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INFLAMMATORY DISORDERS

Clinical characteristics of viral-associated Fuchs uveitis syndrome and Posner-Schlossman syndrome in a Chinese population

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Abstract

Purpose To identify the types of viral infection in aqueous humor (AqH) among patients diagnosed as Fuchs uveitis syndrome (FUS) or Posner-Schlossman syndrome (PSS) and investigate their relevance to clinical manifestations and visual outcome.

Methods A total of 375 patients and 171 patients were diagnosed as FUS or PSS in our department. AqH and serum samples from 68 FUS patients and 16 PSS patients were obtained during eye surgery. The viral etiologies, clinical features, auxiliary tests and visual prognosis of patients with FUS or PSS who underwent AqH analysis were analysed and compared.

Results Among 68 FUS patients, rubella virus (RV), cytomegalovirus (CMV), herpes simplex virus (HSV) and varicella-zoster virus were identified in 17, 11, 1 and 1 patients, respectively. Seven patients with CMV and 1 with HSV were identified in 16 PSS patients. In both FUS and PSS groups, virus-associated eyes had higher proportion of secondary glaucoma and worse visual prognosis as compared with non-virus-associated eyes (all $P < 0.05$). In FUS group, specifically, CMV infection manifested as more obvious anterior segment inflammation and lower corneal endothelial cell density (CECD). RV infection showed a higher percentage of vitritis. In PSS group, CMV-associated PSS had a lower retinal nerve fiber layer thickness and CECD, worse visual prognosis as compared with non-virus-associated PSS (all $P < 0.05$).

Conclusion Our study identified 4 types of viral infection in FUS and 2 types of viral infection in PSS. Virus-associated patients are usually associated with more obvious clinical signs and poor visual prognosis.

Keywords Fuchs uveitis syndrome · Posner-Schlossman syndrome · Viral infection · Herpesvirus · Rubella virus

Key messages

What is known:

- Viral infection has been increasingly implicated in the pathogenesis of Fuchs uveitis syndrome (FUS) and Posner-Schlossman syndrome (PSS). The differences regarding clinical manifestations and visual outcome in FUS and PSS patients with or without viral infection have not been well understood.

What is new:

- This study addressed the similarities and differences among FUS or PSS patients with or without viral infection. FUS and PSS patients with viral-infected have more obvious clinical presentations and should be monitored promptly.
- FUS and PSS patients with the homologous viral infection displayed a more similar constellation of ocular characteristics, and identifying the differences in details may be useful to differentiate these two diseases.

Introduction

Fuchs uveitis syndrome (FUS) is classically considered as a chronic non-granulomatous anterior uveitis characterized by mild inflammation, stellate or medium-sized keratic precipitates (KPs) and iris depigmentation. It accounts for 12.5% of patients with anterior uveitis in China and

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2–11% in European countries [1, 2]. The diagnosis of FUS is principally based on clinical findings, and there are no laboratory tests available. Although FUS can be diagnosed clinically, misdiagnosis is common due to its complex symptoms and diverse manifestations [3, 4]. It has been reported that a number of FUS patients were initially misdiagnosed as Posner-Schlossman syndrome (PSS), which usually presents as recurrent attacks of increased intraocular pressure (IOP) associated with mild non-granulomatous anterior uveitis [4, 5]. In addition, Posner and Schlossman [6] reported that heterochromia, an important sign of FUS, occurred in more than 30% of PSS cases. Evidently, both diseases share some similarities in terms of clinical manifestations.

