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Original article

Experience of scleritis and episcleritis at a tertiary center in Southern Taiwan

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ABSTRACT

Purpose: The purpose of this study was to review the clinical experiences of scleritis and episcleritis in Southern Taiwanese people during a 7-year period.
Methods: The charts of 89 patients (representing 101 eyes) who had visited our clinic from January 2003 to July 2010 were retrospectively reviewed. They were diagnosed as having episcleritis or scleritis. The medical charts, slit lamp photographs, and laboratory data were reviewed. Age, gender, laterality, previous surgery history, systemic diseases, follow-up duration, and ocular complications were collected. The patients were classified as having clinically suspected noninfectious scleritis (CSNIS), clinically suspected infectious scleritis (CSIS), and episcleritis for analysis.
Results: In the series of 89 patients (i.e., 101 eyes), 31 (34.8%; 32 eyes) patients had scleritis and 58 (65.2%; 69 eyes) patients had episcleritis. Episcleritis and scleritis occurred slightly more frequently in women than in men. In the 31 patients (32 eyes) diagnosed with scleritis, 12 (38.7%) patients had CSIS and 19 (61.3%) patients had CSNIS. Patients with scleritis were older than patients with episcleritis ($p < 0.001$). Previous pterygium excision was associated with CSIS and necrotizing scleritis.
Conclusion: Scleritis occurred in a more elderly population. It was more frequently associated with ocular complications, compared to episcleritis. Both CSNIS and CSIS were associated with a history of pterygium excisional surgery. Our series of patients had a high occurrence of necrotizing scleritis. All cases of necrotizing scleritis were associated with a history of previous ocular surgery.

1. Introduction

Scleritis is characterized by deep inflammation of the sclera that can spread to the adjacent cornea, episclera, and uvea, and cause sight-threatening complications.[1–4] The ocular inflammation is often severe, and sometimes requires treatment with systemic immunosuppressive medications.[4,5] Approximately 25–50% of patients with scleritis have an associated systemic illness that is presumably causally related.[6] Comorbid systemic conditions that have been associated with scleritis include rheumatoid arthritis, Wegener's granulomatosis, systemic vasculitis, systemic lupus erythematosis, sarcoidosis, and spondyloarthropathies.[6–9] Episcleritis, by contrast, is generally a less severe inflammation localized to the episclera. Unlike the deeper inflammation in scleritis, episcleral inflammation is relatively superficial and has the characteristic color of bright red or salmon pink, whereas most forms of scleritis present with a violaceous hue. Episcleritis often responds well to topical corticosteroid treatment[10] and seldom causes ocular complications.[1,9]

In the United States, the overall incidence of episcleritis is reportedly 41.0 per 100,000 person-years, and that of scleritis is 3.4 per 100,000 person-years; there is an increased prevalence among the elderly and women.[11]

However, most previous reports were based on Western populations with a distinctly different ethnic composition than that in Taiwan. Furthermore, previously published reports of scleritis from Taiwan mostly focused on scleral inflammation caused by an infectious etiology[12–16] rather than a full scope investigation into both episcleritis and scleritis. Therefore, we conducted this study to evaluate and analyze our experience of the clinical features and etiologies of scleritis and episcleritis in Southern Taiwan.

Conflicts of interest: All authors declare no conflicts of interest.

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2. Materials and methods

Patients diagnosed as having episcleritis or scleritis from January 2003 to July 2010 at the Cornea Service of Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan were included in this study. The medical records, slit lamp photography, and laboratory data were reviewed. Patients without records of slit lamp photographs or whose photographs were of poor quality were excluded. Age, gender, laterality, previous surgery history, systemic diseases, follow-up duration, and ocular complications were recorded for analysis. Ocular complications included: (1) visual acuity impairment, defined as a decrease in visual acuity of two Snellen lines or more; and (2) ocular hypertension, defined as intraocular pressure higher than 21 mmHg. The presence of systemic diseases or autoimmune diseases was recorded for analysis.

