Original Article



# Clinical features and long-term treatment outcome of posterior scleritis

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**Background:** To analyze the clinical characteristics and long-term treatment outcomes of patients with posterior scleritis.

**Methods:** This retrospective, observational case series analyzed medical records of 14 patients diagnosed with infectious or non-infectious posterior scleritis between May 2005 and March 2020 at Severance Hospital and Gangnam Severance Hospital.

**Results:** A total of 12 patients with non-infectious and two with infectious posterior scleritis were treated. Conjunctival injection (85.7%) was the most common symptom, followed by pain on eyeball movement (57.1%), and decreased visual acuity (42.9%). Anterior uveitis (64.3%) was the most common associated clinical finding. In five eyes (35.7%), immunosuppressive agents were administered in addition to corticosteroids to control the inflammation. Recurrence was noted in three eyes (21.4%), all of them showing non-infectious scleritis. The final visual acuity of the patients did not show significant change compared to that at the first visit (P=0.878).

**Conclusions:** Most posterior scleritis patients were of non-infectious type and some needed additional immunosuppressive treatment. In patients with a history of ocular surgery or trauma, especially with the presence of pus-containing nodules, infectious posterior scleritis should always be considered. Since impaired vision does not improve significantly after treatment of posterior scleritis, prompt diagnosis and aggressive treatment are recommended.

**Keywords:** Posterior scleritis; infectious scleritis; uveitis

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## Introduction

Posterior scleritis is an inflammatory disease that involves the sclera posterior to the ora serrata (1). Its occurrence is rare compared to that of anterior scleritis, and a report suggest that only 6.2% of patients with scleritis have posterior scleritis (2). Posterior scleritis is mainly sub-acute, occurs unilaterally, and presents with moderate to severe pain in nearly half of the patients (2). It develops frequently in young individuals and is associated with severe vision impairment, compared to anterior scleritis (2). Depending on the cause of inflammation, it may be classified into infectious and non-infectious posterior scleritis (3). Non-

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infectious posterior scleritis is usually of an idiopathic etiology, but is often associated with rheumatological disorders (4-6).

The diagnosis of posterior scleritis can be challenging, and a step-wise approach with suspecting and approaching posterior scleritis can help in establishing the definitive diagnosis. Serous retinal detachment, optic nerve swelling, chorio-retinal granulomas, or retinal lesions such as cotton wool spots, can be observed upon funduscopic examination (1,7). In case of posterior nodular scleritis, scleral nodules can be observed funduscopically and also using imaging tools such as B-scan ultrasonography, computed tomography (CT), or magnetic resonance imaging (MRI). Posterior scleral thickening associated with fluid surrounding the optic nerve can be seen as a characteristic "T" sign on B-scan ultrasonography, which helps in the definitive diagnosis.

Studies have mainly focused on anterior scleritis; because of the rarity of posterior scleritis, only a few large-scale studies have focused on posterior scleritis (8,9). There are even fewer reports on infectious posterior scleritis (10,11). González-López *et al.* analyzed the clinical characteristics of 18 patients with bilateral posterior scleritis, which is extremely rare, and reported that patients with elevated anti-nuclear antibody titers exhibited increased bilateral involvement (9). Lavric *et al.* reported the recurrence rate of posterior scleritis in 144 patients and its association with systemic disease, in their large-scale study, with only two patients showing an infectious etiology (4). Moreover, there are only a few case reports on posterior scleritis in Korean patients (12,13).

Therefore, we aimed to retrospectively analyze a series of cases of with posterior scleritis with respect to the etiology, clinical features, diagnosis, treatment, and visual outcome. Moreover, we have discussed our experience of two cases of infectious posterior scleritis related to *Pseudomonas aeruginosa* (*P. aeruginosa*) and coagulase-negative *Staphylococci* that were successfully treated with antibiotics and steroids. We present the following article in accordance with the STROBE reporting checklist (available at https://atm.amegroups.com/article/view/10.21037/atm-22-721/rc).

