

The clinical features of posterior scleritis with serous retinal detachment: a retrospective clinical analysis

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Abstract

• **AIM:** To summarize the clinical features, systemic associations, risk factors and choroidal thickness (CT) changing in posterior scleritis (PS) with serous retinal detachment.

• **METHODS:** This retrospective study included 23 patients diagnosed PS with retinal detachment from August 2012 to July 2017. All patients' medical history and clinical features were recorded. The examinations included best corrected visual acuity (BCVA), intraocular pressure (IOP), fundus examination, and routine eye examinations. Posterior coats thickness (PCT) was determined by B-scan ultrasound, the CT was measured by enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT) and clinical data were compiled and analyzed.

• **RESULTS:** After application of extensive exclusion criteria, 23 patients with PS remained (13 females, 10 males). The average age at presentation was 29.5±9.24 years old. Ocular pain and blurred vision were the two most common complained symptoms by patients. Anterior scleritis occurred in 12 patients, which was confirmed by ultrasound biomicroscopy (UBM) examination. Despite all patients displaying serous retinal detachment in their macula, no fluorescein leakage was observed in the macular area. Optic disc swelling was documented in 10 of the 23 eyes. From B-scan ultrasound examination, the PCT increased with fluid in Tenon's capsule demonstrated as a typical T-sign. The average PCT was 2.51±0.81 mm in the

PS-affected eyes and only 1.09±0.29 mm in the unaffected eye ($P<0.0001$). The subfoveal CT was 442.61±55.61 μm, which correlated with axis length ($r=-0.65$, $P=0.001$) and PCT ($r=0.783$, $P<0.001$). The BCVA and IOP did not correlate with either CT or PCT.

• **CONCLUSION:** PS with serous retinal detachment presented a variety of symptoms, such as pain, visual loss, and physical indicators. Typical T-sign detected by B-scan ultrasound is a useful confirmatory sign for PS diagnosis. Pathological increases in CT might be a potential predictive factor for inflammation.

• **KEYWORDS:** choroidal thickness; scleritis; serous retinal detachment; clinical features; posterior scleritis

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INTRODUCTION

Posterior scleritis (PS) is an uncommon and under-diagnosed condition caused by inflammation of the sclera (*i.e.* the fibrous outer layer of the eye)^[1]. Due to its low incidence and variable clinical presentation, the mechanism underlying PS remains unclear and the majority of the research to date has focused instead on characterizing its clinical features, and optimizing diagnosis, treatment, and patient outcome^[2-4]. Based on the anatomical location, PS presents with a range of clinical features, especially in fundus change, and is often misdiagnosed as intraocular inflammation^[5], ocular tumors^[6], or orbital inflammation^[7]. Such misdiagnoses^[8] increase the likelihood of incurring irreversible visual damage including eventual vision loss. Given the high rates of retinal detachment in PS^[4], this manifestation can be easily misdiagnosed central serous chorioretinopathy (CSC), which is characterized by retinal detachment involving macula or not. There is currently a paucity of research dedicated to detailing the differences between these two diseases. These situation motivated our interest in the clinical features and risk factors involved in PS specifically with retinal detachment.

Recently some studies have suggested that choroidal expansion might play an important role in PS^[9-10]. Due to advances in ophthalmic imaging technology, choroidal thickness (CT) can be noninvasively measured by enhanced depth imaging spectral-domain optical coherence tomography (EDI-OCT). While studies have implicated the importance of CT in PS, but none have focused on how CT is involved in PS with retinal detachment^[10-11]. Furthermore, CT involvement is increasingly recognized as a feature of PS. However, little is known about the association between CT and other ocular biometric parameters, such as visual acuity, axial length (AL) and posterior coats thickness (PCT), in PS, let alone in PS with retinal detachment. Therefore, this study aimed to fully characterize the clinical features, systemic associations, and risk factors in PS with retinal detachment and to investigate the clinic findings and association of CT in PS with serous retinal detachment by a retrospective clinical analysis.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the Ethical Review Committee of the Second Affiliated Hospital of Wenzhou Medical University, Wenzhou, China. All procedures adhered to the tenets of the Declaration of Helsinki for research involving human subjects. Written informed consent was obtained from all participants enrolled in this study. All potential study participants were from Chinese Han population and patients of the aforementioned clinic.

