Clinical Features of Sympathetic Ophthalmia in a Tertiary Referral Center in Thailand

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ABSTRACT

Background: Sympathetic ophthalmia is a rare bilateral granulomatous intraocular inflammation, developed after ocular injury in one eye. If untreated, there is a potential risk of developing visual impairment in both eyes. An awareness of this disease is crucial. Studies related to clinical characteristics, treatment outcomes and disease complications would help us more understand about the disease and visual prognosis.

Objective: To report clinical features of sympathetic ophthalmia and potential ocular complications of the disease.

Methods: This study was a descriptive retrospective study. Medical records of patients who were diagnosed with sympathetic ophthalmia at Siriraj Hospital between January 2006 and January 2015 were reviewed. Patient's demographic data, history and details of ocular injuries or surgeries, details of ocular examinations, follow up duration and treatment outcomes were recorded.

Results: Twenty-three sympathetic ophthalmia patients were found. Eighteen patients (78.3%) had histories of ocular trauma and 5 patients (21.7%) had histories of ocular surgery. Duration between ocular injuries and onset of intraocular inflammation ranged from 24 days to 50 years. No associated risk factors of developing sympathetic ophthalmia were identified due to incomplete data and small sample size. The most common complication was secondary glaucoma. There were wide varieties of treatment regimen. Some patients were treated with only corticosteroid eye drops, whereas some patients were treated with systemic corticosteroids and/or immunosuppressive medications. Most patients (17/23; 74%) had visual improvement on their last visit.

Conclusion: Early diagnosis, early detection of disease complications and early initiation of proper treatments can alter disease prognosis and visual outcome in most patients.

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Keywords: Sympathetic ophthalmia; granulomatous; panuveitis; anterior uveitis; ocular injury
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INTRODUCTION

Sympathetic ophthalmia (SO) is a rare bilateral granulomatous panuveitis developed following ocular injuries or ocular surgeries in one eye.[1,2] The injured eye or exciting eye was believed to aggravate the immune system by an unknown intraocular antigen after break down of the blood-ocular barrier. The fellow eye or sympathizing eye was also affected by immune processes and developed intraocular inflammation since it shared the same self-antigen.[3,4] The study from the UK and Republic of Ireland in the year 2000 reported a low incidence of SO at 0.03 per 100,000[5] in contrast to previous

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reports in which incidences ranged from 0.1-0.3% following ocular traumas[6-8] and 0.02% following ocular surgeries.[9] Visual prognosis in sympathizing eye was concerned because of a potential to cause blindness. We aimed to report clinical features and their potential ocular complications in patients with SO.

MATERIALS AND METHODS

This study was a 10-year retrospective charts review of SO patients at Siriraj Hospital, Mahidol University, Thailand between January 2006 and January 2015. We included both newly diagnosed patients and known cases of SO patients who visited our hospital during that period. Patients must have had either a history of ocular surgery or ocular trauma in at least 1 eye prior to the development of intraocular inflammation. For SO, it does not have diagnostic criteria so we made the diagnosis based on clinical presentations of bilateral granulomatous panuveitis, which could present as an acute phase of the disease with granulomatous panuveitis, with or without exudative retinal detachment, optic nerve head swelling, choroidal infiltrates, choroidal thickening and multifocal area of leakage on fluorescein angiography, chronic phase with choroidal depigmentation, optic nerve atrophy, or chronic recurrent phase with bilateral granulomatous anterior uveitis. Demographic data, which were age of onset and gender, were recorded. Mode of injury was divided into ocular injury (including both penetrating injury and blunt trauma) and ocular surgery. For ocular injury group, we collected the date of ocular injury, date of primary repair (if primary repair was necessary), uveal tissue prolapse, and pathological reports (if the patients underwent either enucleation or evisceration with the date that these procedures were performed). For ocular surgery group, we collected the date when the procedures were performed, type of ocular surgery such as phacoemulsification with intraocular lens implantation, extracapsular cataract extraction, or pars plana vitrectomy. Details of ocular examinations on the day that SO was diagnosed were recorded which were initial best corrected visual acuity (BCVA) in excited eye and sympathizing eye, anterior chamber cells grading according to standardization of uveitis nomenclature[10], fundus abnormalities (exudative retinal detachment, optic disc edema, peri-retinal vascular infiltrates, choroidal depigmentation or sunset glow fundus), choroidal thickening on B-scan ultrasonography, multiple leakage on fluorescein angiogram, and multifocal dark dots on indocyanine green angiogram. Ocular complications on sympathizing eyes such as band keratopathy, complicated cataract, secondary glaucoma, or pthisis bulbi were recorded. Treatments were recorded as route of corticosteroids administrations, date when systemic corticosteroids was started and discontinued and in some cases; immunosuppressive therapy and its complications. BCVA in both eyes on their last visit to Siriraj Hospital was also recorded. This study has already been approved by Siriraj Institutional Review Board (Si 567/2558).