Classification was based on the anatomic site and clinical appearance of inflammation. Episcleritis was diagnosed when the inflammation was localized and confined to the episclera and blanched after the instillation of topical 10% phenylephrine. Scleritis was defined as the edema of the episcleral and scleral tissues with congestion of the superficial and the deep episcleral vessels. Application of 10% phenylephrine to the ocular surface blanches the superficial episcleral vessels but not the deeper scleral vascular plexus, thus differentiating between episcleritis and scleritis.

Patients with scleritis were divided into clinically suspected noninfectious scleritis (CSNIS) and clinically suspected infectious scleritis (CSIS). The former was further classified as "anterior scleritis" or "posterior scleritis", based on the anatomical location of the inflammation. Thickening of the posterior sclera in posterior scleritis was confirmed by B-scan ultrasonography. Anterior scleritis was categorized as diffuse scleritis, nodular scleritis, or necrotizing scleritis. Diffuse scleritis was defined as diffuse inflammation and vascular engorgement of the episclera and sclera. Nodular scleritis was characterized by an immobile elevated nodular swelling and inflammation of the sclera. Patients who presented with an avascular patch or ulcerative area on the sclera with or without marked inflammation were classified as having necrotizing scleritis.

Patients classified as having CSIS included: (1) patients with infectious scleritis with positive isolation of the causative microorganism from the lesion, and (2) patients with suspected infectious scleritis that showed favorable clinical response to antibiotic treatment but without laboratory evidence of microbial growth. The clinical picture of CSIS was acute inflammation of the sclera with subconjunctival abscess and suppurative discharge. The specimen for microbial culture was obtained from debridement surgery or scleral scraping in the clinic. Common aerobic, common anaerobic, fungus, and mycobacterial cultures were obtained.

Statistical analyses were performed using SPSS software version 17.0 (SPSS Inc., Chicago, IL, USA). Differences between the two groups were compared and evaluated with the Student t test for continuous variables and with the Chi-square test for categorical variables. Analysis between multiple groups was evaluated with one-way analysis of variance. A value of $p < 0.05$ was considered statistically significant.

3. Results

Eighty-nine patients (representing 101 eyes) diagnosed with episcleritis or scleritis from January 2003 to July 2010 were included in this study. There were 31 (34.8%) cases of scleritis with a mean patient age of 62.2 ± 18.5 years, and 58 (65.2%) cases of episcleritis with a mean patient age of 47.7 ± 17.3 years. Table 1 summarizes the clinical characteristics of the patients. There was a slight female predominance in the episcleritis and scleritis groups, and they accounted for more than one-half of the cases in both groups (episcleritis, 52%; scleritis, 61%). The patients with scleritis were significantly older than patients with episcleritis ($p < 0.001$). When the scleritis group was further divided into the CSNIS group and CSIS group, we found that the CSIS patients were older (CSNIS, 55.0 years old; CSIS, 73.7 years old).

Table 1
Clinical characteristics of patients with episcleritis and scleritis.

	Episcleritis ($n = 58$)	Scleritis ($n = 31$)	p
Age (y)	47.7	62.2	< 0.001
Sex (male:female)	28:30	12:19	0.39
Bilateral involvement	11 (19.0)	1 (3.2)	0.10
Ocular complications			
Ocular hypertension	0 (0)	6 (19.4)	< 0.01
Decreased VA	11 (19.0)	14 (45.2)	0.01
History of pterygium excision	2 (3.4)	18 (58.1)	< 0.001
Follow-up duration (mo)	13.2	27.0	0.01
Systemic autoimmune disease	3 (5.2)	4 (12.9)	0.23
Rheumatoid arthritis	1	1	
Ankylosing spondylitis	0	1	
SLE	2	0	
Sjogren's syndrome	0	1	
Autoimmune thyroiditis	0	1	
Nonautoimmune systemic disease	14 (24.1)	8 (25.8)	0.86
Diabetes mellitus	5	2	
Hypertension	7	4	
Chronic hepatitis	6	2	

Data are presented as n or n (%).
SLE = systemic lupus erythematosus; VA = visual acuity.

