Sympathetic Ophthalmia: Experience from a Tertiary Care Center in Northern India

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Abstract

Purpose: To describe our clinical experience with sympathetic ophthalmia (SO) at a tertiary eye care center in north India.

Methods: In this retrospective case series, analysis of the clinical features and visual outcomes of patients diagnosed with SO between March 2012 and March 2016 were performed.

Results: Ten male and four female patients (median age, 15.5 years) with SO following penetrating trauma (10 patients) or ocular surgery (four patients) were included. SO developed 2 weeks to 3 years after the insult. Mean presenting visual acuity of the sympathizing eyes was 1.086 (LogMAR). Anterior chamber reaction was documented in all eyes in which it could be assessed (14 sympathizing eyes; five exciting eyes). Neurosensory detachment was seen in 10 of 14 patients (71.5%). Five patients (35.7%) were managed with oral steroids alone, whereas nine (64.3%) were treated with intravenous pulse dexamethasone followed by oral steroids. Inflammation recurred in three patients during steroid tapering, necessitating restarting of steroid therapy with or without additional immunosuppressants. At the last follow-up, all 14 patients were in remission with low-dose oral steroids; seven patients were also on immunosuppressants. At the final follow-up, 12 of 14 (85.7%) sympathizing eyes achieved 20/40 or better visual acuity and three exciting eyes achieved at least 6/24 visual acuity.

Conclusion: Although SO is a potentially blinding disorder, early detection and individualized treatment allow most patients achieve good final visual acuity.

Keywords: Granulomatous Uveitis; Immunosuppressants; Neurosensory Detachment; Panuveitis; Sympathetic Ophthalmia

INTRODUCTION

Sympathetic ophthalmia (SO), classically described as a bilateral granulomatous panuveitis, is an uncommonly encountered ocular condition with an incidence of around 0.03 per 100,000 ophthalmic patients seen per year. Nevertheless, it is potentially blinding if not detected in time and managed appropriately. Initially described...
as a response of the sympathizing eye to penetrating trauma, SO is now commonly seen in postsurgical (especially vitreoretinal surgery) cases. SO may also occur after iridectomy, paracentesis, transscleral cyclodestruction, chemical burns, and helium ion therapy for choroidal melanoma. According to the peer-reviewed literature from the 1990s, one-third of patients with SO eventually became legally blind (visual acuity worse than 6/60 in both eyes). Half of patients had a visual acuity worse than 6/12 in their better eye. The purpose of this study was to analyze the clinical profile and visual outcomes in a series of SO in the current era.

METHODS

We retrospectively analyzed a series of cases of SO treated at our tertiary eye care center between March 2012 and March 2016. Our study adhered to the tenets of the Declaration of Helsinki. SO was defined as any form of bilateral uveitis (not necessarily granulomatous) following penetrating ocular trauma or ocular surgery in a patient with no previous history of uveitis. Other causes of bilateral uveitis, including tuberculosis, were excluded when required by necessary history, examination and relevant investigations.

From the hospital records, a detailed history of trauma, surgery, and duration of symptoms was obtained. Ophthalmological examination findings, fundus images, and results of other investigations like fluorescein angiography (FA), optical coherence tomography (OCT), and B-scan ultrasonography were retrieved. Details of treatment and outcomes were recorded. Follow-up data of patients were collected. All visual acuity measurements were obtained using the Snellen chart and converted to the logarithm of minimum angle of resolution (LogMAR).

We used the following LogMAR values to denote the non-numeric visual acuities: finger counting close to face = 1.7 LogMAR, hand movement = 2.0 LogMAR, light perception = 2.3 LogMAR, and no light perception = 3.0 LogMAR.

RESULTS

Clinical Features

We encountered 14 patients (10 male and 4 female) with SO during the study period. Their ages ranged from 10 years to 48 years, with a median age of 15.5 years.

The insult in the “exciting eye” was trauma in 10 patients, pars plana vitrectomy in 1, therapeutic penetrating keratoplasty (TPK) in 1, conjunctival flap in 1, and evisceration for a painful blind eye in 1 [Table 1].