## Methods

This was a retrospective observational study and was conducted using data of 14 patients diagnosed with posterior scleritis at Ophthalmology Department of Severance Hospital and Gangnam Severance Hospital between May 2005 and March 2020. The demographic characteristics, clinical features, and diagnostic test results of patients were analyzed. Details regarding treatment regimens and their results were collected. This study was conducted in accordance with the tenets of the Declaration of Helsinki (as revised in 2013), and was approved by the Institutional Review Board (IRB) of the Gangnam Severance Hospital retrospectively (IRB approval No. 3-2020-0304). The necessity to obtain informed consent was waived by the IRB. The inclusion criteria were patients diagnosed with either infectious or non-infectious posterior scleritis. The diagnosis of posterior scleritis was made when patients with suspected past medico-surgical history and clinical features showed the following characteristic abnormalities on imaging or blood tests: the T sign observed on B-scan ultrasound; increased choroidal thickness observed on optical coherence tomography (OCT); vascular leakage observed on fluorescein angiogram; increased choroidal thickness observed on either CT or MRI; culture results of samples taken from the lesion in cases of suspected infectious scleritis, etc. The exclusion criteria were patients with insufficient evidence of posterior scleritis and those with other ophthalmic conditions such as diabetic retinopathy, age-related macular degeneration, and glaucoma. At the first visit, the best-corrected visual acuity and intraocular pressure were measured. Vision was measured with a Snellen chart and then converted to the logarithm of the minimum angle of resolution vision for statistical analysis. Dilated funduscopic examination and OCT examination were performed. B-scan ultrasonography test confirmed whether the "T" sign was present or whether the scleral thickness had increased. Fluorescein angiography (FA) was also performed to confirm any abnormal findings suggestive of posterior scleritis, such as optic disc leakage or vascular leakage. All patients were tested for complete blood count, erythrocyte sedimentation rate, and C-reactive protein levels; additional serology tests were performed for assessing rheumatologic or infectious diseases, if needed. Patients with suspected infectious posterior scleritis were tested for bacterial and fungal culture for the suspected organism. For differential diagnosis, imaging tests such as CT and MRI, were performed, if necessary.

### *Statistical analysis*

Descriptive statistical analyses of the patients' demographic data were performed using SPSS v25.0 (IBM Inc., Armonk, NY, USA). The Wilcoxon's signed rank test was performed to compare the visual changes.

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**Table 1** Demographics of 14 patients with posterior scleritis

| Demographic | Number (%)/mean ± SD |
|---|---|
| Age, years | 52.6±16.4 |
| Sex (male/female) | 5/9 |
| Known systemic diseases | |
| Rheumatologic diseases | 3 (21.4) |
| Systemic lupus erythematosus | 1 (7.1) |
| Sero-negative spondyloarthropathy | 1 (7.1) |
| Behçet's disease | 1 (7.1) |
| Hypertension | 2 (14.3) |
| Diabetes | 2 (14.3) |
| Pregnancy | 2 (14.3) |
| Tuberculosis | 1 (7.14) |
| Known ocular trauma or surgery | |
| Past ocular surgery | 2 (14.3) |
| Cataract surgery | 1 (7.1) |
| Pterygium removal | 1 (7.1) |
| Types of posterior scleritis | |
| Infectious | 2 (14.3) |
| Superinfection with both *Pseudomonas aeruginosa* and coagulase-negative *Staphylococci* | 2 (14.3) |
| Non-infectious | 12 (85.7) |

SD, standard deviation.

## Results

A total of 14 patients were treated for posterior scleritis, of which two (14.3%) were of infectious origin. The mean age was 52.6±16.4 years. Five (35.7%) patients were male and nine (64.3%) were female. Three (21.4%) patients had rheumatologic disorders, including one with systemic lupus erythematosus (7.1%), one with sero-negative spondyloarthropathy (7.1%), and one with Behçet's disease (7.1%). One patient had a history of tuberculosis. Two patients with infectious scleritis (14.3%) had a history of eye surgery (14.3%). Culturing in pus-filled nodules revealed super-infection with both *P. aeruginosa* and coagulase-negative *Staphylococci* in those two patients (*Table 1*).