Ocular complications were more common among the scleritis patients than among the episcleritis patients. Blurred vision was present in 45.2% of scleritis patients and 19.0% of episcleritis patients ($p = 0.01$). Ocular hypertension was present in 19.4% of scleritis patients, but was not present in any of the episcleritis patients ($p < 0.01$). None of the episcleritis patients progressed to scleritis during the follow-up period.

Concomitant autoimmune disease was relatively low in our series. Only 5.2% of episcleritis patients and 12.9% of scleritis patients had an associated autoimmune disease. In the episcleritis group, there was one case of rheumatoid arthritis and two cases of systemic lupus erythematosus. In the scleritis group, there was one case each of rheumatoid arthritis, ankylosing spondylitis, autoimmune thyroiditis, and Sjogren's syndrome.

A history of previous pterygium excisional surgery was more frequent in the scleritis group than in the episcleritis group ($p < 0.001$). The proportion of patients with previous pterygium excision was 75% in the CSIS group and approximately 47% in the CSNIS group (Fig. 1). In the CSNIS group, most patients who had had previous pterygium excision presented with anterior necrotizing scleritis, which was the most common form of anterior scleritis in our study (Table 2). In 20 patients in this series who had a history of pterygium excision, nine (45%) patients presented with CSIS, eight (40%) patients presented with anterior necrotizing scleritis, two (10%) patients presented with episcleritis, and one (5%) patient presented with anterior nodular scleritis.

In the subset of patients diagnosed with CSIS ($n = 12$), nine patients had a positive microbial culture. The most commonly isolated microorganism was *Pseudomonas aeruginosa* in 6 (50%) of 12 patients, followed by fungus in 2 (12.5%) of 12 patients. Seventy-five percent of patients had previous pterygium excision, whereas one (8.3%) pterygium excision was associated with traumatic injury. Except for one patient, all (91.6%) other patients, underwent surgical debridement for subconjunctival abscess with scleral necrosis (Table 3). The range of time from diagnosis to surgical debridement

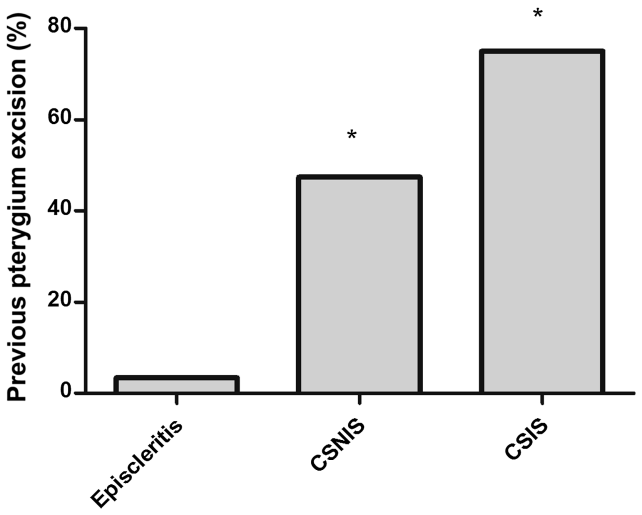

Fig. 1. The percentage of episcleritis and scleritis patients with a previous history of pterygium excision. CSIS = clinically significant infectious scleritis; CSNIS = clinically significant noninfectious scleritis. * Indicates a significant statistical difference between episcleritis and CSNIS, and between episcleritis and CSIS ($p < 0.001$, based on one-way analysis of variance).

was 2–45 days. In the CSIS cases with a bacterial etiology, debridement surgery was performed mostly within 5 days after diagnosis.