Subjects and Enrollment Criteria A retrospective review of patient medical records from the ophthalmological clinic at the Second Affiliated Hospital of Wenzhou Medical University between August 2012 and July 2017 was performed to identify patients with diagnosis of PS. PS was diagnosed by presence of: 1) acute or sub-acute symptom onset; 2) eye pain with or without decreased visual acuity, accompanied by various fundus changes (*e.g.* optic disc edema, retinal phlebectasia, exudative retinal detachment); 3) posterior sclerochoroidal wall thickening and fluid in the Tenon's capsular with low echo and fascial sac edema in the eye coats, defined as typical T-sign^[3-4,12], revealed by B-scan ultrasound examination.

Patients with any of the following conditions were excluded: incomplete clinical information, infection with acute orbital cellulitis, tuberculosis, or syphilis; ocular trauma or tumor; the orbital inflammatory pseudotumor; Graves' ophthalmopathy; macular retinal detachment with vascular leakage in fundus fluorescein angiography (FFA); rhegmatogenous retinal detachment; any obvious cataract leading to an intumescent lens; a history of intraocular surgery; clinically relevant opacities of the optic media; and low-quality images due to unstable fixation or a severe cataract.

Of the 69 records initially identified, 16 were excluded because of insufficient clinical detail to ensure a correct diagnosis or

lack of satisfactory ultrasonography data. Thirty PS patients were not included because no sub retinal fluid was detected in our research. Finally 23 patients were included in this study. All enrolled patients were diagnosed with PS presenting serous retinal detachment over the macula.

Study Measurements Demographic data of age, sex, and blood pressure were collected. Detailed clinical information regarding original diagnosis, disease onset, clinical presentation, ultrasound data, and systemic associations was recorded. All patients were regularly tested with regular blood test, C reactive protein (CRP), erythrocyte sedimentation rate (ERS), P- and C-anti-neutrophil cytoplasmic antibodies (ANCA), antinuclear antibody, PANA, antistreptolysin O antigen test, dsDNA antibody, SS-A and SS-B antibody, complement series, serum amyloid A (SAA), rheumatoid factor, immunoglobulin G and M, and TORCH test (for *Toxoplasma gondii*, Rubella virus, Cytomegalovirus, Herpes simplex virus). All subjects underwent a thorough ophthalmic evaluation, including the best corrected visual acuity (BCVA), slit-lamp biomicroscopy, intraocular pressure (IOP) measurement (applanation tonometry), fundus examination, ultrasonographic biomicroscopy (UBM), ultrasound B-mode scanning (B-scan, Bio-vision Echoscans, France), FFA, refractive error examination, and axial length (AL) measured with partial optical coherence interferometry (IOLMaster, Carl Zeiss Meditec, German). All examinations were performed upon diagnosis by experienced ophthalmologists who were blinded to the patients diagnosis.

EDI-OCT Examination As previously described^[13], CT was determined using the Spectralis device (Heidelberg Engineering, Heidelberg, Germany), by using the device's automatic averaging (about 100 real-time frames were averaged) and eye-tracking features. First of all, in order to estimate optical magnification and achieve accurate comparisons across individuals, keratometry readings and the refraction data were collected and entered into the Spectralis software program. For the aim of ensuring high-quality images, the quality of choroidal imaging was judged according to the signal-to-noise ratio, and only images ratios ≥ 20 dB were collected and used for further analysis. The resulting scans were visualized and measured by the measuring software, the standard Spectralis OCT (v1.5.12.0; Heidelberg Engineering). The CT was measured from the outer portion of the retinal pigment epithelium (RPE) to the inner surface of the sclera as indicated in Figure 1C by arrow. CT was measured at the fovea in all subjects. Experienced ophthalmologists, blinded to the clinical diagnoses of the patients, performed EDI-OCT examinations and measurements and the latter were averaged before further analysis.