The initial logarithm of the minimum angle of resolution (logMAR) best-corrected visual acuity (BCVA) of patients with posterior scleritis was 0.6±0.9. Intraocular pressure was 13.9±7.6 mmHg. The most common initial symptom of patients included conjunctival injection (n=12, 85.7%), followed by pain on eyeball movement (n=8, 57.1%) and decreased visual acuity (n=6, 42.9%). It took an average of 10.4±10.1 days for a patient to visit the outpatient clinic after initial symptom onset. Nine patients (64.3%) had inflammatory cells in the anterior chamber and eight patients (57.1%) had inflammatory cells in the vitreous cavity. During funduscopic evaluation, optic disc swelling was observed in six patients (42.9%); choroidal folding/detachment, vitreous haziness, and retinal folding in three (21.4%); and optic disc hemorrhage and epiretinal membrane in one (7.1%). However, three patients (21.4%) showed no abnormality on funduscopic examination. The mean central macular thickness was 302.9±90.8 μm, and macular edema was present in three patients (21.4%). Eight (57.14%) patients underwent FA, of which four (50.0%) had leakage. Four patients (50.0%) had optic disc leakage, whereas two (25.0%) had vascular leakage. B-scan ultrasonography confirmed an increase in the scleral thickness in all patients and the presence of "T" sign in

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**Table 2** Ocular findings of 14 patients with posterior scleritis

| Finding | Number (%)/ mean ± SD |
|---|---|
| Duration between symptoms and first visit (days) | 10.4±10.1 |
| Initial logMAR BCVA | 0.6±0.9 |
| Intraocular pressure (mmHg) | 13.9±7.6 |
| Spherical equivalent refractive error (D) | −1.6±2.0 |
| Initial symptom | |
| Injection | 12 (85.7) |
| Pain on eyeball movement | 8 (57.1) |
| Decreased visual acuity | 6 (42.9) |
| Ocular findings | |
| Cells in anterior chamber (eyes) | 9 (64.3) |
| SUN grading | 1.6±1.6 |
| Cells in anterior vitreous (eyes) | 8 (57.1) |
| Funduscopic features | |
| Optic disc swelling | 6 (42.9) |
| Vitreous haziness | 3 (21.4) |
| Retinal fold | 3 (21.4) |
| Choroidal fold/detachment | 3 (21.4) |
| No abnormality | 3 (21.4) |
| Optic disc hemorrhage | 1 (7.1) |
| Epiretinal membrane | 1 (7.1) |
| OCT features | |
| Central macular thickness (μm) | 302.9±90.8 |
| Macular edema | 3 (21.4) |
| Fluorescein angiographic leakage | 4/8 (50.0) |
| Disc leak | 4 (50.0) |
| Vascular leak | 2 (25.0) |
| B-scan ultrasonography | |
| Increased scleral thickness | 14 (100.0) |
| T-sign | 10 (71.4) |
| CT/MRI abnormal findings | 6/8 (75.0) |
| Enhancement/high signal intensity | 5/6 (83.3) |
| Thickening of sclera | 4/6 (66.7) |
| Choroidal detachment | 2/6 (33.3) |
| Combined features | |
| Uveitis | 9 (64.3) |
| Optic neuritis | 5 (35.7) |
| Nodular scleritis | 4 (28.6) |
| Idiopathic orbital inflammatory disease | 2 (14.3) |
| Uveal effusion | 1 (7.1) |
| Non-arteritic ischemic optic neuropathy | 1 (7.1) |

SD, standard deviation; logMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity; D, diopter; SUN, the standardization of uveitis nomenclature; OCT, optical coherence tomography; CT, computed tomography; MRI, magnetic resonance imaging.

