Assessment of clinical characteristics of patients with scleritis accompanied by episcleritis

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Abstract: Objective: To evaluate the demographic data, clinical characteristics, eye complications of patients diagnosed with scleritis complicated with episcleritis. Methods: This retrospective case-series study consisting of 84 cases diagnosed with scleritis complicated with episcleritis in the People’s Hospital of Guangxi. The medical history, health status, clinical manifestations and characteristics, eye complications were evaluated to summarize clinical characteristics of this complicated disease. Results: Eighty four patients, aged 5-78 years, mean age (48 ± 15) years, 28 males and 56 females, were recruited in this clinical trial. Thirty four patients had episcleritis and 50 had scleritis. Among 84 cases, two children were aged < 16 years old and had episcleritis, 36 cases aged 17-44 years including 12 episcleritis and 24 scleritis, 28 aged 45-59 years including 8 episcleritis and 20 scleritis and 18 aged ≥ 60 years including 12 episcleritis and 6 scleritis. Eighteen cases had different types of arthritis, and 9 had topical infectious diseases. Eye complications were more frequent overall in patients with scleritis versus in those with episcleritis, including keratitis and ocular hypertension. Conclusions: Scleritis is a rare and potentially life-threatening disease, which occurs in individuals of all ages especially in adults. More and more attention should be paid to the diagnosis and treatment of scleritis complicated with episcleritis.

Keywords: Scleritis, visual acuity, diagnosis, risk factor, episcleritis

Introduction

Scleritis is an ocular disease relatively uncommon in clinic with an incidence taking up about 0.5% of ocular diseases [1-3], with causes are so complicated and remain unclear, which are probably related to exogenous or endogenous infection and diseases of autoimmunity [4-6]. There are many ocular complications caused by scleritis, which will lead to vision decrease or eye damage if they are not treated properly no matter they are acute or chronic. Besides, scleritis is associated with systemic diseases. Under some circumstances, scleritis happens before potentially lethal systemic immune-mediated diseases, so early diagnosis and treatment of scleritis is particularly important [7-12].

Scleritis is classified into anterior, posterior and panscleritis according to the affected sites and categorized into simple or diffuse, nodular and necrotic scleritis according to lesion nature. At present, scleritis is clinically classified into episcleritis and scleritis based upon the affected site and lesion nature. The former includes two types of diffuse and nodular scleritis, and two types of the latter are anterior and posterior scleritis. And anterior scleritis is divided into diffuse, nodular and necrotic types. This classification includes different types ranging from mild to severe scleritis, which can direct clinical therapy. In this study, 84 cases diagnosed as scleritis complicated with episcleritis were recruited to evaluate the clinical characteristics, aiming to provide clinical evidence for physicians.

Materials and methods

Patients’ data

Eighty four cases (98 eyes) that were clinically diagnosed as scleritis and episcleritis in the People’s Hospital of Guangxi were collected. The follow-up endured for 1-27 months, 5
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months on average. The cases were divided into the children, young, middle age and elderly groups. Confirmed consents were obtained from all participants prior to formal study.

Diagnostic criteria of episcleritis and scleritis

According to the lesion site and severity, ocular disease was classified into episcleritis and scleritis as according to the Watson Classification System. Episcleritis is characterized by radial congestion and dilation of surface scleral blood vessels, the scleral tissue does not develop edema generally. The patients feel ocular distending pain or discomfort. This type includes diffuse and nodular episcleritis. Diffuse episcleritis refers to superficial scleral swelling whereas nodular episcleritis manifests as nodular bulge into the superficial sclera. Scleritis is characterized by significant dilation of deep vascular plexus and scleral edema. The patients had pain, occasionally local haphalgesia and radiating pain. Scleritis is classified into the anterior and posterior scleritis by the lesion site. According to the nature of lesions, it is classified into the diffuse, nodular and necrotic scleritis.

Episcleritis and scleritis could be identified by red-free light after administration of 10% phenylephrine hydrochloride eye drops. The superficial vascular congestion was alleviated and scleral tissue was not involved. While in scleritis patients, the scleral edema and apparent dilation of deep vascular plexus were not eased. In the cases with posterior scleritis, B-scan revealed ocular wall thickening with a typical "T" shape.