The time interval between the initial insult and the development of SO was quite variable. It ranged from 2 weeks (patient 8) to 3 years (patient 9), with a mean interval of 33 weeks (± standard deviation [SD], 45.5 weeks) [Table 1]. Patient 8 lost vision in one eye in early childhood (around 10 years back) following a penetrating trauma. This patient developed pain in his blind traumatized eye 10 years after the trauma. He subsequently underwent an evisceration for this painful blind eye. Two weeks after the evisceration, he presented with anterior uveitis in the normal eye. In this case, we considered evisceration, and not the original trauma, as the insult. Thus, the time for the development of SO after the insult was considered as 2 weeks. However, the pain in the right eye may also have been due to a late presentation of SO after the initial trauma, which is usually more severe in the exciting eye and may start earlier than in the sympathizing eye.

Notably, patient 2 had a history of repeated trauma in the same eye. This patient had a penetrating ocular injury of his left eye at 4 years of age with a wooden stick. The patient lost useful vision in the left eye after this injury, but the eye was quiet. He sustained trauma to the left eye again at 11 years of age. SO developed around 11 months after the second trauma. In this case also, we considered the time for development of SO after the second insult as 11 months.

Visual acuity of the sympathizing eye at presentation ranged from the perception of light to 6/6 (mean Snellen equivalent of 6/73) or 2.3-0 LogMAR (mean ± SD, 1.086 ± 0.81 LogMAR). All of our patients regained good vision in the sympathizing eye after treatment 6/6 to 6/60 (0.0-1 LogMAR), with a mean ± SD value of 0.1 ± 0.28 LogMAR and a mean Snellen equivalent of 20/25. Visual acuity of the exciting eye ranged from no perception of light to counting fingers at 3 m (1.3-3 LogMAR) at presentation. Seven of the 14 patients did not appreciate light in the exciting eye, three could just appreciate light, and 2 could count fingers close to the face [Table 2]. Patients 3 and 11 had a presenting visual acuity of 3/60 and 2/60, respectively, in the exciting eye. After treatment of the acute episode, three patients (21.43%; patients 3, 4, and 11) regained useful vision in the traumatized eye, and one (patient 4, who was reported previously) improved to the best-corrected visual acuity of 6/9.

The most common presenting symptom was diminution of distance vision in the sympathizing eye in 11 of the 14 patients (78.5%). Three of the 14 (21.43%) patients presented with redness, pain, and photophobia in the sympathizing eye. In two of the 14 patients (14%; patients 8 and 14), anterior uveitis was noted early during routine outpatient follow-up even prior to the onset of any significant symptoms in the sympathizing eye. All patients had a significant cellular reaction in the anterior chamber with around 4+ cells in the sympathizing eye according to the Standardization of Uveitis Nomenclature working group. Active anterior segment inflammation with anterior chamber cells was also documented in the exciting eye.
Eyes. Anterior chamber cells could be appreciated in all five exciting eyes in which anatomy of anterior segment was maintained (patients 3, 4, 11, 12, and 14) during the acute episode.

Retrolental cells were visible in all of the sympathizing and exciting eyes in which the retrolental space could be assessed (patients 3, 4, 11, 12, and 14). Patient 2 had total cataract and mild-amplitude point spikes in the vitreous on ocular ultrasonography in the sympathizing eye.

Neurosensory detachments [Figures 1a-c] were present in the sympathizing eye of 10 of the 14 patients (71.4%; except patients 2, 8, 11, and 14) at presentation [Table 3]. The exciting eye in patient 3 had multifocal visible neurosensory detachments. Patient 4 had retinal detachment on ultrasonography performed at presentation.

The classically described Dalen-Fuchs nodules were seen on follow-up in the sympathizing eye of only three patients (21.43%; patients 2, 5, and 10), and sunset glow [Figure 1d] was documented in the sympathizing eye of two patients (patients 2 and 10) on follow-up.