10 patients (71.4%). Eight patients underwent either CT or MRI, of which six patients (75.0%) showed abnormal findings in the eyeball. Five of these patients (83.3%) showed an enhancement on CT or hyperintensity on MRI, and 4 (66.7%) showed scleral wall thickening. Choroidal detachment was found in 2 patients (33.3%). Associated ocular diseases were uveitis (n=9, 64.3%), optic neuritis (n=5, 35.7%), nodular scleritis (n=4, 28.6%), idiopathic orbital inflammatory disease (n=2, 14.3%), uveal effusion (n=1, 7.1%), and non-arteritic ischemic optic neuropathy (n=1, 7.1%) (*Table 2*).

Systemic steroids were administered in 11 (78.6%) patients, and intravenous steroid pulse therapy was administered in 5 (45.5%). In four patients (28.6%), immunosuppressive agents were additionally used, including cyclosporine (Cipol-N®, Chong Kun Dang, Seoul, Republic of Korea) in two, cyclophosphamide (Alkyloxan®, JW Pharmaceutical, Seoul, Republic of Korea) in one, and methotrexate (Methotrexate®, Yuhan, Seoul, Republic of Korea) in one. Intra-vitreal dexamethasone injections (Ozurdex®, Allergan, Irvine, CA, USA) were administered in two patients (14.3%). Biological therapeutic agent adalimumab (Humira®, AbbVie Inc., North Chicago, IL, USA) was administered in one patient who was refractory to corticosteroid and immunosuppressive therapy. Pars plana vitrectomy with silicone oil injection was performed in one patient (7.1%) for exudative retinal detachment with

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**Table 3** Treatment and follow-up outcomes of 14 patients with posterior scleritis

| Variable | Number (%)/mean ± SD |
|---|---|
| Treatment | |
| Topical antibiotics and steroids | 13 (92.9) |
| Topical NSAIDs | 4 (28.6) |
| Systemic steroids | 11 (78.6) |
| Systemic NSAIDs | 2 (14.3) |
| Systemic immunosuppressants | 4 (28.6) |
| Cyclosporine | 2 (14.3) |
| Cyclophosphamide | 1 (7.1) |
| Methotrexate | 1 (7.1) |
| Systemic biologics | 1 (7.1) |
| Intravitreal dexamethasone injection | 2 (14.3) |
| Vitrectomy | 1 (7.1) |
| Recurrence (eyes, events) | 3 (21.4%, 1.6±0.7) |
| Follow-up duration (months) | 31.6±39.2 |
| Final logMAR BCVA | 0.6±1.0 (P=0.878*) |

*, comparison of initial and final visual acuity using Wilcoxon's signed rank test. SD, standard deviation; NSAID, non-steroidal anti-inflammatory drugs; logMAR, logarithm of the minimum angle of resolution; BCVA, best-corrected visual acuity.

vitreous opacity. Patients were followed up for an average of 31.6±39.2 months. Recurrence was noted in three patients (21.4%), with an average recurrence rate of 1.6±0.7 times. The final LogMAR BCVA was 0.6±1.0, which did not significantly differ from that at the first visit (P=0.878) (*Table 3*).

Of the three patients with recurrence, one showed posterior scleritis associated with optic neuritis and idiopathic orbital inflammatory disease, which recurred despite administering intravenous steroid pulse therapy. Further recurrence was not observed after the administration of oral methotrexate. One patient in her 50s received intravenous steroid pulse therapy due to idiopathic orbital inflammatory disease, posterior scleral thickening, and choroidal detachment. Her initial visual acuity was limited to just perception of light. After 2 months of treatment, posterior scleritis with exudative retinal detachment developed, and despite intensive intravenous steroid pulse therapy and oral steroid administration, the condition did not improve; vitreous opacity developed subsequently. After vitrectomy with silicone oil tamponade, the retina re-attached, and the patient remained stable without recurrence. One patient with posterior scleritis had initially been under control with oral steroids; however, the patient had a recurrence after a few months. Improvement was observed after the administration of oral cyclosporine, with no further recurrence. All three relapsed patients did not have any rheumatologic disease.