The exact etiology and pathogenesis underlying FUS and PSS are not completely understood. Viral infections with rubella virus (RV), cytomegalovirus (CMV) and varicella-zoster virus (VZV) have been considered to be associated with both diseases [4, 7, 8]. Chee et al. [8] reported that CMV infection was observed in 52% of PSS patients and 42% of FUS patients, and characterized the clinical features of CMV-positive and negative cases. However, no study addressed the clinical characteristics and visual prognosis of CMV-associated FUS and CMV-associated PSS, a situation whereby both diseases may be mutually misdiagnosed. Furthermore, the wide spectrum of ocular manifestations and visual function of FUS and PSS patients with viral infection has not been adequately investigated in Chinese population. In this study, we identified viral etiologies in aqueous humor (AqH) among patients diagnosed as FUS or PSS and investigated their relevance to clinical signs as well as visual prognosis. We also compared the similarities and differences with respect to the clinical profiles of FUS and PSS patients with the homologous viral infection.

Methods

Subjects

A total of 2996 consecutive patients with anterior uveitis were referred to the First Affiliated Hospital of Chongqing Medical University from June 2019 to March 2023. Of these patients, 375 (13%) were diagnosed with FUS and 171 (6%) diagnosed with PSS. The diagnosis of FUS was based on recently proposed criteria that included three essential findings (iris depigmentation, absence of posterior synechiae, mild inflammation in the anterior chamber at presentation) and five associated findings (unilateral involvement, cataract, vitreous opacities, absence of acute symptoms and characteristic iris nodules). The diagnosis of FUS required all essential findings, and the presence of associated findings further strengthened the diagnosis [3]. The clinical diagnostic criteria for PSS were based on the following clinical characteristics [9]: (a) recurrent attacks of unilateral elevated IOP in association with mild nongranulomatous anterior uveitis, and attacks last few hours to few weeks; (b) patients usually complain about decreased vision, mild discomfort, halos; (c) corneal edema, elevated IOP, open angle, KPs, few cells and minimal flare are usually seen in the affected eye; (d) normal visual fields and optic disc, and normal IOP between attacks. Patients with trauma, retinal disease, or any other ocular disorder, and those with less than 3 months of follow-up were excluded from this study. During the follow-up period of 3–42 months, 105 FUS patients and 28 PSS patients developed complicated cataract, while 21 FUS and 16 PSS patients developed glaucoma as evidenced by glaucomatous disc and visual field changes [10, 11]. Among them, 68 FUS patients and 16 PSS patients underwent corresponding ocular surgery in our department, and their AqH and serum were simultaneously collected during the surgery. As the chronic nature of FUS and polymerase chain reaction (PCR) assay may show negative results for patients with a long history of the disease, it has been suggested that Goldmann-Witmer coefficient (GWC) can be a relatively reliable parameter for identifying viral infection in infectious uveitis [12, 13]. The concentrations of specific immunoglobulin G (IgG) against herpes simplex virus (HSV), VZV, CMV, RV and total IgG in AqH and serum were determined by enzyme-linked immunosorbent assay using commercial kits (Ruixin Biotechnology) and used to calculate GWC. To ascertain the presence of viral infection in the AqH excluding other possibilities, positive laboratory results were defined as GWC > 4 as it has been definitely considered as an indicator for the local antibody production [14, 15]. AqH and serum samples from 10 patients with age-related cataract were obtained during cataract surgery serving as controls. All individuals signed informed consent forms. The study was approved by the Institutional Review Board of the First Affiliated Hospital of Chongqing Medical University and complied with the Declaration of Helsinki.

Data collection and treatment

We have established a protocol for the collection of database and samples from patients with variety uveitis, including FUS and PSS, based nomenclature, categorization and diagnostic criteria endorsed by the International Uveitis Study Group and Standardization of Uveitis Nomenclature Working Group as well as the generally acknowledged system in evaluating the intraocular inflammation [16]. Data were extracted from

medical records including demographics, diagnosis, uveitis laterality, best-corrected visual acuity (BCVA), IOP, ocular manifestations, complication, and auxiliary examinations such as corneal specular microscopy, optical coherence tomography (OCT), visual field, ultrasound biomicroscopy (UBM), B-scan ultrasonography were performed according to clinical necessary. FUS and PSS patients were analyzed for preoperative auxiliary examination results after intraocular inflammation subsided, and the corresponding results were obtained from the same machine. The level of anterior segment inflammation was evaluated based on the Standardization of Uveitis Nomenclature criteria [17]. The grade of iris depigmentation has been described in our previous study by using a slit-lamp biomicroscope with a narrow slit-beam to observe the translucent zone of iris [3].