Clinically apparent vasculitis was not seen in any patients. Other delayed features, such as optic atrophy, choroidal neovascular membrane, and subretinal

| Table 1. Demographic details of the patients with sympathetic ophthalmia |
|--------------------------|--------------------------|------------------|--------------------------|--------------------------|
| Patient | Age (year) | Sex | Injury/surgery | Interval between injury and presentation | Duration between symptoms to initiation of treatment |
|----------|-----------|-----|----------------|------------------------------------------|------------------------------------------|
| 1        | 25        | Male | Trauma with stone | 2 years | 15 days |
| 2        | 11        | Male | Penetrating trauma with a wooden stick at the age of 4, repeat trauma at the age of 11 | 11 months after the second trauma | 1 month |
| 3        | 25        | Male | 23G pars plana vitrectomy | 1 year | 5 days |
| 4        | 26        | Male | Conjunctival flap | 1 month | 5 days |
| 5        | 16        | Female | Trauma | 8 months | 15 days |
| 6        | 11        | Female | Penetrating trauma with a stick | 2 months | 2 months |
| 7        | 48        | Female | TPK | 6 months | 3 days |
| 8        | 14        | Male | Evisceration | 2 weeks | 1 day |
| 9        | 10        | Male | Globe rupture, (trauma) | 3 years | 2 weeks |
| 10       | 20        | Female | Penetrating trauma | 1 month | 1 month |
| 11       | 20        | Male | Penetrating trauma | 6 weeks | 5 days |
| 12       | 12        | Male | Penetrating trauma | 5 weeks | 2 days |
| 13       | 15        | Male | Penetrating trauma | 7 weeks | 1 week |
| 14       | 12        | Male | Penetrating trauma | 6 weeks | 1 day |

TPK, therapeutic penetrating keratoplasty

Table 2. Visual acuity of patients with sympathetic ophthalmia

| Patient | Presenting visual acuity in the exciting eye in Snellen (LogMAR) | Visual acuity in the exciting eye in Snellen (LogMAR) at the final follow-up | Presenting visual acuity of the sympathizing eye in Snellen (LogMAR) | Visual acuity of the sympathizing eye at the last follow-up in Snellen (LogMAR) | Duration of follow-up |
|---------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|---------------------------------------------------------------|-----------------------|
| 1       | No perception of light (3)                                   | No perception of light (3)                                    | 4/60 (1.2)                                                   | 6/6 (0.0)                                                    | 18 months             |
| 2       | No perception of light (3)                                   | No perception of light (3)                                    | Perception of light (2.3)                                    | 6/60 (1)                                                     | 17 months             |
| 3       | 3/60 (1.3)                                                   | 6/24 (0.6)                                                   | 6/60 (1)                                                     | 6/6 (0)                                                      | 8 months              |
| 4       | Perception of light (2.3)                                   | 6/9 (0.2)                                                    | Hand movements (2)                                           | 6/9 (0.2)                                                    | 24 months             |
| 5       | No perception of light (3)                                   | No perception of light (3)                                    | Hand movements (2)                                           | 6/9 (0.2)                                                    | 48 months             |
| 6       | Perception of light (2.3)                                   | Perception of light (2.3)                                    | 6/24 (0.6)                                                   | 6/12 (0.3)                                                   | 4 months              |
| 7       | No perception of light (3)                                   | No perception of light (3)                                    | Finger counting (1.7)                                       | 6/12 (0.3)                                                   | 8 months              |
| 8       | No perception of light (3)                                   | No perception of light (3)                                    | 6/6 (0)                                                      | 6/6 (0.0)                                                    | 22 months             |
| 9       | No perception of light (3)                                   | No perception of light (3)                                    | 6/9 (0.2)                                                    | 6/6 (0.0)                                                    | 27 months             |
| 10      | Perception of light (2.3)                                   | Perception of light (2.3)                                    | Finger counting (1.7)                                       | 6/18 (0.5)                                                   | 48 months             |
| 11      | 2/60 (1.5)                                                   | 6/18 (0.5)                                                   | 6/6 (0)                                                      | 6/6 (0.0)                                                    | 5 months              |
| 12      | Finger counting (1.7)                                       | Finger counting (1.7)                                       | 2/60 (1.5)                                                   | 6/6 (0.0)                                                    | 8 months              |
| 13      | No perception of light (3)                                   | No perception of light (3)                                    | 6/60 (1)                                                     | 6/6 (0.0)                                                    | 7 months              |
| 14      | Finger counting (1.7)                                       | Finger counting (1.7)                                       | 6/6 (0)                                                      | 6/6 (0.0)                                                    | 6 months              |

LogMAR, logarithm of the minimum angle of resolution
Sympathetic Ophthalmia; Chawla et al

fibrosis, were also not seen in any patients in this series during follow-up.