4. Discussion

Consistent with the results of previous studies,[1,9–11] we found an older age in the scleritis group and female predominance in the scleritis and episcleritis groups. In a large cohort study by Sainz de la Maza et al[1] and an epidemiological study by Honik et al,[11] the reported mean age was 45.6–47.4 years for patients with episcleritis and 52.6–53.7 years for patients with scleritis. In our study, the mean age for patients with episcleritis was 47.7 years, which was comparable to their results; however, the mean age in our group of scleritis patients was 62.2 years, which is slightly older than the age previously reported in the literature.[1,11]

Ocular complications are more frequently encountered in scleritis and reportedly occurs in 29.4–84.6% of patients.[1,4,9,10,17] These complications include loss in visual acuity, ocular hypertension, anterior uveitis, peripheral ulcerative keratitis, cataract, scleral thinning, and in severe cases involve the posterior segment, cystoid macular edema or exudative retinal detachment. In our study, 45.2% of scleritis patients presented with decreased vision.

Table 2
Association between a history of previous pterygium excision and autoimmune disease in patients with scleritis.

	CSNIS ($n = 19$)				CSIS ($n = 12$)
	Anterior nodular scleritis ($n = 4$)	Anterior diffuse scleritis ($n = 5$)	Anterior necrotizing scleritis ($n = 8$)	Posterior scleritis ($n = 2$)	
History of pterygium excision	1 (25)	0 (0)	8 (100)	0 (0)	9 (75)
Autoimmune disease	1 (25)	1 (20)	0 (0)	1 (50)	1 (8.3)

Data are presented as *n* (%).
CSIS = clinically significant infectious scleritis; CSNIS = clinically significant noninfectious scleritis.

Table 3
Summary of the clinical characteristics of patients with clinically significant infectious scleritis.

Case No.	Sex	Age	Predisposing factor	Surgical debridement	Time from diagnosis to debridement	Culture
1	F	72	Pterygium surgery	Yes	3 d	No growth
2	F	68	Pterygium surgery	Yes	3 d	*Pseudomonas aeruginosa*
3	M	73	Pterygium surgery	No	—	No growth
4	F	87	Idiopathic	Yes	10 d	*Haemophilus influenza*
5	F	75	Pterygium surgery	Yes	5 d	*P. aeruginosa*
6	M	75	Trauma	Yes	23 d	Fungus
7	M	68	Idiopathic	Yes	30 d	Fungus
8	F	76	Pterygium surgery	Yes	45 d	No growth
9	F	48	Pterygium surgery	Yes	3 d	*P. aeruginosa*
10	F	75	Pterygium surgery	Yes	2 d	*P. aeruginosa*
11	F	94	Pterygium surgery	Yes	5 d	*P. aeruginosa*
12	F	73	Pterygium surgery	Yes	4 d	*P. aeruginosa*

Sainz de la Maza et al[1] found that predictive factors associated with loss in visual acuity were the presence of anterior uveitis, ocular hypertension, and the subtype of necrotizing scleritis. However, a study by Jabs et al[10] and a recent study by Wieringa et al[4] found that decreased visual acuity was associated with concomitant systemic disease, but was not associated with the type of scleritis.

By comparison, episcleritis tends to be a milder ocular disorder with fewer ocular complications and better responsiveness to topical medications, compared to scleritis. Most cases of episcleritis remain localized to the episclera and do not progress to scleritis.[10] In our study, no patient diagnosed with episcleritis progressed to scleritis within the follow-up period.

In this study, we found that the rate of associated autoimmune disease was much lower than that previously reported. The systemic disease association rate in scleritis had been reported as high as 29.8–39.2%.[1,4,7,9,10] However, in a more recent study, Honik et al[11] also reported a relatively low systemic disease rate of 1.2% in episcleritis and 6% in scleritis in their epidemiologic study. Raiji and coworkers[8] in their community-based study on the association between scleritis and systemic disease also pointed out that differences in the reported rate of autoimmune diseases may be largely influenced by the study population and the clinical setting where the study is conducted. Because most previous studies have been conducted at large tertiary university-based referral centers where patients with more severe diseases are concentrated, referral bias may have resulted in the high rate of disease association.