The patients were determined whether accompanied with systemic diseases, infectious scleritis and perioperative scleritis. Systemic diseases include rheumatoid arthritis, systemic angiopathy, Wegener granulomatosis and recurrent polychondritis. And infectious diseases include bacterial, fungal, virus and parasitic infection.

Routine examination

General conditions, cases histories, clinical examination results of sclera, cornea, iris and anterior chamber were all recorded by electronic medical records. The ocular conditions were recorded by colorful digital camera. Besides, microbiological examinations (mainly ocular scrapers for bacteriological test and virological immunological test) and ocular B-scan were performed.

Eye complications

Ocular complications: (1) decrease in vision: vision acuity decrease ≥ 2 lines or vision acuity ≤ 0.25 after affected or in time of follow-up visit; (2) keratitis: mainly marginally sclerosing keratitis and ulcerative keratitis; (3) anterior uveitis: more than one planktonic cell in anterior segment; (4) ocular hypertension: intraocular pressure higher than 21 mmHg (1 mmHg = 0.133 kPa); (5) cataract; (6) diseases of retina and optic neuritis: retinal edema at posterior pole, exudative detachment, flocculent exudation in front of retina, papilledema, Macular edema and ischemic optic neuropathy.

Episcleritis and scleritis management

Episcleritis: local application of glucocorticoid eye drops in low concentration or NSAIDs eye drops 4 times/day, and gradually reducing dose 1 week later.

Scleritis: local treatment: application of glucocorticoid eye drops in relatively high concentration 6 times/day, 4 times/day 3 days later, and glucocorticoid in low concentration 1–2 weeks later 2 times/day to maintain for 2 weeks. Systemic treatment: NSAIDs and cyclooxygenase inhibitors for non-necrotic scleritis, such as ibuprofen tablet 0.25 mg, three times/day. For severe or necrotic scleritis, oral administration of prednisone is needed, 1.0–1.5 mg/kg, gradually reducing the dose depending on the conditions 1–2 weeks later, maintenance dose of 5 mg/day for at least 6 months.

Medical treatment when accompanied with systemic diseases, and corresponding treatment for ocular complications. Scleral transplant is needed for severe sclera attenuation or necrotic scleritis with a threatening of rupture.

Statistical analysis

SPSS 19.0 statistical software was used for all data analysis. χ² test was applied for evaluation of gender and other enumeration data between episcleritis and scleritis groups. P < 0.05 was considered as significantly different. For the
Results

Clinical data

Eighty four cases of episcleritis and scleritis were collected. Sixty two cases were biocularly while 22 cases were monocularly affected. Patients’ age ranged from 5 to 78 years old with an average age of (48 ± 15) years old.

Among 84 cases, 36 cases were diagnosed with episcleritis, who visited a doctor mainly because of redness, mild pain or discomfort. And 27 cases had diffuse episcleritis, manifested by diffuse congestion and superficial scleral edema and bulbar conjunctiva and four nodular episcleritis, manifested with a nodular bulge into the superficial sclera, its color varied from bright red to pink, with irregular vessels on or around it. Solitary nodule was constantly observed with not apparent stimulous symptoms.

Forty eight cases were scleritis, which was characterized by pain, sometimes was haphalgesia locally. And 38 cases were anterior scleritis and 10 cases were posterior scleritis. Among the anterior scleritis, 30 were diffuse ones, manifested by congestion and edema of bulbar conjunctiva, patchy diffuse congestion of deep scleral vessels, which can be restricted to one quadrant, but also can involve in the whole anterior segment. Six cases were nodular scleritis, in which haphalgesia was obvious, and non-palpable nodules may exist. The local sclera was edema. Two cases were necrotic scleritis, presenting with scleral necrosis and capillary non-perfusion area. The posterior scleritis patients mainly showed ocular dull pain and decrease in visual acuity, sever pain can radiate to scalp, ear, jaw and teeth, typically aggravating during night and woke up because of pain. The sign was not typical, sometimes only the sclera had edema, ocular B-scan showed ocular wall thickening, interspace under the Tenon capsule, showing typical “T” shape.

Disease conditions for both genders

Twenty eight cases were male and 56 were female. In the episcleritis cases, 15 cases were male, 21 female. In scleritis cases, 15 cases were male, 39 female. The number of female cases was significantly higher than male cases ($\chi^2 = 10.000, P < 0.01$).