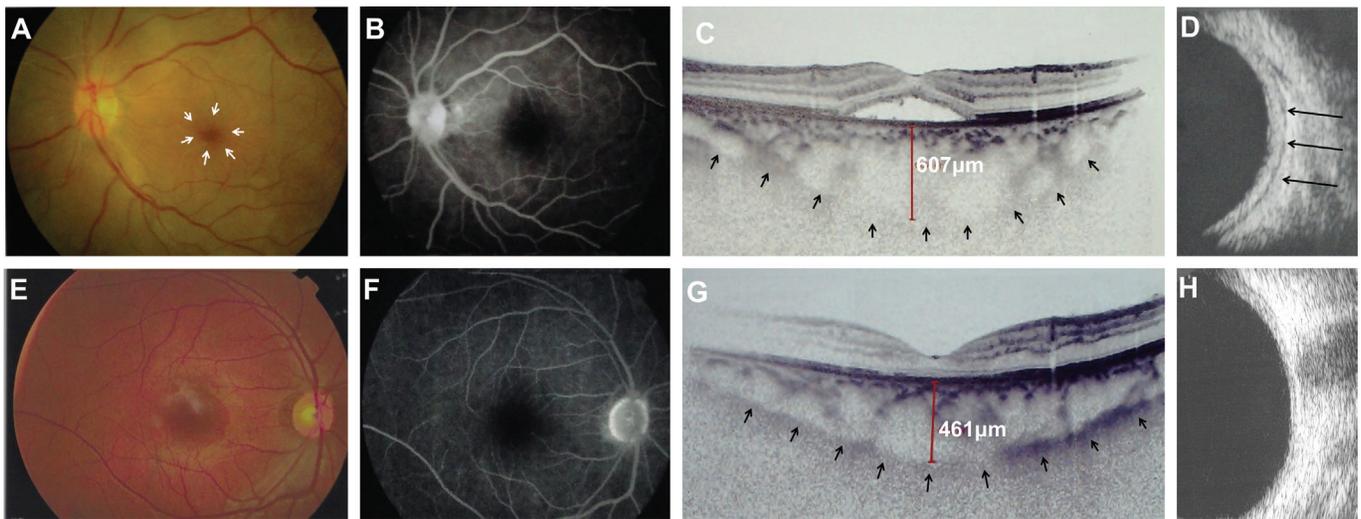


Figure 1 Clinical findings of posterior scleritis in case 1 A: Fundus imaging of disc swelling, retinal phlebotasia, and serous retinal detachment (white arrow) at the macula; B: Fluorescein leakage around the optic nerve at the late stage in FFA; C: EDI-OCT scanning of serous detachment over the macula. The short arrows indicate the chorioscleral interface and red segment length indicate subfoveal CT (the CT of the left eye was 607 μm at the initial visit); D: Ultrasound scan of scleral thickening and black arrows denote the posterior boundary of the sclera. E-H: Normal structure in the unaffected eye of case 1; fundus photography (E), FFA (F), EDI-OCT (G) and B-scan ultrasonography (H).

Statistical Analysis Data were analyzed using SPSS 17.0 software (SPSS, Chicago, IL, USA). Levene's test was used to confirm normal distribution. A paired *t*-test was used to determine changes in macular CT. Pearson's correlation analysis was performed to evaluate the relationships between the changes in CT, BCVA, AL, and PCT. $P < 0.05$ was considered statistically significant.

RESULTS

Demographic Characteristics During the five-year period from August 2012 to July 2017, nearly 300 000 patients were referred to the Ophthalmology Department of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University. Of these, 69 patients (0.023%) had PS and 33.33% of the patients with PS also presented with retinal detachment; therefore, a total of 23 patients (23 eyes) included in the study population (Table 1).

Clinical Characteristics The main characteristics of the study participants are presented in Table 1. This study included 13 female and 10 male patients from 19 to 57 years old (mean age 29.5 ± 9.24 y), 78.26% of which were between 21 and 40 years old. Unilateral involvement was present in all of the patients. Ocular pain (78.26%) and vision loss (86.96%) were the two most commonly reported symptoms. Interestingly, there were 2 patients (8.96%) without symptoms identified just through routine physical examination. Around 26.09% patients were diagnosed during their first visit, while the remaining 73.91% patients were initially diagnosed with and treated for other retinal diseases (e.g. CSC with 7 cases, neuroretinitis with 10 cases). Sixteen patients (69.5%) visited the clinic within one month of symptom onset. At the time of presentation, four patients (17%) were documented as having systemic

associations including ANA+, hypertension, allergic rhinitis, and Sjögren syndrome. Eighteen patients (78.26%) had a single episode of PS and five patients had multiple episodes of PS, less than 4 episodes.