Three patients with posterior scleritis showed no abnormalities on funduscopic examination. They visited the outpatient clinic after an average of 7.7±4.0 days after the onset of symptoms, and their initial visual acuity was 20/20. They had subjective visual deterioration, red eyes, and pain during eyeball movement. "T" sign and increased scleral thickness were observed on B-scan ultrasonography in all patients; however, only one patient showed the presence of inflammatory cells in the anterior chamber and vitreous cavity.

Two of the four patients with posterior scleritis associated with anterior nodules had an infectious origin; both had a history of ocular surgery. One patient had a cataract surgery 10 years ago, and visited with the symptom of decreased vision since 1 month. At the first visit, visual acuity was limited to counting fingers, and intraocular pressure was 4 mmHg. Conjunctival hyperemia and a pus-discharging scleral nodule were seen. B-scan ultrasonography confirmed the presence of choroidal detachment with choroidal effusion. From the results of the culture examination of the pus draining from the nodules, a superinfection with *P. aeruginosa* and coagulase-negative *Staphylococci* was noted. There were no signs of other systemic infections, as confirmed by head and neck, chest, and liver CT. The patient was successfully treated with intravenous administration of 3$^{rd}$ generation cephalosporin and ciprofloxacin. The patient's final vision improved slightly to 20/133. The other patient had undergone resection of pterygium on the right eye 15 years ago. Because of a newly developed scleral melting, the patient received a scleral graft 2 months ago. Conjunctival hyperemia and nodules were observed. The patient's initial visual acuity was 20/50 and intraocular pressure was 6 mmHg. Choroidal detachment was also noted. From the results of culture examination of the nodule sample, a superinfection with *P. aeruginosa* and coagulase-negative *Staphylococci* was identified. The patient was treated with intravenous administration of ampicillin/sulbactam and ciprofloxacin. The final visual acuity of the patient was 20/50, which did not differ compared to the first visit.

Representative pictures of non-infectious and infectious

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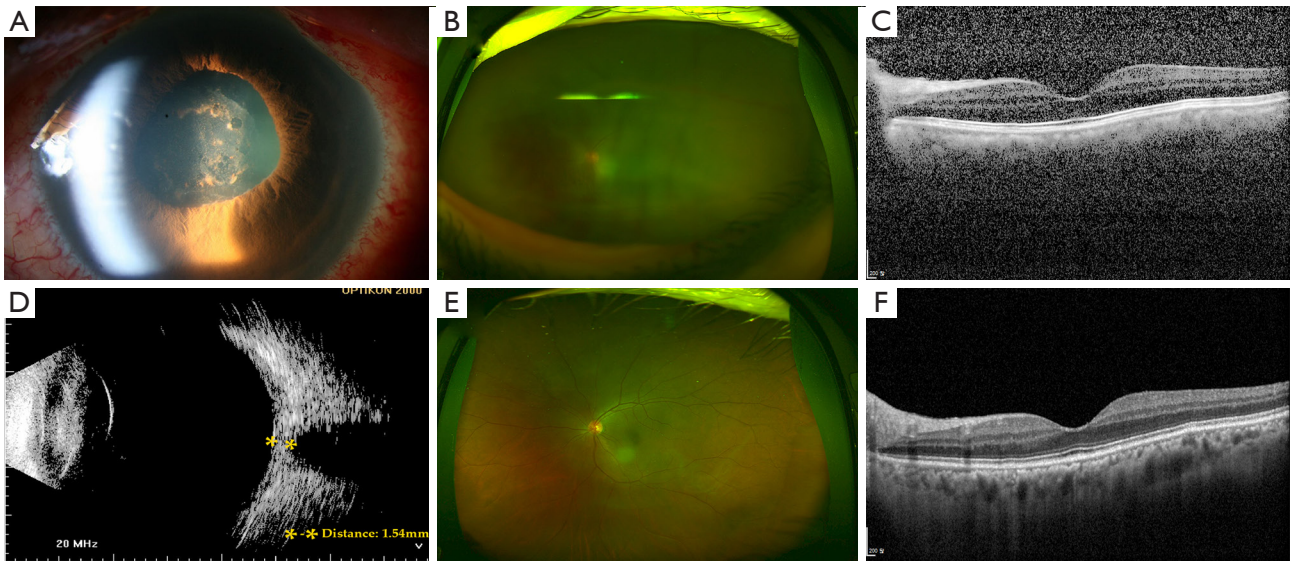


