Case Report

SURGICALLY INDUCED SCLERITIS: A CASE SERIES

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ABSTRACT

Surgical induced scleritis (SIS) is a potentially devastating complication following ocular surgeries. The objective of this case study was to review the clinical experience of SIS at Hospital Selayang. A retrospective observational case series review of SIS cases at Hospital Selayang from year 2008 to 2017. The result found that there were 13 patients with age ranging from 38 to 78 years old. Four patients (30.8%) had glaucoma filtering surgery, three (23.1%) had pterygium excision, three (23.1%) had scleral buckling and cryotherapy, two (15.4%) had cataract extraction and one (7.7%) had vitrectomy as the initial ocular surgery prior to onset of SIS. Majority (53.8%) had history of multiple ocular procedures. Necrotising scleritis was the commonest subtype. Eight patients (61.6%) achieved vision of ≥6/24. Four patients (30.8%) had vision of ≤6/60. In conclusion, SIS may have favourable visual prognosis when treated accordingly. Intraoperative cytotoxic agent usage in ocular surgeries should be with extreme care due to risk of SIS.

INTRODUCTION

Despite its rarity, surgical induced scleritis (SIS) is distressing and has been observed following a variety of ocular procedures such as glaucoma filtering surgery, cataract extraction ,pterygium excision, retinal detachment surgery, penetrating keratoplasty and strabismus surgery [1-9]. While immune mediated scleritis is quite commonly reported in patients with coexisting systemic illness like rheumatoid arthritis and other vascular collagen disorders and may occur in this group of patients after surgery, we report SIS in patients without any known underlying systemic vascular collagen diseases. This condition requires early recognition and prompt effective treatment with non-steroidal anti-inflammatory drugs (NSAIDs) and immunosuppressive agents to prevent dreadful sequelae of loss of vision. Surgical induced necrotising scleritis (SINS) is a severe form of SIS Various etiological mechanisms, disease patterns, treatment administered, and visual outcomes is presented in this case series review.

METHODOLOGY

This is a retrospective case series over a 9-year period between 1st January 2008 and 31st December 2017. Electronic medical records of all patients who were diagnosed and treated as SIS in Ophthalmology clinic, Selayang Hospital between the period stated were retrospectively reviewed, which included a total of 16 eyes from 16 patients. Thirteen eyes met the study criteria and thus included in this study. Scleritis was diagnosed clinically on the basis of a painful red eye with associated photophobia and blurring of vision. Surgical induced diffuse scleritis type was recognized by the presence of inflamed scleral tissue with congested deep episcleral vascular plexus usually adjacent to operative wound [4,10]. Surgical induced necrotizing scleritis type was identified by the presence of a localized patch of scleritis associated with acute congestion, avascular overlying episcleral tissue or scleral necrosis in advanced disease[10]. Finally, posterior scleritis type demonstrated presence of mainly posterior segment involvement such as choroidal detachment or effusion, exudative retinal detachment or disc edema; with the absence of marked anterior scleral involvement [11]. Depending on the severity of each condition, all of the above conditions portrayed clinical improvement either with non-steroidal anti-inflammatory drugs (NSAIDs), topical or oral corticosteroids with or without second-line immunosuppressive therapy. Demographic data, number and type of ocular surgeries performed, onset and clinical manifestation of disease, treatment modalities and visual acuity were collected and documented. Patients with evidence of infectious post-operative scleritis, known or newly diagnosed collagen vascular disease or autoimmune diseases or incomplete documentation were excluded from this case review.

RESULTS

There were 13 patients involving 13 eyes in this study, with age at diagnosis ranging between 34 to 78 years old. There were nine males (mean age 56 years) and four females (mean age 78.5 years) affected. All patients had unilateral eye involvement. None of them had history of scleritis prior to surgery (Table 1).