FUS patients generally may not require corticosteroids, topical use of corticosteroids for short time (5–7 days) may be needed if there are obvious anterior chamber inflammation. PSS patients were usually treated with topical corticosteroid in combination with topical antiglaucoma agents to suppress intraocular inflammation and reduce the increased IOP during disease attacks. Mannitol was used for the treatment of PSS patients with higher IOP unresponsive to the topical antiglaucoma therapy. As for the treatment of complicated cataract, ultrasound phacoemulsification with intraocular lens implantation was performed in these FUS and PSS patients. Antiglaucoma surgery including glaucoma valve implantation and trabeculectomy was recommended for the FUS or PSS patients with glaucoma if they failed to response to the antiglaucoma agents.

Statistical analysis

Statistical analysis was performed using SPSS version 25.0. Quantitative variables were presented as means ± standard deviations or medians and interquartile range, and assessed using the independent samples *t*-test and Mann–Whitney *U* test. Categorical variables were presented as numbers and percentages and compared with χ^2 test and Fisher exact test. Convert BCVA to logarithm of the minimum angle of resolution (logMAR) for calculation. Final LogMAR BCVA was defined as the patient's visual outcome at six months after surgery. For assessment of the association between retinal nerve fiber layer (RNFL) thickness and peak IOP, as well as the association between CMV-IgG in AqH and corneal endothelial cell density (CECD), Pearson and Spearman rank tests were used. $P < 0.05$ was considered statistically significant.

Results

AqH analysis was performed in 68 FUS patients and 16 PSS patients. All of them had unilateral involvement. According to the GWC results, among these 68 FUS patients, 1 (1%),1 (1%),11 (16%) and 17 (25%) patients were affected by HSV, VZV, CMV, and RV, respectively. Seven out of 16 cases of PSS were diagnosed as CMV-associated PSS (44%) and 1 case diagnosed as HSV-associated PSS (6%). All 10 patients with age-related cataract had a GWC-negative result.

Comparison of clinical manifestations between Fuchs uveitis syndrome and Posner-Schlossman syndrome

The demographics, clinical characteristics, auxiliary examinations and visual prognosis of patients diagnosed as FUS or PSS are shown in Table 1. The mean age of disease onset of FUS and PSS patients was 34.0 and 42.6 years, respectively, showing a significant difference between both groups ($P = 0.014$). Male patients were observed in 44% of FUS and 56% of PSS, and there was no statistical difference concerning male-to-female ratio between the two groups. As for clinical signs, there was no significant difference with regard to initial visual function between both groups. However, A poor visual prognosis was seen in PSS patients as compared to FUS patients ($P = 0.015$). Fourteen out of 16 (88%) PSS patients had an IOP > 22 mmHg at their first visit to our uveitis center, whereas this sign was observed only in 19% of FUS patients. The median peak IOP in FUS patients and PSS patients was 16.0 and 33.5 mmHg during the follow-up, with significant differences between both groups ($P < 0.001$). More than 70% of FUS patients and PSS patients had KPs at their first visit to our uveitis center. FUS patients mostly showed stellate or medium-sized KPs with a diffuse distribution pattern, whereas PSS patients mainly had a few medium-sized KPs mostly distributed in the lower area of the pupil. All FUS patients presented with various degree of diffuse iris depigmentation, while only 44% of PSS patients had iris depigmentation which was uneven in appearance and different from that observed in FUS patients ($P < 0.001$) (Fig. 1). Approximately 30% of FUS patients had Koeppe nodules and/or Busacca nodules, usually presenting with a fluffy appearance, which are different from those observed in granulomatous uveitis (Fig. 2), whereas none of the PSS patients had these nodules($P = 0.038$). Neither FUS nor PSS patients had posterior synechia. As for auxiliary examinations, OCT was nonselectively performed in 13 PSS patients and 47 FUS patients. Eight PSS patients had varying degrees of reduced RNFL thickness in all quadrants, whereas 6 FUS patients had thin RNFL mostly in association with elevated IOP. Visual field defect was observed in 56% of PSS patients, while it was detected only in 21% of FUS patients ($P = 0.017$). The mean CECD was significantly lower in the PSS group (1,979.3 cells/mm^2) than in the FUS group (2,663.8 cells/mm^2) ($P < 0.001$).