**Figure 1** A case of non-infectious posterior scleritis. A 57-year-old woman visited our clinic, complaining of lowered vision, pain, and hyperemia in the left eye for 3 days. The patient had a history of sero-negative spondyloarthropathy and was positive for HLA-B27. At that time, her visual acuity was 20/1,000 and intraocular pressure was 13 mmHg. (A) Severe conjunctival injection, corneal edema with folding of the Descemet's membrane, and inflammatory cells (4+) in the anterior chamber are observed. Synechia with dysmorphic pupil, and multiple iridial pigments on the lens surface are present. (B) Funduscopic examination revealed vitreous haziness. The optic disc alone is visible, though faintly. (C) OCT revealed absence of macular edema. Because of vitreous haziness, OCT signals are reduced. (D) B-scan ultrasonography revealed an increase in the choroid and scleral thickness. The patient was administered topical steroids eight times a day, topical cycloplegic three times a day, and oral prednisolone 60 mg daily. After 1 week, the signs and symptoms improved. The dose of prednisolone was tapered by 10 mg each week over 6 weeks, and that topical steroids was tapered to end the treatment after 6 weeks. After 2 months of treatment, the visual acuity of the left eye improved to 20/25, and conjunctival injection disappeared. The cornea was clear, and there were no inflammatory cells in the anterior chamber. (E) Funduscopic examination revealed absence of vitreous haziness or abnormal findings. (F) OCT demonstrated absence of any definite structural abnormality. OCT, optical coherence tomography.

posterior scleritis are presented in *Figures 1*,*2*.

## Discussion

This study demonstrated that most posterior scleritis cases are of non-infectious origin. Uveitis and anterior nodular scleritis are commonly present. However, some patients cannot be diagnosed using funduscopic and slit lamp examination alone, and additional B-scan ultrasonography may be required. Most patients can be treated using topical and systemic steroids, whereas some patients require additional immunosuppressive and biological therapeutics.

Diagnosis of posterior scleritis is sometimes challenging. Funduscopic or OCT findings involving the posterior segment, such as choroidal effusion and detachment, and cystoid macular edema, are helpful in the diagnosis (8,14,15); however, we encountered three patients who did not show abnormal funduscopic findings. B-scan ultrasonography was of diagnostic value in all patients, particularly in these three patients who showed no abnormalities on funduscopic examination. In this study, patients who did not show unusual funduscopic findings complained of subjective vision loss, injected conjunctiva, and severe pain during eye movement. Performing additional tests such as B-scan ultrasonography to identify the "T" sign and/or increased scleral thickness could help in the early diagnosis and management of posterior scleritis without abnormal fundus features.

Imaging modalities such as CT and MRI can also be useful in patients with posterior scleritis. CT or MRI was performed in eight out of 14 patients in this study, of whom six showed abnormal findings. CT findings commonly seen in posterior scleritis include eccentric enhancement of the globe wall and eccentric thickening of the sclero-uveal rim;