In this case series, the mean interval between initial surgery to onset of SIS was 75.5 months (ranged five - 144 months). Four patients (30.8%) had glaucoma filtering surgery, three (23.1%) had pterygium excision, three (23.1%) had scleral buckling and cryotherapy, two (15.4%) had cataract extraction and one (7.7%) had vitrectomy as the initial ocular surgery done before occurrence of SIS (Table 2). Of the 13 eyes, seven (53.8%) had history of multiple ocular procedures (Table 3).

Most patients showed necrotising scleritis pattern which was identified in seven eyes (53.8%). The rest of the patients demonstrated either diffuse anterior scleritis (23.1%) or posterior scleritis (23.1%) (Table 4). Except from three patients (all males; two had necrotising scleritis; one had diffuse anterior scleritis), all other patients were screened and negative for autoimmune or connective tissue diseases.

We observed a variety of ocular surgical procedures which preceded the onset of necrotising scleritis in our patients (Table 4). Patients presented with a range of symptoms included eye redness, pain and some had reduced vision. In all patients, the site of scleral necrosis was intimately related to the previous surgical incision site. All patients were treated with immunosuppressive therapy (topical and oral prednisolone), however four out of seven (57.%) required second line

Table 1: Demographic data of patients.

Demography	Number of patients (n=13)
Gender	
Male	9
Female	4
Eye involvement	
Unilateral	13
Bilateral	0
Age (years)	
Range	Male (34-78) Female (44- 69)
Mean	Male (56) Female (78.5)

Table 2: Onset and cases of SIS by types of ocular surgery.

Types of Ocular Surgery	Number of eyes n=13 (%)	Onset of SIS* months (mean)
Glaucoma Filtering Surgery	4 (30.8)	5-26 (15.5)
- Trabeculectomy with MMC**	3 (23.1)	6-26 (16)
- Glaucoma Drainage Device	1 (7.7)	5
Cataract Extraction	2 (15.4)	49-84 (66.5)
- Phaco converted ECCE/ACIOL***	1 (7.7)	49
- ICCE/Scleral Fixated IOL****	1 (7.7)	84
Pterygium excision	3 (23.1)	60-144 (102)
- with MMC**	2 (15.4)	108-144 (126)
- unknown usage of MMC**	1 (7.7)	60
Scleral buckle/ Cryotherapy	3 (23.1)	5-24 (14.5)
Pars plana vitrectomy	1 (7.7)	19

* surgical induced scleritis
** mitomycin-C
*** anterior chamber intraocular lens
**** intraocular lens

Table 3: Number of ocular procedures prior to SIS

Single Procedure (n=6)
3 – pterygium excision
1 – trabeculectomy
1 – scleral buckle/ cryotherapy
1 - cataract extraction
Multiple Procedures (n=7)
2 - multiple glaucoma filtering surgeries
1 – cataract extraction followed by trabeculectomy
1 – cataract extraction followed by scleral buckle/ cryotherapy
1 – multiple retinal detachment repair surgeries
1 – vitrectomy followed by cataract extraction
1 – complicated cataract extraction (phaco converted ECCE*/ anterior vitrectomy/ ACIOL**)

* phacoemulsification converted extracapsular cataract extraction
** anterior chamber intraocular lens

Table 4: Clinical manifestations of SIS.

	Diffuse	**Necrotising**	**Posterior**
Number of eyes, n (%)	3 (23.1)	7 (53.8)	3 (23.1)
Prior ocular surgery, (n)	(1) Cataract extraction (1) Trabeculectomy/ MMC (1) Vitrectomy	(2) Pterygium/MMC (1) Pterygium/unknown MMC (1) Scleral buckle/ cryotherapy (1) Cataract extraction (1) Scleral buckle/ cryotherapy followed by vitrectomy (1) Cataract extraction followed by scleral buckle/ cryotherapy	(2) Multiple glaucoma filtering surgeries/ MMC (1) Cataract extraction followed by trabeculectomy/ MMC
Second line therapy, n (%)	0 (0)	4 (57.1)	2 (66.7)
Visual outcome, n (overall %)			
≥6/24	2 (15.4)	5 (38.5)	1 (7.7)
6/36- 6/60	-	-	1 (7.7)
<6/60	1 (7.7)	2 (15.4)	1 (7.7)