Eye complications

Ocular complications were more frequent overall in patients with scleritis versus in those with episcleritis ($\chi^2 = 30.0, P < 0.05$), including decrease in vision, keratitis, and ocular hypertension ($\chi^2 = 130.200, 67.200$ and $54.444, P < 0.01$) (Table 1). Thirty five cases had a decrease in vision to different extent. Twenty two cases had corneal complications, in which marginally sclerosing keratitis were significantly more than ulcerative keratitis ($\chi^2 = 321.3, P < 0.05$). In total, 18 cases had anterior uveitis in the patients with episcleritis and scleritis with no statistical significance ($\chi^2 = 0.40, P > 0.05$). In patients with episcleritis and scleritis, one case was diagnosed with cataract, and one case of flocculent exudation in front of the reti-

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**Table 1.** Eye complications between patients diagnosed with scleritis and episcleritis

<table>
<thead>
<tr>
<th>Eye complications</th>
<th>Scleritis group</th>
<th>Episcleritis group</th>
<th>Total number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ocular complications</td>
<td>37 (77.1%)</td>
<td>12 (25.0%)</td>
<td>49 (59.0%)</td>
</tr>
<tr>
<td>Decreased vision</td>
<td>30 (62.5%)</td>
<td>4 (11.1%)</td>
<td>34 (40.5%)</td>
</tr>
<tr>
<td>Anterior uveitis</td>
<td>18 (37.5%)</td>
<td>20 (55.6%)</td>
<td>38 (45.2%)</td>
</tr>
<tr>
<td>Keratitis</td>
<td>15 (31.3%)</td>
<td>7 (19.4%)</td>
<td>22 (26.2%)</td>
</tr>
<tr>
<td>Ocular hypertension</td>
<td>12 (25.0%)</td>
<td>2 (5.6%)</td>
<td>14 (16.7%)</td>
</tr>
<tr>
<td>Cataract</td>
<td>1 (2.1%)</td>
<td>0 (0%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>12 (25.0%)</td>
<td>6 (16.7%)</td>
<td>18 (21.4%)</td>
</tr>
<tr>
<td>Nocardia infection</td>
<td>1 (2.1%)</td>
<td>0 (0%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Herpes simplex infection</td>
<td>6 (12.5%)</td>
<td>3 (8.3%)</td>
<td>9 (10.7%)</td>
</tr>
</tbody>
</table>
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na and the exudation was fully absorbed after treatment.

The number of cases with episcleritis was significantly more than scleritis ($\chi^2 = 145.6, P < 0.05$). A total of 18 cases had arthritis of varying degree and two necrotic scleritis cases had server rheumatic arthritis. Nine cases had topical infectious diseases including one infected by Nocardia after PPV and nine cases infected by virus.

Discussion

Scleritis is involved in individuals of all ages, dominantly bilaterally affected. In present study, patients' age ranged from 5 to 78 years old, among whom young and middle-aged subjects were the majority and 74.4% of the patients were bilaterally affected. In correspondence with abroad researches, female patients were more than male patients. The age of episcleritis had a wide range, it is relatively mild with acute onset, and the ocular symptoms of pain and discomfort is not specific so the diagnosis is mainly based on clinical signs and histories. Episcleritis is thought to be a self-limited, recurrent and benign disease. Patients in outpatient service are usually those who had a persistent disease needing to be treated and the symptoms can be rapidly eased by locally administration of glucocorticoid in low concentration. Patients with recurrent episcleritis should be carefully emphasized because they may suffer from associated diseases, especially rheumatic arthritis.

Physiopathologic mechanism of scleritis is complicated. Most cases have a local or systemic cause, but there still exist ones that are idiopathic. Rao et al thought that most idiopathic cases would show autoimmunization, the Specific remained unclear. There was once a study on one scleritis case with treatment by mouse monoclonal antibody, thinking that deposit of immunocomplex is an important pathogenic factor. Approximately 40%-50% patients with scleritis had systemic immune-mediated diseases [8, 13-15] based on previous study. In the present study, 21.1% cases had a history of arthritis, and both two cases with necrotic anterior scleritis were diagnosed with arthritis.