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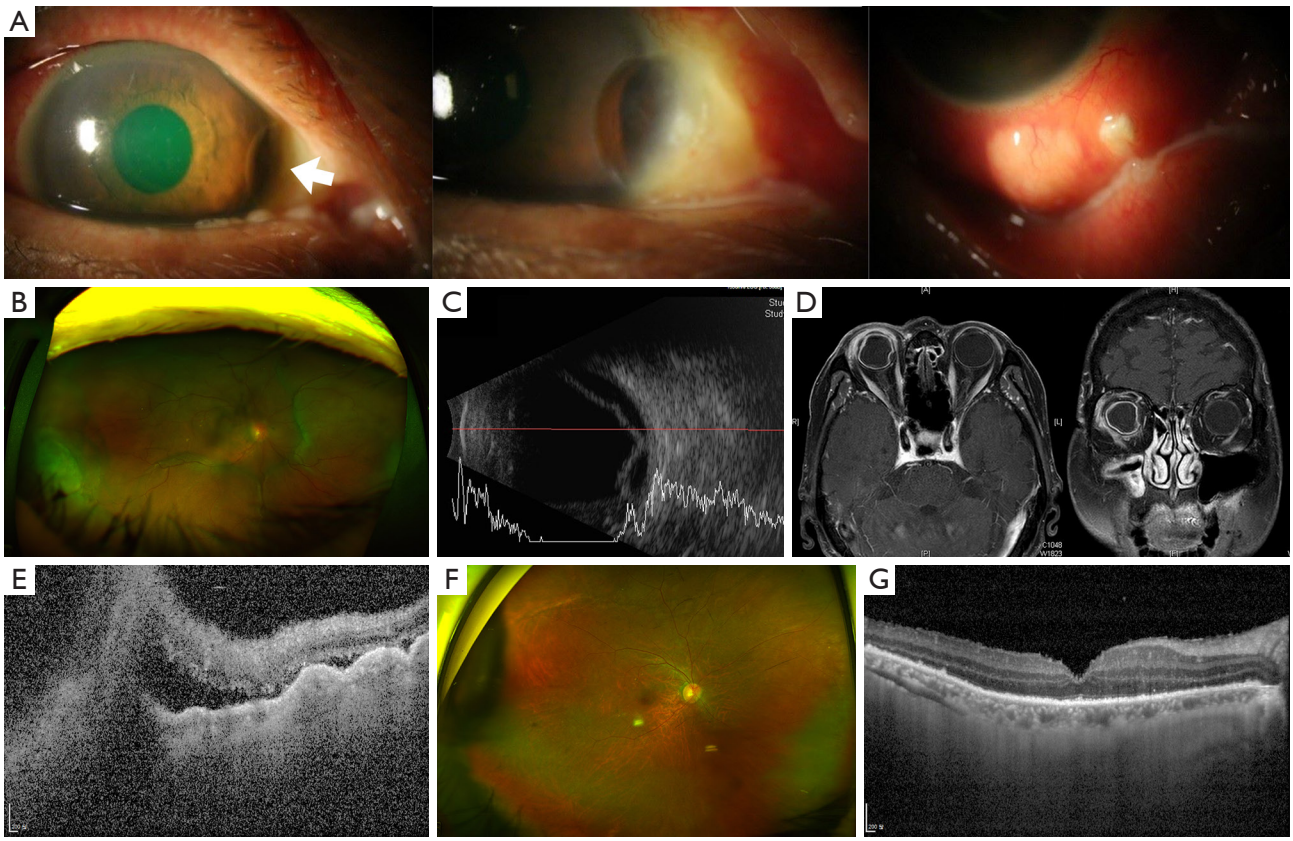


**Figure 2** A case of infectious posterior scleritis. An 80-year-old woman presented with a reduction in visual acuity for 1 month. She had been operated for cataract 10 years ago. At the first visit, visual acuity was ability to count fingers, and intraocular pressure was 4 mmHg. Cells were present in the anterior chamber (3+). (A) Severe hyperemia of the conjunctiva, a yellowish nodular protruding mass around the limbus, and focal scleral thinning are seen (arrow). (B) Funduscopic examination revealed choroidal folding. (C) B-scan ultrasonography confirmed choroidal detachment. (D) Left: T1-weighted fat suppression magnetic resonance imaging revealed high signal intensity of the scleral wall and adjacent peri-ocular tissue, and high signal intensity in front of the lateral rectus muscle; right: coronal plane showed high signal intensity of the scleral wall and the maxillary sinus wall. (E) OCT demonstrated choroidal folding, choroidal effusion, and subretinal fluid. Third generation cephalosporin and ciprofloxacin were administered intravenously for 5 days, and then orally for another week. Five months after the patient's first visit, visual acuity improved to 20/133, and intraocular pressure was 8 mmHg. (F) Choroidal folding disappeared and the fundus appeared stable. (G) OCT reveals absence of subretinal fluid. OCT, optical coherence tomography.

scleral enhancement and thickening are frequently observed on MRI (16). In these patients, findings such as scleral enhancement, scleral thickening, and choroidal detachment were assessed to establish the diagnosis. However, because two patients did not show any specific findings on CT or MRI, we speculated that CT or MRI may be inconclusive. This reaffirms the significance of careful clinical examination along with the interpretation of multimodal imaging modalities including B-scan, CT, and/or MRI.