immunosuppression (Methotrexate or Azathioprine) to control disease activity. With appropriate treatment, most (71.4%) had good visual outcome of 6/24 or better. One patient had vision of counting finger at 2 feet due to progression of underlying glaucoma. Another patient who underwent pterygium excision with mitomycin C (MMC) experienced a more severe form of scleritis whereby he had scleral necrosis with microperforation requiring lamellar grafting alongside second line immunosuppressive therapy. He had two episodes of disease reactivations while on tapering dose of oral prednisolone 7.5mg daily. Disease control was achieved after 15 months of initial diagnosis with Methotrexate 10mg weekly while maintaining long-term low dose of oral prednisolone 5mg daily. Despite treatment, he had poor final visual outcome of counting finger at 2 feet attributed by dense cataract and maculopathy secondary to age-related macular disease. Full autoimmune and connective tissue workup which consisted of erythrocyte sedimentation rate (ESR), antinuclear antibody (ANA), viral and syphilis serology, Mantoux and chest X ray test results were not significant for this patient. Figure 1 shows anterior segment photos of patients with necrotising scleritis.

Posterior scleritis was observed in three patients. Apart from typical symptoms of eye pain and redness, patients significantly complained of deterioration of vision. All three patients demonstrated signs of posterior scleral

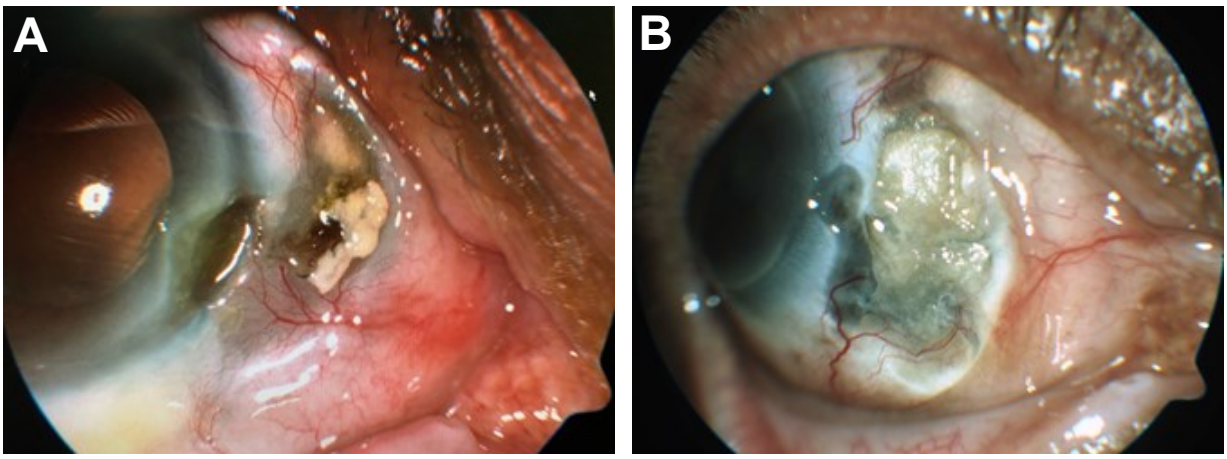

Figure 1: (A, B) Anterior segment photo of two patients with focal area of scleral necrosis with adjacent inflammation following pterygium excision with mitomycin C usage.