Table 1 Comparison of clinical features between Fuchs uveitis syndrome and Posner-Schlossman syndrome

Items	FUS ($n=68$ eyes)	PSS ($n=16$ eyes)	*P* Value
Age of disease onset, mean ± SD, y	34.0 ± 11.5	42.6 ± 15.4	0.014[¶]
Male gender, *n* (%)	30/68 (44%)	9/16 (56%)	0.381[†]
Initial LogMAR BCVA, median (IQR)	0.4 (0.2–0.8)	0.7 (0.4–0.9)	0.055[§]
Final LogMAR BCVA, median (IQR)	0.1 (0.0–0.2)	0.3 (0.0–0.9)	0.015[§]
Highest intraocular pressure, median (IQR), mmHg	16.0 (14.0–19.8)	33.5 (26.8–49.5)	< 0.001[§]
Keratic precipitates, *n* (%)	49/68 (72%)	12/16 (75%)	1.000[†]
Iris depigmentation, *n* (%)	68/68 (100%)	7/16 (44%)	< 0.001[†]
Iris nodules, *n* (%)	19/68 (28%)	0/16 (0%)	0.038[†]
Absence of posterior synechia, *n* (%)	68/68 (100%)	16/16 (100%)	NA
Secondary glaucoma, *n* (%)	10/68 (15%)	6/16 (38%)	0.083[†]
Visual field defect, *n* (%)	11/52 (21%)	9/16 (56%)	0.017[†]
CECD, mean ± SD, cells/mm^2	2663.8 ± 463.3	1979.3 ± 539.6	< 0.001[¶]

FUS, Fuchs uveitis syndrome; *PSS*, Posner-Schlossman syndrome; *LogMAR*, logarithm of the minimum angle of resolution; *BCVA*, best-corrected visual acuity; *CECD*, corneal endothelial cell density; *NA*, not applicable; *SD*, standard deviation; *IQR*, interquartile range

[¶]Statistical differences were assessed by independent samples *t*-test

[†]Statistical differences were assessed by χ^2 test or Fisher's exact test, as appropriate