Ultrawide-field imaging (Optos Inc., Marlborough, MA, USA) was performed in few patients. This modality may be helpful in patients with uveitis, considering the small pupil and media haze. FA was performed in nine patients to confirm the diagnosis. It revealed a classical picture of multiple small hyperfluorescent leaks with late pooling of dye in the neurosensory detachment with disc leakage [Figure 1b]. OCT also demonstrated neurosensory detachments and fluid pockets in the outer retina [Figure 1c], which corroborated with the clinical findings. Although the diagnosis was clinical, multimodal imaging helped in confirming the diagnosis and monitoring treatment response.

Enhanced-depth imaging OCT was performed in two patients and choroidal thickness was noted to be high in the acute phase, which reduced with treatment.

Management

All of our patients were started on topical steroids and cycloplegics to manage the anterior segment inflammation. At our center, we generally initiate the treatment of SO with pulse dexamethasone therapy followed by oral steroids. Nine of our 14 (64.2%) patients were treated with 100 mg intravenous pulse dexamethasone in 250 ml of 5% dextrose once daily for 3 days, followed by oral steroids. Five of the 14 (35.7%) patients were managed with only oral steroids at presentation, as they did not provide consent for pulse dexamethasone therapy.

Oral steroids were started at a dose of 1-1.5 mg/kg body weight and were slowly tapered over 3 to 6 months to a dose less than 10 mg/day. Seven patients (50%) were started on immunosuppressant therapy either due to recurrence of disease activity while the steroids were being tapered (three patients), or because of significant systemic side effects of steroids (three patients), or both (patient 2).

Patient 2 had a total cataract and had been previously diagnosed with SO and was on systemic steroids for the past 8 months. This child had developed significant Cushingoid facies, gained weight, and developed hypertension. The child was slowly tapered off systemic steroids and 10 mg/week of oral methotrexate was started. For early rehabilitation, we performed lens aspiration and intraocular lens implantation (AcrySof IQ SN60WF, Alcon, Texas, USA) under cover of steroids and methotrexate after his anterior chamber reaction subsided. The child regained ambulatory vision and was asymptomatic for 7 months following surgery. However, he developed a recurrence with severe anterior segment inflammation and was treated again with intravenous pulse dexamethasone. Additionally, intraocular lens explantation was performed after control of the acute condition. The child is now stable on maintenance therapy with 15 mg/week of oral methotrexate and low-dose steroids with a best-corrected visual acuity of 6/60 (1.0 LogMAR) for more than 1 year.

Of our 14 patients, seven are stable and in remission (on not more than 7.5 mg prednisolone a day) and seven are on a combination of prednisolone with methotrexate or azathioprine. No patient is completely off therapy. All patients were stable until the last follow-up. A summary of the details of management is given in Table 4.

Side Effects

Follow-up time of patients ranged from 4 months to 48 months, with a mean of 17.8 months. Four patients developed significant Cushingoid facies and two developed hypertension due to systemic steroid use. None of the patients developed any life-threatening systemic side effects with immunosuppressants. Patient 2 had a cataract at presentation, which could be due to long-term topical and systemic steroid use or secondary to the uveitis itself. Patient 10 also developed steroid-induced ocular hypertension and posterior subcapsular cataract while on treatment. These were successfully managed with topical antiglaucoma medications and phacoemulsification, respectively. Azathioprine was stopped in patient 7 as the patient’s liver function test values were elevated. The patient is maintaining remission with low-dose steroid alone and the values have normalized.

Relapse

Patient 2 had one relapse when the steroids were reduced below 10 mg in his 17th month of follow-up.
This was managed by stepping up the steroids and adding methotrexate. The patient is now in remission on a combination of 10 mg prednisolone once daily and 15 mg methotrexate once a week. Patient 9 had one relapse, but as the patient presented early with just anterior uveitis without the involvement of the posterior segment, the patient could be managed by only stepping up the topical steroids. The patient is also stable on 7.5 mg methotrexate once a week and 10 mg prednisolone once daily. Patient 10 has had three relapses in her 48 months of follow-up. This is perhaps due to her poor compliance with azathioprine owing to financial constraints. She is stable on 10 mg prednisolone and 15 mg methotrexate (a cheaper drug than azathioprine) once a week at present.