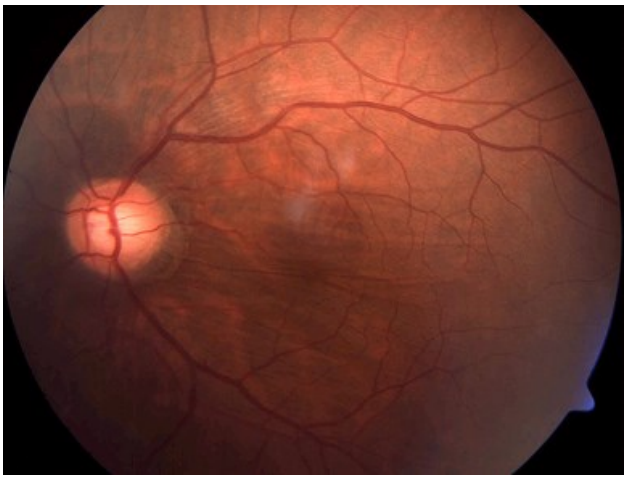

Figure 2: Chorioretinal folds in a patient with posterior scleritis.

inflammation such as choroidal detachment, thickening of sclera (all had more than 1.8mm scleral thickness), chorioretinal folds and presence of fluid in subtenon space (T- sign) which were evident on B scan ultrasonography. Patients showed more aggressive disease spectrums whereby two patients experienced multiple episodes of disease reactivations upon oral prednisolone tapering, despite early addition of second-line immunosuppression. One patient had light perception only vision during her last review. She had two trabeculectomy with MMC and one glaucoma drainage device implantation surgery performed prior to the onset of posterior scleritis. She was treated with topical and oral prednisolone (at dose of 1mg/kg daily with subsequent tapering) for about two months duration during the first episode of scleritis. Azathioprine was added subsequently when her disease recurred after three months of immunosuppressive free period. Unfortunately, due to low absolute lymphocyte count (0.5x109/L) Azathioprine was later withheld. During one of three episodes of disease reactivations, intravenous methylprednisolone was required to control the disease. Nevertheless her disease progressed with development of appositional (kissing) choroidals. Her eye later became phthisical with visual acuity of only light perception. Figure 2 shows a patient with posterior scleritis with chorioretinal folds.

Diffuse type of post-operative scleritis showed a more benign spectrum of disease. This was seen in three patients in which disease activities were adequately controlled using oral non-steroidal anti-inflammatory drugs (NSAIDs) and topical prednisolone only. All patients experienced ocular redness and pain and clinically diffuse scleral inflammation adjacent to site of previous surgical wound were observed. One patient had the characteristic severe pain which awakened him from sleep. Anterior chamber activity was documented in two of the patients. Nevertheless patients with diffuse anterior scleritis showed generally milder course of illness and had good visual outcome. Only one patient documented poor vision of hand movement due to pre-existing myopic maculopathy.

DISCUSSION

Glaucoma filtering surgery has shown to be the leading cause of surgical induced scleritis (SIS) in our centre likewise previously reported [12]. Mean

time to presentation from surgery has been reported as 9 months ranging from day one to 40 years by others [6,12]. However, in our case series, the onset of disease ranged from 5 months to 12 years (144 months) post initial surgery, with glaucoma filtering surgery showing the earliest onset of scleritis. Interestingly in our case series, post-operative scleritis involved more male patients. E O'Donoghue at al documented predominance of females patients (70%) and linked it to the increased associations of autoimmune diseases in this group of patients [6]. Contrary, we excluded patients with autoimmune or collagen vascular diseases thus similar observations were not observed. Majority of patients (53.8%) had history of multiple ocular procedures which were consistent with reports from previous authors[6,14]. An increased number of ocular procedures have previously been associated with higher incidence of SIS, similarly seen in our study.