[§]Statistical differences were assessed by Mann–Whitney *U* test

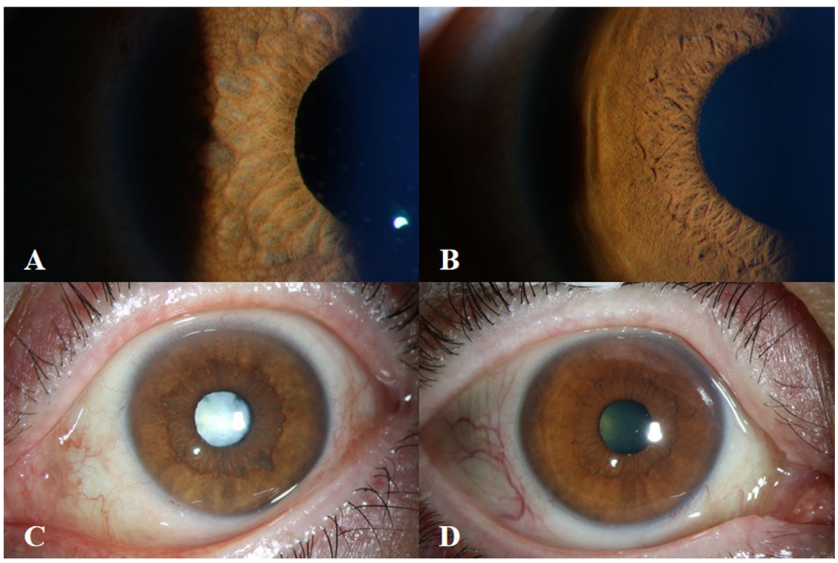

Fig. 1 Iris depigmentation observed in patients with Fuchs uveitis syndrome or Posner-Schlossman syndrome. **A** (affected eye) and **B** (normal eye) from the same Fuchs uveitis syndrome patient. The affected eye (**A**) showed diffuse iris depigmentation as compared to the normal eye (**B**). **C** (affected eye) and **D** (normal eye) from the same Posner-Schlossman syndrome patient. The affected eye (**C**) presented with uneven or somewhat focal iris depigmentation as compared to the normal eye (**D**)

The similarities and differences between CMV-associated FUS and CMV-associated PSS are listed in Table S1. Four out of 11 CMV-associated FUS patients were misdiagnosed as PSS before being referred to our department, and approximately 45% of CMV-associated PSS patients (3 out of 7 cases) were misdiagnosed as FUS. The misdiagnosis was not observed in FUS or PSS patients without viral infection or in combination with other types of viral infection. Generally, higher IOP, CMV-IgG in AqH and proportion of visual field defect, lower RNFL thickness of superior quadrant and CECD, and worse visual prognosis were noted in CMV-associated PSS patients, as compared with CMV-associated FUS patients (all $P<0.05$). In both CMV-PSS and CMV-FUS patients, the RNFL thickness of superior quadrant was negatively correlated with peak IOP (Pearson rho, -0.671, $P=0.009$), and the CECD was negatively correlated with CMV-IgG in AqH (Spearman rho, -0.913, $P<0.001$). There were no significant differences with respect to ocular findings such as KPs, anterior chamber inflammation, iris

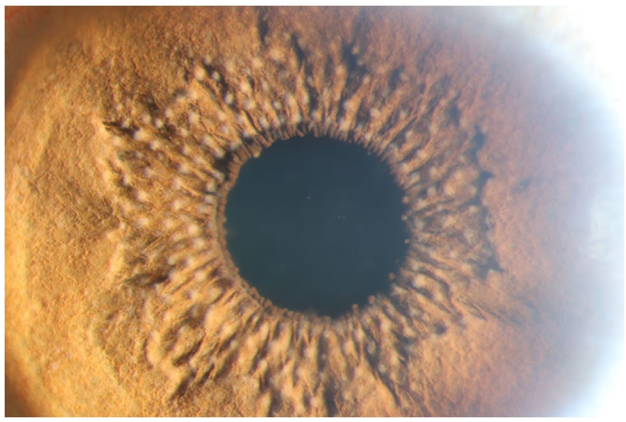

Fig. 2 Fuchs uveitis syndrome patient usually displayed Koeppe nodules and Busacca nodules with a fluffy appearance, which are different from those observed in granulomatous uveitis

depigmentation, absence of posterior synechia and glaucoma in both groups.

Comparison of clinical manifestations in Fuchs uveitis syndrome with or without viral infection

There was no difference concerning the age at disease onset and sex among FUS patients with or without viral infection. A higher proportion of intraocular inflammation (anterior segment cells ≥ 1 + and presence of vitreous cell) was noted in patients with viral infection, as compared with those without viral infection ($P = 0.011$ and $P = 0.006$). Although all FUS patients had iris depigmentation, the grade of iris depigmentation was more obvious (≥II) in virus-associated eyes as compared to the non-virus-associated eyes ($P = 0.002$). A higher percentage of secondary glaucoma was observed in patients with viral infection as compared to patients without viral infection ($P = 0.033$). The mean CECD in patients with or without viral infection was 2381.4 and 2886.4 cells/mm^2, respectively, showing a significant difference ($P < 0.001$). A good prognosis visual function was seen in non-virus-associated patients as compared with the virus-associated patients ($P = 0.029$)(Table 2).