Anterior scleritis is the most common type of scleritis, which happens in the population of any age, but mainly in young and middle-aged adults. In this study, it mainly happened in 24-65 years old, accounting for 47.8%. Among which diffuse anterior scleritis was the most common, whereas nodular and necrotic cases accounted for the least percentage. Though almost all necrotic scleritis cases were characterized by acute onset with server pain, certain patients showed an ocular inflammatory reaction with mild pain. These patients generally received low dose glucocorticoid treatment because of systemic diseases such as rheumatic arthritis. As a result, detailed examination and early diagnosis were particularly important. Posterior scleritis has no typical clinical manifestations, which usually showed a progressive decrease in vision with ocular pain, sometimes accompanied with choroid wrinkles, papilledema, choroid exudation and retinal detachment. The diagnosis is relied on ultrasonoscopy, which taking up 8.9% cases in the present study. An analysis on 500 scleritis cases showed 6.2% incidence of posterior scleritis. As there is no obvious symptom for posterior scleritis, while inflammation is close to macule, retinal and optic nerve, so the potential damage is great. Posterior scleritis of any type that cannot be diagnosed or treated will rapidly lead to blindness. For patients of posterior scleritis, the most step of treatment is seriously asking for medical history, detailed examinations and completely system review. And then rule out possible systemic diseases and other diseases that should be taken into consideration according to the results of clinical evaluations.

Scleritis caused by infection and operation is not rare, in new patients in an ocular disease therapeutic center, inflammatory scleral diseases made up 0.08%, and about 10% scleritis patients had a history of associated infectious diseases [7]. Various kinds of microorganisms (virus, bacterium, fungus and parasite) can cause infectious scleritis, among which varicella-zoster virus is the most common cause [4]. Marsh and Cooper found that 37 cases (3%) had scleritis in 1365 herpes zoster affected patients. In the present study, 9 cases infected with herpes virus made up 10% of all cases. 1 case was proved by laboratory test to be infected with nocardia with server pain, eyelid swelling and exophthalmos postoperatively. The mechanism of infectious scleritis may have two sides, one is directive invasion of pathogen...
after tissue damage, and the other one is a series immunoreaction caused by infective factors.

Ocular complications caused by scleritis are not rare, including decrease in vision, keratitis, ocular hypertension, anterior uveitis, cataract, and diseases of retina, among which decrease in vision is the most common one. Jabs et al [8] reported that 15.9% scleritis patients had a decrease in visual acuity by Sainz et al [9] showed 37.2% scleritis had a decrease in vision. While our study showed 41.4% cases with visual acuity decrease, most patients had a decrease in vision of varying degrees, and recurrent episcleritis also led to a decrease in visual acuity. Corneal complications included sclerokeratitis and edge ulcerative keratitis, in this study, 20.0% cases had edge sclerosing keratitis, 6.7% of cases had ulcerative keratitis. Those were close to the results of abroad studies previously [8, 9, 13]. Anterior scleritis will infiltrate to adjacent periphery of the cornea, which leads to attenuation of adjacent cornea and keratoplasty is needed when rupture may happens. There are many reasons why ocular hypertension happens in scleritis, the most common one is anterior diffuse scleritis, especially trabeculitis close to edge of the sclera. Secondly, long-term or irregular administration of gluocorticoid will lead a side effect of ocular hypertension. In this study, 21.1% scleritis cases had anterior uveitis, which was lower than 42.4% reported in an abroad study [9], and was close to that reported by Sainz et al [14]. Complicated uveitis was mild generally and would disappear when the scleritis was controlled. Cataract derived from scleritis is usually posterior subcapsular cataract. The posterior scleritis can give rise to retinitis and optic neuritis, retinal edema at posterior pole, exudative detachment, flocculent exudation in front of retina; papilledema, macular edema and ischemic optic neuropathy. One case in this study had a flocculent exudation in front of retina and was absorbed after systemic treatment. In terms of relative server exudative retinal detachment, perpetual detachment will leave because viscous or organizational fluid could not to be absorbed. Scleritis is a disease worthy of paying attention to. Systemic and local factors need to be taken into consideration to make early diagnosis and appropriate treatment. Furthermore, it is essential to understand that many ocular complications will be derived from scleritis so inflammatory response should be controlled actively so that complications will decrease and visual acuity will be saved to the greatest extent.

Disclosure of conflict of interest

None.

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