RESULTS

There were a total of 23 SO patients who were seen at Siriraj Hospital between January 2006 and January 2015. Eighteen patients (78.3%) were male and 5 patients (21.7%) were female. Age at onset ranged between 15-83 years (median 44 years). Eighteen patients (78.3%) had histories of ocular trauma {penetrating injuries 12/19 (63.2%), blunt ocular injury 1/19 (5.3%) and the rest 5/19 (26.3%) data were not available} and 5 patients (21.7%) had previous ocular surgeries {1/5 (20%) underwent phacoemulsification, 1/5 (20%) underwent extracapsular cataract extraction, 1/5 (20%) underwent 20 guage pars plana vitrectomy, 1/5 (20%) underwent combined phacoemulsification with pars plana vitrectomy (unavailable surgical details), and 1/5 (20%) had triple operation}. For patients who had penetrating ocular injury10/12 (83.3%) had primary wound repaired, but most medical records were incomplete because most of our patients were referred from other hospitals, only 2 medical records indicated that 1 of them had primary repair 1 day after the accident and 1 patient had primary repair 14 days after the injury. One patient (1/18; 5.55%) had uveal tissue prolapse, one had no prolapsed uveal tissue, but for 16/18 (88.9%) data were not available. Duration since the patients had ocular traumas until developing SO ranged from 24 days to 50 years. Only 1 patient (5.55%) had enucleation and it was done more than 2 weeks after the accident. BCVA in excited eye in ocular injury group ranged from 6/60 to no perception of light and BCVA in sympathizing eyes ranged from 6/6 to light projection. Presence of anterior chamber cells at least 1+ were found in 13/18 patients (72.2%) while only 3/18 patients (16.7%) had anterior chamber cells less than 1+ and 2/18 patients (11.1%) data were not available. Fundus examination of 13/18 traumatized patients (72.2%) revealed fundus abnormalities {acute phase 7/13 patients (53.8%) and convalescent phase 6/13 patients (46.2%)}, 4/18 patients (22.2%) had no posterior eye segment involvement, and 1/18 patient (5.6%) had no data. Choroidal thickening was determined by B-scan ultrasonography, in ocular injury group and 12/18 patients had ultrasonography done. Choroidal thickening was detected in 7/12 patients

(58.3%), whereas 5/12 patients (41.7%) had no choroidal thickening detected on ultrasonography. For patients who were found to have choroidal thickening, 2/7 (28.6%) had fundus findings compatible with convalescent phase and 4/7 (57.1%) were compatible with acute phase, and 1/7 (14.3%) was indeterminate. Patients who had no choroidal thickening detected presented with acute uveitic phase for 2 patients (40%) and convalescent phase for 3 patients (60%). Fluorescein angiogram was done in 5 traumatized patients. Four patients who presented with acute intraocular inflammation had multifocal leakage, and one who presented with convalescent phase had no abnormality found in fundus fluorescein angiogram. Only one patient in this study had indocyanine green angiography done during the convalescent phase and the result was unremarkable. For ocular surgery group, duration between the surgeries until onset of inflammation ranged from less than 1 month to 14 years. BCVA in excited eye was 6/240 in 1 patient (1/5; 20%) and 4/5 patients (80%) had no light perception. BCVA in sympathizing eyes ranged from 6/12 to light projection. None of the patients in this group had anterior chamber cells more than 1+. All of the patients in this group had fundus abnormalities, 2/5 (40%) presented with acute uveitic phase and 3/5 (60%) presented with convalescent phase. Only 2/5 patients (40%) had B-scan ultrasonography done and both of them were found to have choroidal thickening (1 presented with acute phase and 1 presented with convalescent phase). Fundus fluorescein angiogram and indocyanine green angiogram were not done in all of these patients. Ocular complications in sympathizing eye were summarized in Table 1. Treatments included systemic corticosteroids in 20/23 patients (87%) and immunosuppressive medications 12/23 patients (52.2%). There were 2 patients (8.7%) who were treated with purely topical corticosteroids.

Details of initial and final BCVA, follow up duration, number of systemic medications, and treatment outcomes on their last visit are shown in Table 2.

TABLE 1. Number of ocular complications in sympathizing eyes in ocular injury group and ocular surgery group.