Our further analysis showed that higher percentage of anterior chamber cells (≥ 1 +), worse visual prognosis, lower CECD were observed in CMV-associated FUS, as compared with RV-associated FUS (all $P < 0.05$). The proportion of vitreous cells identified by B-scan ultrasonography in RV-associated FUS was significantly higher than that in CMV-associated FUS ($P = 0.024$)(Table S2).

Comparison of clinical manifestations in Posner-Schlossman syndrome with or without viral infection

Table 3 summarizes the clinical manifestations, auxiliary examinations and visual prognosis in PSS patients with or without viral infection. The frequency of disease recurrence was significantly higher in the virus-associated eyes than that in the non-virus-associated eyes ($P = 0.047$). A good visual outcome at final visit was noted in PSS patients with non-viral infection as compared to those with viral infection patients ($P = 0.001$). Anterior segment cells (≥ 1 +) and secondary glaucoma were found in more than 70% of patients with viral infection, which was

Table 2 Comparison of clinical features in Fuchs uveitis syndrome with or without viral infection

Items	Virus-associated ($n = 30$ eyes)	Non-virus-associated ($n = 38$ eyes)	*P* Value
Age of disease onset, mean ± SD, y	35.7 ± 11.4	32.6 ± 11.6	0.281[¶]
Male gender, n (%)	14/30 (47%)	16/38 (42%)	0.707[†]
Initial LogMAR BCVA, median (IQR)	0.4 (0.2–0.9)	0.4 (0.2–0.5)	0.273[§]
Final LogMAR BCVA, median (IQR)	0.1 (0.0–0.3)	0.0 (0.0–0.1)	0.029[§]
Highest intraocular pressure, median (IQR), mmHg	15.5 (13.8–21.5)	16.0 (14.0–19.3)	0.442[§]
Stellate or medium-sized keratic precipitates, n (%)	20/30 (67%)	29/38 (76%)	0.379[†]
Anterior chamber cells ≥ 1 +, n (%)	12/30 (40%)	5/38 (13%)	0.011[†]
Grade of iris depigmentation ≥ II, n (%)	26/30 (87%)	19/38 (50%)	0.002[†]
Vitreous cell, n (%)	14/30 (47%)	6/38 (16%)	0.006[†]
Secondary glaucoma, n (%)	8/30 (27%)	2/38 (5%)	0.033[†]
CECD, mean ± SD, cells/mm^2	2381.4 ± 418.1	2886.4 ± 369.5	< 0.001[¶]

LogMAR, logarithm of the minimum angle of resolution; *BCVA*, best-corrected visual acuity; *CECD*, corneal endothelial cell density; *SD*, standard deviation; *IQR*, interquartile range

[¶]Statistical differences were assessed by independent samples *t*-test

[†]Statistical differences were assessed by χ^2 test or Fisher's exact test, as appropriate

[§]Statistical differences were assessed by Mann–Whitney *U* test

Table 3 Comparison of clinical features in Posner-Schlossman syndrome with or without viral infection