In our centre, most patients demonstrated necrotising scleritis pattern followed by diffuse anterior scleritis and posterior scleritis [6,15]. Necrotising scleritis is a rare but possible sequalae of ocular surgery. Despite its rarity, this subtype of scleritis is the commonest to be associated with following surgical procedures [6,14]. Surgical induced necrosting scleritis (SINS) represents a more severe form of disorder requiring early aggressive immunosuppression to control disease activity and reduce ocular complications [16]. Extensive sclera destructions and necrosis may warrant prolonged, potentially hazardous immuno-suppressive therapy requirement in some patients [17]. More aggressive disease can present with scleral thinning and perforation necessitating lamellar graft which was done in 1 of our patients. Another patient recorded poor vision due to underlying glaucoma which made worst by the use of prolonged immunosuppressive medications. Our findings showed that good visual outcome was achievable by most patients with SINS hence proving that early diagnosis and prompt treatment results in good visual outcome [1]. On the other hand, diffuse anterior scleritis represents a more benign and self-limiting condition, where treatment with oral non-steroidal anti-inflammatory drugs (NSAIDs) adequately controlled disease activity [4,17]. These observations were seen in all of our patients diagnosed with diffuse anterior scleritis whereby they showed milder spectrum of disease which completely responded to oral NSAIDs. Posterior scleritis more often carried a poorer visual prognosis despite optimal management instituted [16,17]. Similarly to necrotising scleritis, patients often require systemic corticosteroid with or without second line immunosuppression in the form of immunomodulating agents (Azathioprine, Methotrexate, Mycophenolate Mofetil) to achieve disease control [18]. Posterior scleritis carries most threat to vision due to the involvement of the retina, choroid and optic disc [17]. In our patients, only one third of patients with posterior scleritis achieved vision of 6/24 or better. Recurrences in SIS are not uncommon and were seen in our patients particularly in the necrotising and posterior scleritis subtypes[14].

The precise underlying mechanism of SIS remains unknown to date. As proposed by Watson, local vascular closure in the sclera was contributed by both mechanical trauma (including surgery) and biological trauma such as infections and immune complexes [16]. The resultant hypoxic condition initiated a chain of catabolic events leading to progressive scleral necrosis. Clinicopathological study by Maite de Sanza at el have demonstrated evidence of immune complex mediated vasculitis following observation of increased deposition of inflammatory cells and HLA-DR expression in the scleral tissues of post-operative scleritis patients [19]. While scleritis has been linked with various connective tissue disorders, in majority of cases, evidence of underlying diseases could not be detected [10]. In a clinical-pathologic review of post -operative scleritis by Rishi et al, patients who developed SINS were those with underlying systemic autoimmune diseases [12]. They also postulated that pterygium surgery with or without use of adjunctive agents were associated with higher rate of secondary infection which contributed to scleral inflammation and necrosis. In our case series, pterygium excision surgery was the second commonest ocular procedure performed prior the onset of scleritis, and except one patient (who was not screened for systemic disease), rest of them did not have evidence of systemic vasculitic disease. Except in one case who complained of on and off eye discharge for one year (whereby the swab culture taken was negative), we did not find other evidence to suggest possible concurrent infection in the rest of the patients. Being a retrospective study, our findings and observations is also limited by the involvement of multiple ophthalmologists ,with various level of experience in the managements.

The risk of scleritis increases with the use of anti-metabolites, such as MMC in trabeculectomy and pterygium operation[1]. Mitomycin C is an antineoplastic antibiotic agent isolated from Streptomyces caespitosus. It alkylates and cross-links DNA thus inhibits protein synthesis and imposes long term inhibition to cellular proliferation [20]. Ischemic scleral necrosis induced by excessive cauterization during bare sclera technique is another possible cause of scleral necrosis [21]. Cheng HC et al has suggested intra-operative usage of lower concentration of MMC ie 0.02% for a safer yet effective technique to reduce the recurrence rate after bare sclera excision of pterygium [22]. Use of MMC in high risk patients with eye conditions which predisposed to poor wound healing such as Sjogren syndrome, kerato-conjunctivitis sicca, meibomitis or blepharitis were not advisable as they were more likely to develop complications. Alternatively, pterygium excision with conjunctival autografting may provide better option in effort to reduce intraoperative MMC usage [12].

CONCLUSION

SIS when treated according and promptly has a favorable visual prognosis. In this case series,

glaucoma surgeries with intraoperative cytotoxic agent usage is leading cause of surgical induced scleritis. Hence usage of this cytotoxic agent should be with extreme care.

DECLARATION OF CONFLICT OF INTEREST

The authors report no conflict of interest.

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