Complications	Ocular injury group (n=18)	Ocular surgery group (n=5)
Glaucoma	6 (33.3%)	2 (40%)
Complicated cataract	3 (16.7%)	2 (40%)
Retinal detachment	2 (11.1%)	0
Band keratopathy	2 (11.1%)	0
Choroidal neovascularization	0	1 (20%)
Optic atrophy	1 (0.6%)	0
Pthisis bulbi	1 (0.6%)	0

DISCUSSION

SO is considerably rare. Our hospital is a university-based referral center, but there were only 23 patients found in 10 years. Thus, statistical analysis was impossible and associated risk factors of developing SO were unable to be identified. Although SO rarely occurs, the importance is the disease itself can aggravate intraocular inflammation aggressively in both eyes. Patients can lose their sight permanently and become legally blind. Most of our patients developed SO after ocular trauma. However, some reports indicated that incidence of SO was increasing after ocular surgery especially retinal surgery.[11, 12] The indication of early enucleation to prevent SO is controversial.[2] The benefit of early enucleation of injured eye in this study was also unable to evaluate since we had no data of patients who had a history of ocular trauma, but had no SO to compare. Sen et al., reported that the factors most often associated with decreased vision were active inflammation, cataract, and optic nerve abnormalities.[2] Like our study, the most common ocular complication in sympathizing eye was glaucoma and the second most common complication was cataract, which the latter was curable. Median duration from ocular injury/surgery to onset of ocular inflammation in this study was 7 years, which differed more from previous reports that 80% of SO developed within 3 months after injuries.[13] In this study we had to estimate date of ocular injury/surgery and the date when ocular inflammation began in some

TABLE 2. Best corrected visual acuity (BCVA*) in sympathizing eyes at presentation and on their last visit at Siriraj Hospital. The first 5 patients developed SO after ocular surgery and the rests had previous ocular trauma. This table also named systemic medications that each patient had ever received. Some were in remission on their last visit but some were recalcitrant to therapies.

No.	BCVA* at presentation	BCVA at last visit	Follow up duration	Systemic Medications	Subsided inflammation on last visit
1	Fc † ½ ft	6/6	2yr 3mo	Steroids, CYP ||	Yes
2	PJ ‡	6/36	4 yr 1mo	Steroids	Yes
3	Fc 1 ½ ft	6/120	6mo	-	No
4	6/48	6/38	3yr 4mo	Steroids, MTX ¶, AZA**, MMF ††	Yes
5	6/19	6/9	5yr 9mo	Steroids	Yes
6	Fc 2ft	6/12	1yr	Steroids, CYP, Chlorambucil	No
7	6/48	6/48	6mo	Steroids, AZA	No
8	6/60	6/7.5	6yr	Steroids	Yes
9	6/9	NPL §	13yr	Steroids, CSA ††, pulse CYP	No
10	Fc 1ft	6/60	2yr 6mo	Steroids, CSA, CYP	Yes
11	PJ	NPL	2mo	Steroids	No
12	Fc 1ft	1 visit	1 visit	-	No
13	PJ	6/9.5	5yr 6mo	Steroids	Yes
14	6/9	6/6	6yr 11mo	Steroids, AZA	Yes
15	6/24	6/12	3mo	Steroids	Not available
16	6/192	6/7.5	4yr 4mo	Steroids, MTX, AZA	Yes
17	Fc 1ft	6/60	12yr 10mo	Steroids, CYP, chlorambucil	Yes
18	6/152	6/24	3yr 1mo	Steroids, AZA, chlorambucil	Yes
19	6/24	6/9.5	1mo	-	Yes
20	6/6	6/9.5	5yr 5 mo	Steroids, CSA, CYP	Yes
21	6/18	6/6	2yr	Steroids, CYP	Yes
22	Fc ½ ft	1 visit	1 visit	Steroids	Yes
23	6/12	6/7.5	7yr 1mo	Steroids	No

Abbreviations: Fc† = Finger counting, PJ‡ = projection of light, NPL§ = no perception of light, CYP|| = cyclophosphamide, MTX¶ = methotrexate, AZA** = azathioprine, MMF†† = mycofenolate mofetil, CSA‡‡ = cyclosporine A.