Items	Virus-associated ($n=8$ eyes)	Non-virus-associated ($n=8$ eyes)	*P* Value
Age of disease onset, mean ± SD, y	44.9 ± 19.8	40.3 ± 10.2	0.566¶
Male gender, n (%)	5/8 (63%)	4/8 (50%)	1.000†
Recurrent attacks, mean ± SD, times per year	3.6 ± 3.2	0.9 ± 0.8	0.047¶
Initial LogMAR BCVA, median (IQR)	0.7 (0.6–1.0)	0.5 (0.2–0.7)	0.049§
Final LogMAR BCVA, median (IQR)	0.9 (0.7–1.0)	0.1 (0.0–0.1)	0.001§
Highest IOP, mean ± SD, mmHg	41.3 ± 15.2	31.4 ± 6.3	0.123¶
Keratic precipitates, n (%)	6/8 (75%)	6/8 (75%)	1.000†
Anterior chamber cells ≥ 1 +, n (%)	7/8 (88%)	2/8 (25%)	0.041†
Iris depigmentation, n (%)	5/8 (63%)	2/8 (25%)	0.315†
Secondary glaucoma, n (%)	6/8 (75%)	0/8 (0%)	0.007†
Retinal nerve fiber layer thickness, μm			
Global, mean ± SD	60.7 ± 23.4	96.5 ± 24.5	0.021¶
Superior quadrant, mean ± SD	62.7 ± 23.6	109.2 ± 32.1	0.012¶
Inferior quadrant, median (IQR)	50.0 (41.0–83.0)	134.5 (103.5–159.3)	0.063§
Nasal quadrant, mean ± SD	45.0 ± 17.9	67.7 ± 16.2	0.037¶
Temporal quadrant, mean ± SD	62.3 ± 14.9	79.3 ± 23.5	0.141¶
Visual field defect, n (%)	7/8 (88%)	2/8 (25%)	0.041†
CECD, mean ± SD, cells/mm^2	1682.4 ± 439.2	2276.3 ± 479.0	0.022¶

LogMAR, logarithm of the minimum angle of resolution; *BCVA*, best-corrected visual acuity; *IOP*, intraocular pressure; *CECD*, corneal endothelial cell density; *SD*, standard deviation; *IQR*, interquartile range

¶Statistical differences were assessed by independent samples *t*-test

†Statistical differences were assessed by Fisher's exact test

§Statistical differences were assessed by Mann–Whitney *U* test

higher than that in patients without viral infection (25% and 0%)($P=0.041$ and $P=0.007$). Lower RNFL thickness of superior, nasal quadrants and global, decreased CECD, and a higher proportion of visual field defect were detected in virus-associated patients, as compared with non-virus-associated patients (all $P<0.05$). All patients with PSS showed an open angle by UBM examination.

Discussion

This study characterized the clinical manifestations of FUS patients with or without viral infection and PSS patients with or without viral infection. In both FUS and PSS groups, viral infected eyes were typically associated with obvious intraocular inflammation, higher proportion of glaucoma, and worse visual outcome as compared to non-viral infected eyes. CMV infection mainly affected the anterior chamber in association with decreased CECD, whereas RV infection could result in vitritis in most FUS patients.

In general, FUS and PSS have their own typical clinical features for diagnosis and differentiation. However, both diseases also share some similarities with respect to ocular manifestations such as unilateral involvement, iris depigmentation and absence of posterior synechia. It indicates that there may be a similar pathogenesis underlying these two diseases.

Recently, viral infection has been increasingly implicated in the pathogenesis of PSS and FUS [8, 18, 19]. It has been shown that PSS is predominantly associated with CMV infection [20]. In a large-scale study reported previously, 35 out of 67 PSS patients (52%) had CMV infection [8]. The present study showed a similar result. We also identified 1 PSS patient with HSV infection, which is generally consistent with the result of an earlier study [21]. FUS in Western countries is principally RV-infected, whereas CMV infection is more common in Asia [8, 22, 23]. Our study identified 4 types of viral infection in FUS, with CMV and RV being more prevalent, which is also in line with previous reports [8, 19, 23]. We confirmed that both diseases are associated with viral infection and therefore they may have a similar basis for pathogenesis. More importantly, we found that FUS and PSS patients with the homologous viral infection displayed a more similar constellation of ocular characteristics and were prone to be misdiagnosed mutually. Due to limitations in diagnostic tools, the diagnosis of FUS and