Visual Acuity The BCVA (logMAR) was determined for all patients. As described in Table 2, three (13.04%) patients had a BCVA of 0 logMAR at presentation, 11 (47.83%) patients were below 0.5 logMAR, 3 (13.04%) patients between 0.5-1 logMAR, and 6 (26.09%) patients over 1 logMAR. No patients were found to be amaurosis or light perception using this test. The mean of the logMAR visual acuity was 0.61 ± 0.54 logMAR. In their other eyes, 20 (86.96%) patients had a BCVA of 0 logMAR and 3 (13.04%) patients were between 0.08-0.2 logMAR (average 0.017 ± 0.045). As expected, the BCVA in PS-affected eyes was worse than in the unaffected eyes. The BCVA decrease in PS was not related to the unaffected eyes according to Pearson's correlation coefficient ($r = 0.105$; $P = 0.635$).

Anterior Segment PS occurred in 12 (52.17%) patients with associated anterior scleritis, which can cause symptoms of conjunctival congestion and tenderness in the superficial sclera (Figure 2A). UBM examination confirmed the presence of swelling in the sclera (Figure 2B). Anterior uveitis occurred in 8 (34.78%) patients with PS as indicated by anterior chamber cell or flare at the time of presentation. There were no hypopyon, synechia, or cataracts found in any of the cases. In the unaffected eye, the anterior ocular portion remained within expected limits. Ocular hypertension was detected neither in the PS-affected eye (14.21 ± 6.61 mm Hg) nor in the unaffected one (15.10 ± 2.36 mm Hg). No statistically significant differences were observed in IOP between the PS-affected and unaffected eyes.

Posterior scleritis with serous retinal detachment

Table 1 Demographic characteristics of the 23 patients

No.	Sex	Age, y	Ocular pain	Visual acuity ^a	Anterior scleritis	AC cell or flare	Retinal phlebectasia	Annular retinal detachment	Optic nerve swelling	Systemic factors
1	M	23	Yes	1	Yes	Yes	Yes	Yes	Yes	No
2	M	23	Yes	0.1	Yes	Yes	Yes	Yes	Yes	No
3	F	41	Yes	0.5	Yes	No	Yes	Yes	Yes	ANA+
4	F	24	Yes	0.2	Yes	Yes	Yes	Yes	Yes	No
5	F	19	Yes	0.7	No	Yes	Yes	Yes	Yes	No
6	M	24	Yes	0.4	Yes	Yes	Yes	Yes	No	No
7	F	36	Yes	0.7	No	No	Yes	Yes	No	No
8	F	57	Yes	0	No	No	No	Yes	No	No
9	F	28	Yes	0.5	No	No	Yes	Yes	Yes	No
10	F	26	Yes	1.1	No	No	No	Yes	No	No
11	M	27	Yes	0	Yes	Yes	Yes	Yes	No	No
12	M	25	Yes	0.5	No	No	No	Yes	No	No
13	M	21	Yes	1.2	No	No	No	Yes	Yes	Rhinallergosis
14	F	26	Yes	0.2	Yes	No	No	Yes	No	No
15	M	37	No	1.7	Yes	No	Yes	Yes	No	No
16	F	19	No	1	No	No	Yes	Yes	No	Hypertension
17	F	38	Yes	0.4	No	No	Yes	Yes	No	No
18	F	46	No	2	No	No	No	Yes	No	SS
19	M	23	Yes	0.1	No	No	No	Yes	No	No
20	F	22	Yes	0.2	Yes	No	No	Yes	No	No
21	F	22	Yes	1.3	Yes	Yes	Yes	Yes	Yes	No
22	M	35	No	0	Yes	Yes	Yes	Yes	Yes	No
23	M	36	No	0.1	Yes	No	Yes	Yes	Yes	No
<i>n</i> (%)			18 (78.26)	20 (86.96)	12 (52.17)	8 (34.78)	15 (65.22)	23 (100)	10 (43.48)	4 (17.39)

AC: Anterior chamber; ANA: Antinuclear antibody; SS: Sjögren syndrome. ^alogMAR best corrected visual acuity.