cases. This might have caused unreliable data and probably partially explained why our result was so different from other studies. We found that most of our patients had visual improvement in the sympathizing eye even though our patients received different treatment regimens. As many patients as 17/23 patients (74%) had visual improvement on their last follow up visit. One patient (4.3%) had stable BCVA and 3/23 patients (13%) had worse BCVA on their last visit. For patients who experienced worse visual outcomes, one was recalcitrant to therapy with pulse cyclophosphamide, oral cyclosporine and prednisolone, one had poor visual prognosis since the beginning and had visual deterioration from light projection to no light perception, and one had insignificant change

in vision from 6/6 to 6/9.5. Two patients visited our hospital only once. Interestingly, as many as 5 patients (21.7%) required systemic corticosteroids alone without any immunosuppressive medication to control their ocular inflammation and 1 patient (4.3%) required solely short-term topical corticosteroids. This was in contrast with some previous reports, in which most of their patients who were diagnosed with SO required systemic immunosuppressive medication.[14] For patients who presented with mild degree of anterior segment inflammation without active choroidal inflammation, steroid eye drops can be considered as a mainstay therapy. This is in contrast with patients who present with panuveitis, which warrants systemic medication. Stepladders approach can be considered in this situation. High dose systemic corticosteroids (such as 1 MKD of oral prednisolone or 1 g of pulse methylprednisolone infusions) which are gradually tapered can probably adequately control ocular inflammation in some patients without systemic immunosuppressant. From this study, we would like to presume that early diagnosis and appropriate treatment with corticosteroids and/or immunosuppressive therapy would improve visual outcome in sympathizing eye. Further study with a larger number in the study-group would be beneficial.

CONCLUSION

Sympathetic ophthalmia is treatable. Proper treatment can improve visual outcome in sympathizing eye. Early detection with prompt management to control intraocular inflammation and prevent further ocular complications can alter disease prognosis.

Limitations

This study has a lot of limitations due to the nature of a retrospective study. It has small sample size and it was limited by missing data and variable duration of follow up. Statistical analysis to evaluate associated risk factors of developing SO, treatment outcomes and visual prognosis was impractical.

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Conflict of interests

All authors declare no conflicts of interests.

REFERENCES

1. de la Fuente MA, Alejandre N, Ferrer P, Fernandez G, Sarasa JL, Sanchez O. Sympathetic ophthalmia in HIV infection. A clinicopathological case report. J Ophthalmic Inflamm Infect 2012;2(3):161-4.
2. Sen HN, Nussenblatt RB. Nussenblatt, Sympathetic ophthalmia: what have we learned? Am J Ophthalmol 2009;148(5):632-3.
3. Guzman-Salas PJ, Serna-Ojeda JC, Guinto-Arcos EB, Pedroza-Seres M. Characteristics of Sympathetic Ophthalmia in a Single International Center. Open Ophthalmol J 2016;10:154-9.
4. Aziz HA, Flynn HW Jr, Young RC, Davis JL, Dubovy SR. Sympathetic ophthalmia: Clinicopathologic Correlation in a Consecutive Case Series. Retina 2015;35(8):1696-703.
5. Kilmartin DJ, Dick AD, Forrester JV. Prospective surveillance of sympathetic ophthalmia in the UK and Republic of Ireland. Br J Ophthalmol 2000;84(3):259-63.
6. Allen JC. Sympathetic ophthalmia, a disappearing disease. JAMA 1969;209(7):1090.
7. Liddy L, Stuart J. Sympathetic ophthalmia in Canada. Can J Ophthalmol 1972;7(2):157-9.
8. Kraus-Mackiw E, Müller-Ruchholtz W. Sympathetic eye diseases: diagnosis and therapy. Klin Monbl Augenheilkd 1980;176(1):131-9.
9. Gass JD. Sympathetic ophthalmia following vitrectomy. Am J Ophthalmol 1982;93(5):552-8.
10. Jabs DA, Nussenblatt RB, Rosenbaum JT; Standardization of Uveitis Nomenclature (SUN) Working Group. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J Ophthalmol 2005;140(3):509-16.
11. Chan CC, Roberge RG, Whitcup SM, Nussenblatt RB. 32 cases of sympathetic ophthalmia. A retrospective study at the National Eye Institute, Bethesda, Md., from 1982 to 1992. Arch Ophthalmol 1995;113(5):597-600.
12. Kilmartin DJ, Dick AD, Forrester JV. Sympathetic ophthalmia risk following vitrectomy: should we counsel patients? Br J Ophthalmol 2000;84(5):448-9.
13. Marak GE Jr. Recent advances in sympathetic ophthalmia. Surv Ophthalmol 1979;24(3):141-56.
14. Patel SS, Dodds EM, Echandi LV, Couto CA, Schlaen A, Tessler HH, et al. Long-term, drug-free remission of sympathetic ophthalmia with high-dose, short-term chlorambucil therapy. Ophthalmolog. 2014;121(2):596-602.