PSS lacks a gold standard and remains controversial. Consequently, diagnosis based on clinical presentations alone can be a challenge, and identifying the differences in details may be useful to differentiate these two diseases. A striking difference between CMV-associated FUS and CMV-associated PSS was the glaucomatous pattern. CMV-PSS patients had lower RNFL thickness of superior quadrant, higher IOP and an increased proportion of visual field defect. These findings are in agreement with an earlier report from the largest European cohort of CMV-associated PSS patients (52 eyes), which showed that RNFL thickness reduction was more pronounced in the superior and inferior quadrants [24]. Their report further emphasised the impact of elevated IOP on RNFL thickness. In the present study, we demonstrated that RNFL thickness of superior quadrant was negatively correlated with peak IOP. We also found a higher CMV-IgG in AqH of CMV-positive PSS as compared to CMV-positive FUS and showed a negative correlation between CMV-IgG and CECD. These results are supported by the study of Miyanaga et al. [25], which showed a significant correlation between CMV viral load and corneal endothelial cell loss. However, it is not completely understood how CMV plays a role in these two diseases, and further studies are warranted to elucidate this issue. In addition, there are significant differences regarding the clinical manifestations of different types of viral infection. CMV-associated FUS had a more obvious anterior segment inflammation and lower CECD, whereas RV-positive FUS mostly displayed vitritis as evidenced by vitreous opacities shown on B-scan ultrasonography. This finding is in agreement with previous reports, suggesting that vitritis may be a prominent clinical sign of RV-associated FUS [19, 26]. However, the mechanisms underlying CMV and RV are unclear and need to be explored in future studies.

Interestingly, there is a considerable variation in PSS and FUS patients with or without viral infection. As compared with PSS patients without viral infection, viral-infected PSS patients had a higher percentage of secondary glaucoma and more severe optic nerve damage as evidenced by decreased RNFL thickness and severe visual field loss. Furthermore, virus-associated PSS patients had worse final vision despite the IOP was controlled in most patients after antiglaucoma surgery, possibly due to optic nerve damage caused by preoperative recurrent increased IOP. Our study, for the first time, compared clinical differences in FUS with or without viral infection. Based on long-term follow-up, we also found a higher proportion of secondary glaucoma in FUS patients with virus-associated than in those without viral infection. However, the exact mechanism underlying the increased IOP caused by viral infection remains unclear. As regards to CECD, a previous study reported that viral anterior uveitis can lead to corneal endothelial damage [13]. In this study, we also revealed a decreased CECD both in FUS and PSS patients with viral infection. These results collectively suggest that FUS and PSS patients with viral-infected have more obvious clinical symptoms, and much more attention should be payed during follow up visits.

The study has some limitations. First, it was a retrospective study, and the number of PSS patients enrolled for AqH analysis was relative small due to the rarity of PSS patients, especially those who necessitate surgery intervention. Further large-scale studies are warranted to validate the findings of this study. Second, although FUS and PSS have been demonstrated to be associated with viral infection in some cases in previous reports and the present study, the underlying mechanisms as well as their relevance to management are needed to be investigated in future studies. Third, all patients enrolled were Chinese from one uveitis centre, and validation of the results in other populations is expected to be carried out in future study. Fourth, due to the small amount of AqH obtained from patients with FUS or PSS, we did not perform PCR assay on the patients who underwent GWC assessment. The results obtained in this study are expected to be validated by PCR in the future and analyzed for sensitivity and specificity of PCR and GWC.

In conclusion, we characterized the clinical features and the types of viral infection among 68 FUS patients and 16 PSS patients by AqH analysis. Our study addressed the similarities and differences among FUS or PSS patients with or without viral infection, and ancillary tests can be helpful in differentiating these two diseases with CMV infection.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s00417-024-06502-0.

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Declarations

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional Review Board of the First Affiliated Hospital of Chongqing Medical University and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no confict of interests.

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