Table 2 The basic clinical features of posterior scleritis in 23 cases

Clinical features	Eyes (%)
Age	
≤20y	2 (8.70)
21-40y	18 (78.26)
>40y	3 (13.04)
Gender	
Male	10 (43.48)
Female	13 (56.52)
Complaint pain	18 (78.26)
Complaint vision loss	20 (86.96)
Diagnosis rate	6 (26.09)
Onset time (1mo)	16 (69.57)
Visual acuity (logMAR)	
0	3 (13.04)
>0-0.5	11 (47.83)
>0.5-1	3 (13.04)
>1	6 (26.09)
Total	23 (100)

Posterior Segment A number of abnormalities were observed in PS-affected eyes. All of the patients displayed dome-shaped macular retinal detachment (Figures 1A, 2C, white arrows)

but varied in area and sizes (*e.g.* case 14 was larger than that case 1). All patients were tested using OCT scanning, which confirmed serous detachment over the macula (Figures 1C, 2E) and no abnormal findings were detected in the unaffected eye (Figure 1G). In order to figure out whether retinal detachment was due to exudation causing by RPE dysfunction, FFA examination was performed and no fluorescein leakage was observed around the macula regardless of stage (Figures 1B, 2D). The only positive association identified was between mild fluorescein leakage around the optic nerve and optic disc edema (Figure 1B). Mild optic nerve swelling was observed in 10 patients (43.48%) and about 15 (65.22%) patients were found to have retinal phlebectasia in the fundus examination (Figure 1A). No choroidal detachment or choroidal folds were observed in this study. In the unaffected eye, fundus imaging revealed normal structures (Figure 1E), which were further confirmed by FFA and OCT examination (Figure 1F, 1G).

Ultrasonography Examination B-scan ultrasonography is the most useful confirmatory analysis for PS diagnosis^[12], so all eyes had been examined with B-scan ultrasound. The longitudinal B-mode ultrasound scan showed diffuse PCT with fluid both in the Tenon's capsule and around the nerve sheath

Table 3 Clinical measurements in posterior scleritis and fellow eyes

n=23, mean±SD

Measurements	Posterior scleritis	Fellow eyes	Difference, mean (95%CI)	<i>t</i>	^a <i>P</i>
Visual acuity, logMAR	0.61±0.54	0.017±0.045	0.593 (0.36 to 0.83)	5.03	0.000
IOP, mm Hg	14.21±6.61	15.1±2.36	-0.89 (-2.5 to -0.69)	-1.19	0.248
AL, mm	22.94±1.24	24.4±0.58	-1.46 (-1.98 to -0.92)	-5.64	0.000
Choroid thickness, μm	442.61±55.61	246±42.31	196.61 (183.78 to 209.43)	31.8	0.000
Posterior coats thickness, mm	2.51±0.81	1.09±0.29	1.48 (1.26 to 1.93)	9.8	0.000

AL: Axial length; IOP: Intraocular pressure; CI: Confidence interval. ^a*P*<0.05 was considered statistically significant.