Furthermore, previous studies have all been conducted on Caucasian populations,[1,4,7–10] which have all identified rheumatoid arthritis as the most commonly associated systemic autoimmune disease. In contrast to a Caucasian population, Cohen et al[18] in their study of 153 Chinese rheumatoid arthritis patients found that extra-articular manifestation was relatively uncommon and that the only extra-articular manifestations were rheumatoid nodules (4.6%), episcleritis (0.7%), and cutaneous vasculitis (0.7%). In our study, the association between rheumatoid arthritis and episcleritis and scleritis was low with only one (1.7%) case of rheumatoid arthritis in the episcleritis group and one (3.2%) case of rheumatoid

arthritis in the scleritis group. Racial differences in ocular manifestations of systemic diseases may have likely also contributed to the low autoimmune disease rate observed in our study.

Twenty (22.5%) patients in this case series had a previous history of pterygium excision on the diseased eye. In these patients, the most common presentation was infectious scleritis (45%), followed closely by necrotizing scleritis (40%). In a recent meta-analysis, Liu et al[19] reported a world-wide prevalence of 10.2% for pterygium with an increasing prevalence in regions with a latitude close to the equator. Significant risk factors included old age, sun exposure, and outdoor activity.[19] In Taiwanese aborigines, the prevalence of pterygium was as high as 44.1%.[20] In Taiwan, pterygium excisional surgery is common clinically, probably because of the high prevalence of pterygium and easy medical access.

Several studies of infectious scleritis from Taiwan have previously been published.[12–16] In these studies, pterygium surgery was the most common inciting factor with *Pseudomonas aeruginosa* being the most common microbe. Our study had both factors.

However, the association between pterygium surgery and noninfectious necrotizing scleritis has been less reported in Taiwan. Surgically induced necrotizing scleritis has typically been considered a rare complication after cataract, glaucoma, strabismus, and retinal surgery with as many as 63% of patients having an underlying systemic disease.[21] However, in recent years, there have been several reports of necrotizing scleritis occurring after pterygium surgery.[22–25] In these case reports, none of the patients had an associated autoimmune disease, despite a complete systemic workup. In our series, all patients ($n = 8$) with necrotizing scleritis had a history of pterygium excision, and no patient had an underlying autoimmune disease. Ahn et al[26] report findings similar to ours, and found that 96.3% of their patients with necrotizing scleritis had a previous pterygium excision surgery, whereas only 7.4% of patients had an underlying autoimmune disease. Autoimmunity or delayed-hypersensitivity has been proposed as a possible mechanism for surgically induced necrotizing scleritis,[21] although the mechanism in these pterygium surgery cases is probably more related to localized ischemia at the surgical site that is promoted by excessive cauterization during surgery.[22]

This study has several limitations. The major limitation is its retrospective nature and the relatively small sample size. Furthermore, the results of our study need to be carefully interpreted because this data was based on a single hospital experience, which was not meant to represent the epidemiology of episcleritis and scleritis in the entire Taiwanese population. Future study with a representative sample size in a multi-institutional setting or a population-based study is needed to provide further clarifications and insights into the results of our study. However, the strength of our study is that it highlights the possible influence of geographic regions and ethnicity on the presentation and etiology of scleritis.

In conclusion, we found that scleritis was a severe inflammatory ocular disorder that occurs in the elderly population and is more frequently associated with ocular complications, compared to episcleritis. The most common presentations of scleritis in patients who have had previous pterygium surgery were infectious scleritis and necrotizing scleritis. The results of our study also suggest that the occurrence of necrotizing scleritis may be greater in Southern Taiwan than has previously been reported in the Western population. In our patients, the etiology may more likely be surgically induced rather than autoimmune-associated.

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