**Statistical Analysis**

Regression analysis revealed that the presenting visual acuity predicts final visual acuity statistically significantly (multiple R = 0.63; P = 0.01). After excluding patients (patients 8 and 14) who were detected on routine follow-up and did not have obvious symptoms, all other cases who received treatment within 15 days of onset of symptoms, had a final visual acuity of at least 6/12 in the sympathizing eye. Three patients (patients 2, 6, and 10) presented late, and in two of them (patients 2 and 10), the sympathizing eyes had a final vision worse than 6/12. The number of patients was small for any meaningful comparison between the visual outcomes based on the timing of presentation (early vs. late).

## DISCUSSION

Although trauma has been classically considered the main predisposing factor for SO, the number of non-traumatic cases seems to be increasing. This is likely due to an increase in the number of intraocular procedures. Studies report the incidence of SO to range from 0.2% to 0.5% after trauma and 0.01% following intraocular surgery. In the Indian pediatric population (age ≤16 years), one of the studies reported the incidence of SO to be 0.24% in 2511 children with open globe injuries over a period of 10 years. We had eight patients in our case series with age ≤16 years. In the current series, there are four patients (28.57%) who developed SO after ocular injury.
surgery. Patient 7 developed SO after TPK for a perforated fungal corneal ulcer. SO has been previously reported after TPK alone and after TPK with cataract extraction. Another patient (patient 4) developed SO following a conjunctival flap procedure. A recent study reported that 50% of their SO cases developed after ocular surgery.

The incidence is higher with repeated surgical trauma especially vitreoretinal procedures, where the incidence has been quoted up to 1 in 800 vitreoretinal surgeries. As the current study is a case series, we cannot comment on the incidence of SO. In the current case series, one young male patient developed SO after 23G transconjunctival vitrectomy for non-resolving vitreous hemorrhage. Prior to this, there have been other case reports of SO following 23G transconjunctival vitrectomy.

The latent period has been variably shown to be between 5 days to 66 years after trauma. In the current study, the latent period ranged from 2 weeks to 3 years, with a mean period of 33 weeks (nearly 8 months; SD, 45.5 weeks).

One patient (case 8) in this series developed SO following evisceration of a previously traumatized eye. This highlights that the sequestered antigens can be released even years later in elective procedures done with utmost care to remove all uveal tissue. To the best of our knowledge, very few cases of SO after secondary evisceration for a painful blind eye similar to our case have been reported. However, an asymmetric earlier involvement of the exciting eye compared to the sympathizing eye due to late-onset SO secondary to the primary penetrating trauma cannot be excluded in this case. As of today, most ophthalmologists do not prefer primary enucleation as a prophylactic measure as the incidence of SO is quite low and the exciting eye may eventually have a good vision, which may even be better than that of the sympathizing eye. Even in this series of 14 patients, three patients (patients 4, 11, and 13) regained a visual acuity of 6/9, 6/18, and 6/24, respectively, in the exciting eye after the control of inflammation. Most authors agree that there is no role for enucleation after the onset of SO.

In this study, most patients presented with symptoms of uveitis and loss of vision. All patients had a significant cellular reaction in the anterior chamber. Ten of the 14 patients also manifested neurosensory detachments. Twelve patients had panuveitis and not an isolated posterior presentation. This is in contrast to that of a study on SO by Gupta et al. wherein they found 22 out of 40 eyes had only fundus lesions and no anterior segment inflammation. In contrast, two of our patients presented with isolated anterior uveitis, which was