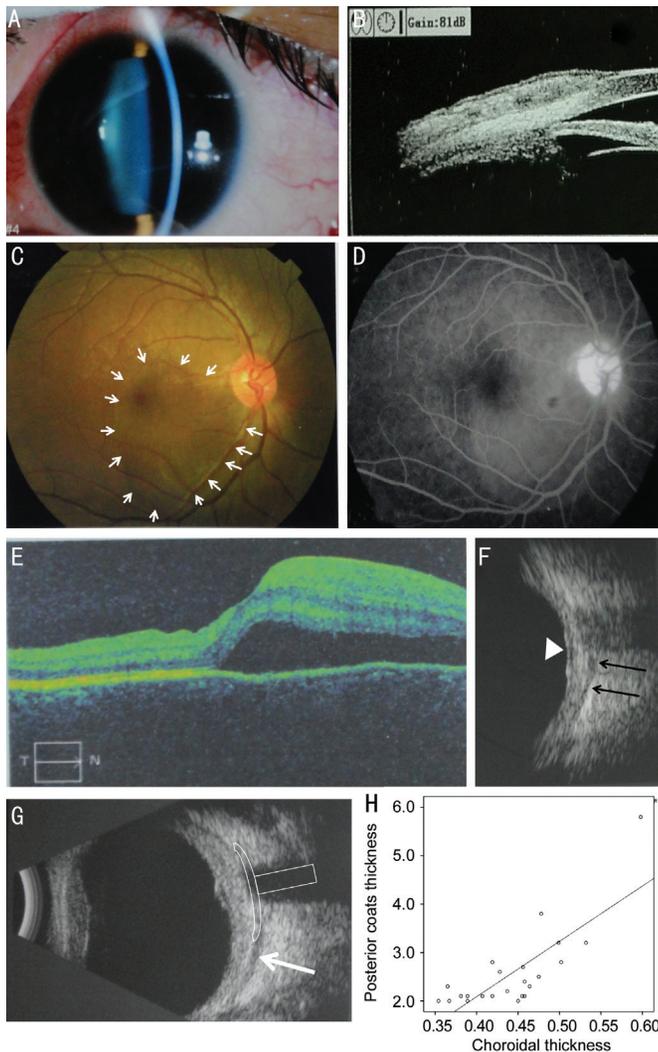


Figure 2 Clinical findings of posterior scleritis with serous retinal detachment

A: Anterior segment examination showed conjunctival congestion and anterior scleritis with tenderness in the upper part of the sclera; **B:** UBM examination detected swelling and hyperemia in the superficial fasciitis and sclera at the 12 o'clock; **C:** Posterior segment examination revealed retinal detachment at the macula (white arrow); **D:** FFA illuminated the serous retinal detachment at the macula but no fluorescein leakage was detected; **E:** The OCT scanning confirmed serous retinal detachment at the macula; **F:** B-scan ultrasonography confirmed scleral thickening (black arrows indicate the posterior boundary of the sclera and the retinal detachment is indicated by the white triangle); **G:** B-scan ultrasonography showing diffuse thickening of the posterior coats of the eye (3.6 mm) together with fluid in the Tenon's capsule (white arrow). The "T" sign is indicated by the white hollow shape. **H:** The increases in the PCT correlated positively with the increasing CT ($r=0.783$, $P<0.001$).

(Figures 1D, 2F, black arrows). A typical T-sign was observed in all cases (Figure 2G, white hollow shape). Furthermore, a B-scan ultrasound confirmed the retinal detachment (Figure 2F, white triangle) and optic nerve swelling in 10 cases (Figure 2G). In the unaffected eyes, the B-scan ultrasound revealed no abnormality (Figure 1H). The average PCT was 2.51 ± 0.81 mm in the PS-affected eyes, compared to 1.09 ± 0.29 mm in the unaffected eyes ($P<0.0001$; Table 3). The AL in the PS-affected eyes was 22.94 ± 1.24 mm and 24.4 ± 0.58 mm in the unaffected eyes (Table 3). The increase in PCT was related to the change in AL ($r=-0.795$, $P<0.001$) but not related to the BCVA ($r=0.117$, $P=0.596$).

Choroidal Thickness Changes in the Macula The CT of the subfoveal area was examined by EDI-OCT (Figure 1C, 1G, black arrows). In the macular region, the mean CT was highest at the subfoveal level in both eyes and it decreased gradually from the fovea. The average thickness of the subfoveal choroid was 442.61 ± 55.61 μm in the PS-affected eye and 246 ± 42.31 μm in the unaffected eye ($t=31.8$, $P<0.0001$; Table 3). In order to explore the parameters affected along with the change of CT in PS, we analyzed correlations between changes in CT and changes in BCVA, IOP, PCT and AL. At the subfoveal level, there were significant relationships between CT and PCT ($r=0.783$, $P<0.001$; Figure 2H) and also between CT and AL ($r=-0.65$, $P=0.001$); while there were no significant associations between CT and BCVA ($r=0.181$, $P=0.409$) and also no correlation with IOP ($r=0.59$, $P=0.79$).

DISCUSSION

This study analyzed the clinical features of PS with serous retinal detachment in 23 Han Chinese patients. Demographically, participants in our study were much younger at disease onset (29.5y, 78% below 40 years old) compared to a previous study performed in England (49.3y)^[12] but similar to a report from Yang *et al*^[2] (29.2y) which also based on Chinese patients. This finding suggests that young adults might have a higher risk of developing PS in the Chinese population.

