.
According to Galor et al., traumatic cause, exudative RD, and active inflammation were associated with poor visual outcome. A more severe course with traumatic SO theoretically may be the result of high-doses of antigenic exposure. Patients treated promptly with prednisone and/or immunosuppression were more likely to achieve quiescence and seemed to do so more quickly.

Poor visual outcome was observed in the inciting and SEs in Group II as compared to Group I. Whether this difference could have been due to the earlier presentation in the trauma group, cannot be inferred. Our study sample size is not large enough to conclude a statistically significant difference in the presentation and the outcome; however, we still feel that patients with multiple surgeries, who are at higher risks of developing SO, if detected and managed at the earliest may give a good visual outcome.

Kilmartin et al. argued that early enucleation did not affect the visual outcome. In our study, eyes which were advised enucleation did not have any recurrences throughout the follow-up. Recurrences and severe inflammations when present were managed by stepping up the doses of steroids and use of additional immunosuppressive agents.

**Conclusion**

Persistent, low-grade uveitis, or isolated posterior segment features following VR surgery should alert the ophthalmologist to the possibility of SO. SO patients with antecedent penetrating trauma present early with a CSR-like picture. Prior use of systemic steroids might have a bearing on the clinical presentation and treatment outcome. The presence of superadded infection/further surgical insults to the IE in the active phase of inflammation is likely to be associated with multiple recurrences of SO and poor visual prognosis in the IEs.

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**Conflicts of interest**

There are no conflicts of interest.

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