In this study, the recurrence rate was 21.4%. Two of the three patients who relapsed were stabilized after administration of immunosuppressants, following which there was no recurrence. The recurrence rate of posterior scleritis is higher in younger patients, those with Crohn's disease, and those receiving immunosuppressive drugs such as mycophenolate mofetil (4). In our study, no cases of recurrence in patients with posterior scleritis associated with systemic rheumatologic diseases were observed. The relapse rate was also within the previously known range of 15.8–40% (4,8). Interestingly, two of the three relapsed patients received intravenous steroid pulse therapy for the accompanying idiopathic orbital inflammatory

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disease. Based on the relationship between idiopathic inflammatory scleritis and extraocular abnormalities, it has been hypothesized that idiopathic inflammatory scleritis falls under the spectrum of idiopathic orbital inflammatory diseases (16,17). In this study, patients with idiopathic orbital inflammatory disease had a higher relapse rate probably because the inflammation developed in an area wider than the sclera alone. Aggressive immunosuppressive therapy and careful follow-up may be helpful in successful treatment and prevention of relapse.

Two patients with infectious posterior scleritis showed pus-containing scleral nodules. Infectious scleritis is often associated with risk factors such as previous ocular surgery or trauma (18), and *Pseudomonas*, gram-negative bacilli, and *Staphylococcus* are the main causative strains. Systemic antibiotics and/or surgical treatment is often required (19). In this study, two patients diagnosed with infectious scleritis had a history of ocular surgery, and importantly, one of these developed infectious posterior scleritis after receiving a scleral graft for the treatment of scleral melting. Bacterial culture was performed, and empirical antibiotic therapy was started immediately, resulting in complete resolution of the infection and globe salvage. Misdiagnosis as non-infectious inflammatory scleritis and treatment with steroids, without the coverage of antibiotics, can worsen the infection. Hence, if patients present with a history of ocular surgery or trauma, with ocular findings suggestive of scleritis, especially with pus-containing nodules, infectious posterior scleritis should always be considered as a differential diagnosis.

This is the first study to analyze the clinical characteristics of Korean patients diagnosed with posterior scleritis. Moreover, this study comprised a relatively large group of patients, analyzing a total of 14 patients with infectious and non-infectious posterior scleritis. However, the limitations of this study include its retrospective study design, small number of patients with infectious posterior scleritis, and the large variation in the patients' follow-up period. Since the number of patients with posterior scleritis visiting a single institution is limited, better results can be obtained in a multi-centric prospective clinical analysis of clinical features.

## Conclusions

In conclusion, early diagnosis and aggressive treatment of posterior scleritis are recommended, since impaired vision does not improve significantly after treatment. Differential diagnosis of posterior scleritis may be challenging, particularly in those with the absence of typical funduscopic features. Therefore, it is advisable to include the possibility of posterior scleritis in the differential diagnosis, especially in those with poor vision, ocular pain, or severe conjunctival injection. If there are concomitant systemic or orbital diseases, aggressive treatment using immunosuppressants or biological therapeutics might be helpful in the treatment and prevention of recurrence.

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## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://atm.amegroups.com/article/view/10.21037/atm-22-721/rc

*Data Sharing Statement:* Available at https://atm.amegroups.com/article/view/10.21037/atm-22-721/dss

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*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. This study was conducted in accordance with the tenets of the Declaration

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of Helsinki (as revised in 2013), and was approved by the Institutional Review Board (IRB) of the Gangnam Severance Hospital retrospectively (IRB approval No. 3-2020-0304). The necessity to obtain informed consent was waived by the IRB.

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