It had been reported that systemic or local diseases may contribute to the development of PS^[2]. The present study found that 17% of patients with PS had systemic or local diseases, which was lower than described in studies conducted in England^[12] and Singapore (37%)^[4] but, again, consistent

with the study in China (13%)^[2]. These results suggest that the association between PS and autoimmune diseases may be weaker in China than in England and Singapore.

In the present study, we found that while blurred vision was one of the most common symptoms of PS, but the BCVA (logMAR) remained below 0.5 in half of our patients. McCluskey *et al*^[12] also found that around 17% of patients were not affected visually and that those older than 50 years old had a higher risk of experiencing vision loss. Similarly, Yang *et al*^[2] reported that around 61.4% of PS patients were observed with decreased vision. Taken together, these results indicate that BCVA might not be severely affected in PS, especially in its early stages. Potential explanations are: the relatively young age of the patients in our study; the original inflammation occurring in the sclera, not in the retina; and, the shorter duration between onset and diagnosis reported by the patients in this study.

Many studies have indicated that PS is highly associated with anterior scleritis at rates that range from 20% to 80% overall^[3-4,12]; specifically, 19% in Singapore^[4], 59% in England^[12], 24% in China^[2] and 52% in this current study. The incidence of comorbidity between PS and anterior scleritis seems to be higher in this report than previously documented. However, Yang *et al*^[2] and Wieringa *et al*^[14] used the term “panscleritis” to describe the scleritis that involves both the anterior and posterior segments. This difference in the definition of PS might contribute to the inconsistencies observed between these studies. Taken together, these results beg the question of whether the inflammation of the anterior scleritis secondary to the posterior segments and which risk factors are involved.

As expected, physical manifestations of PS varied in this study and included swollen discs, retinal neuroepithelial folds, macular edema, serous retinal detachment, and more. Importantly, we found 74% patients were initially misdiagnosed. This observation hints at the importance of differential diagnosis for PS with retinal detachment. In this and previous studies^[12,15], B-scan documented a range of ocular abnormalities in patients with PS corresponding to the fundus examination, thereby, the typical T-sign and PCT detected by ultrasonography were confirming signs, potentially necessary for the accurate diagnosis of PS. However, posterior coats thickening can occur under other conditions (*e.g.* presence of a tumor^[16] or orbital inflammatory disease, but the typical symptoms and signs could help us make the right differential diagnosis), so we suggest that PS should be diagnosed using well-established symptoms and B-scan results.

Recently, an abnormal increase in CT has been hypothesized to contribute to CSC^[17], primary open angle glaucoma^[18], and primary angle closure glaucoma^[13]. Given its anatomical

location, scleral inflammation can spread to the choroid, so CT was supposed to be affected due to inflammation in PS. In a previous study, Uchihori *et al*^[11] reported a PS patient that the subfoveal CT had grown to 418 μm in PS-affected eye by the initial examination, which is in line with our work (average of 442.61 μm). These observations further support that the increased CT might result from inflammation in PS but future studies that focus on the role of the immune system are needed to draw causal connections. Research on other diseases has revealed associations between pathological CT increases and clinical factors, such as AL, choroidal inflammation, and IOP^[19]. Based on data from this study, CT correlated with AL and PCT but not with IOP and BCVA. Given that the CT measurement included portions of the eyeball, the correlation between CT and PCT is intuitive. Since PCT was expected to positively correlate with inflammation in PS^[12], CT likely represents an additional and promising predictive factor. Some researchers have reported CT increases during the active inflammation period that decreased with anti-inflammation treatment over time^[10-11]. Despite the promising nature of the CT results for monitoring inflammation in PS, it does not seem to be related to BCVA. However, due to the limitations imposed by this study's sample size, further efforts are needed to elucidate the role of CT in PS pathology.

In addition to small study size, this study has some limitations. The retrospective nature of this study greatly limits the significance. And we rule out the infectious factor which was supposed to be associated with PS^[20]. Furthermore, most patients were referred by other hospitals and our study population may, therefore, represent the most serious cases.

In conclusion, our study characterized the clinical features of PS with retinal detachment, which frequently manifested as ocular pain and blurred vision in symptom, while serous retinal detachment and optic nerve swelling in sign. Typical T-sign detected by B-scan ultrasound provided a critical indicator for diagnosis. Pathological increases in CT and PCT might be a potential predictive factor for inflammation.

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