| Patient | Intravenous pulse dexamethasone | Immunosuppressant | Maintenance therapy | Surgical intervention |
|---------|---------------------------------|-------------------|---------------------|----------------------|
| 1       | ✓                               | ✗                 | Prednisolone 5 mg OD| Lens aspiration       |
| 2       | ✓                               | Methotrexate 15 mg weekly | Prednisolone 10 mg OD Methotrexate 15 mg weekly | Pars plana vitrectomy Intraocular lens explantation |
| 3       | ✓                               | ✗                 | Prednisolone 5 mg OD| Silicone oil removal and cataract surgery in the vitrectomized eye |
| 4       | ✓                               | Azathioprine 100 mg OD | Azathioprine 100 mg OD Prednisolone 10 mg OD | Nil |
| 5       | ✓                               | Methotrexate 15 mg weekly | Methotrexate 5 mg weekly Prednisolone 5 mg OD | Nil |
| 6       | ✓                               | Methotrexate 7.5 mg weekly | Methotrexate 7.5 mg weekly Prednisolone 10 mg OD | Nil |
| 7       | ✓                               | Azathioprine 100 mg OD | Prednisolone 7.5 mg OD | Nil |
| 8       | ✗                               | ✗                 | Prednisolone 5 mg OD | Nil |
| 9       | ✗                               | Methotrexate 7.5 mg | Methotrexate 7.5 mg weekly Prednisolone 10 mg OD | Nil |
| 10      | ✓                               | Azathioprine 100 mg (defaulter) Methotrexate 25 mg | Methotrexate 15 mg weekly Prednisolone 10 mg OD | Phacoemulsification |
| 11      | ✗                               | ✗                 | Prednisolone 5 mg OD | Nil |
| 12      | ✗                               | Prednisolone 2.5 mg OD | Prednisolone 2.5 mg OD | Nil |
| 13      | ✓                               | ✗                 | Prednisolone 5 mg OD | Nil |
| 14      | ✗                               | ✗                 | Prednisolone 5 mg OD | Nil |

OD, once daily
detected early in routine follow-up of the other eye after surgery (namely evisceration and perforation repair) and were subsequently treated for SO. In the present series, isolated anterior uveitis was found at the time of relapse in one patient (patient 9). This was detected very early on follow-up and was treated appropriately before it progressed to panuveitis. All patients who received treatment within 15 days of onset of symptoms achieved a visual acuity of 6/12 or better. This reinforces the fact that prompt diagnosis and treatment result in better visual outcomes in patients with SO. At the final follow-up, 12 of 14 (85.7%) sympathizing eyes achieved a visual acuity of 20/40 or better and three exciting eyes achieved a visual acuity of at least 6/24. In a recent report, Payal and Foster reported that around 13 of 19 patients (68.4%) maintained at least 20/50 visual acuity in the sympathizing eye with a minimum follow-up of 2.5 years and a median follow-up of 7.1 years. Galor et al. reviewed the reports of 85 patients with SO. Around 60% of sympathizing eyes in this series maintained a visual acuity of at least 20/50 and 75% maintained a visual acuity better than 20/100. Four patients (patients 8, 9, 11, and 14) in the current series had a visual acuity of 6/9 or better at presentation, of whom two (patients 8 and 14) did not have any posterior segment involvement. Thus, we reiterate that a vigilant examination can pick up such patients early, enabling prompt management before the patients begin to lose vision. We treated the acute panuveitis due to SO by using pulse dexamethasone, as it is cheaper than methylprednisolone and has good safety and efficacy in ocular inflammatory disorders. Five patients received only oral steroids at presentation.

Limitations of this study include the small sample size and limited duration of follow-up. Moreover, controversies exist as to whether the visual acuity of light perception or no light perception can be quantitated.

An early diagnosis with appropriate immunosuppressive therapy led to a good visual outcome in all patients. This could be attributed to the fact that most of the patients (nine of 14) were started on treatment early, i.e., within 15 days of onset of symptoms (mean, 13.8 days; range, 1-60 days). The main issue in managing these patients is that they require a very long term, perhaps even a lifetime, of immunosuppression to maintain remission. Thus, it is recommended that ophthalmologists treating such patients have a good knowledge about the use of these drugs. Owing to financial constraints and a high risk of tuberculosis in our country, we did not start any of our patients on biologic therapy.

Early recognition of SO with rapid institution of therapy and further titration of the dosage of immunosuppressive agents to minimize side effects is the key to success in the management of this blinding disease.

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Conflicts of Interest
There are no conflicts of interest.

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