Clinical Outcomes in Cytomegalovirus-Positive Posner-Schlossman Syndrome Patients Treated With Topical Ganciclovir Therapy

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• PURPOSE: To evaluate the clinical characteristics and therapeutic outcomes of cytomegalovirus (CMV)-positive Posner-Schlossman syndrome patients undergoing topical ganciclovir treatment.

• DESIGN: Retrospective, comparative, and interventional case series.

• METHODS: One eye of each of 126 consecutive Posner-Schlossman syndrome patients was investigated using aqueous polymerase chain reaction (PCR) between January 2006 and June 2013. The initial presentations and follow-up data of the CMV-positive patients (68 eyes) and CMV-negative patients (58 eyes) were compared.

• RESULTS: Severe endothelial cell loss ($P < .001$) and a higher number of eyes requiring glaucoma filtering surgery ($P = .017$) were observed in CMV-positive Posner-Schlossman syndrome patients. All CMV-infected eyes treated with continual topical 2% ganciclovir exhibited an undetectable CMV level at the following taps. During follow-up, the average number of antiglaucomatous agents decreased, and a similar frequency of intraocular pressure (IOP) spikes was observed in both groups ($P = .358$). Patients with CMV-positive eyes with a disease duration over 5 years were likely to require glaucoma surgery ($P = .024$, log-rank test). All patients receiving surgery exhibited CMV-negative PCR during the IOP attack, but experienced severe peripheral anterior synechiae and pigment clogging. Both groups exhibited a similar endothelial cell decrease ($P = .243$) and probability of progressive endothelial cell loss ($P = .219$, log-rank test).

• CONCLUSION: Ganciclovir treatment was effective for clearing the viral load, assisting the IOP control, and preserving the corneal endothelium of CMV-positive Posner-Schlossman syndrome patients. Early diagnosis and proper treatment could decrease the risk of advanced glaucoma and avoid glaucoma surgery in long-lasting cases. (Am J Ophthalmol 2014;158:1024–1031.
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CYTOMEGALOVIRUS (CMV) INFECTION IN THE anterior chamber of the eyes is a newly identified clinical entity that is the result of CMV reactivation in immunocompetent patients.[1] Clinical manifestations of CMV infection include anterior uveitis with anterior chamber (AC) inflammation and keratic precipitates (KPs), elevated intraocular pressure (IOP), and corneal endothelial cell damage.[2] CMV infection in the anterior chamber has been detected in patients diagnosed with Posner-Schlossman syndrome or Fuchs heterochromic iridocyclitis, diseases that were previously believed to be idiopathic.[3]

The corneotrabecular endothelium is a vulnerable tissue in this virus-related anterior segment infection. Although the route of infection remains unclear, CMV particles have been detected in the corneal endothelium and trabeculum in patients with acquired immunodeficiency syndrome, and the condition has been diagnosed as CMV panuveitis.[4] A marked loss of corneal endothelial cells has been detected in correlation to viral loads in CMV-associated iridocyclitis and corneal endotheliitis.[5] A high CMV copy number was also identified as a substantial risk factor for IOP elevations.[6] In 1 recent study, Sobolewska and associates reported that 36.4% of patients required surgical treatment in addition to oral valganciclovir administration to stabilize the IOP in CMV-related Posner-Schlossman syndrome.[7]

Proper and early ganciclovir treatments can halt CMV activity; thus, the damage to the trabecular meshwork and corneal endothelium may be avoided. However, this disease is notorious for its high recurrence rate.[8] Continual administration of ganciclovir was considered to control the reactivation of CMV in an immunocompetent group.[8–10] In our previous report, we determined that topical administration of 2% ganciclovir eye drops could effectively clear the viral load in CMV endotheliitis.[10] A continual topical ganciclovir treatment avoids the side effects of long-term systemic and intravitreal ganciclovir treatments, including pancytopenia, renal impairment, retinal detachment, and endophthalmitis.[11–13]

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In the literature, induction therapy for CMV infection included the systemic administration of ganciclovir and valganciclovir[1,2,5,9,14–17] and the intravitreal injection of ganciclovir.[18] Patients experienced a high recurrence rate after ceasing the treatment.[8] Topical antiviral agents such as acyclovir, ganciclovir, and valganciclovir have been used as a maintenance therapy in previous studies.[1,2,17] In our daily practice, we use topical 2% ganciclovir as a long-term maintenance therapy without interruption for Posner-Schlossman syndrome patients with CMV-positive eyes.[10]

Until now, no large-scale study of the long-term clinical outcomes in CMV-positive Posner-Schlossman syndrome patients has been reported. The influence of CMV infection and the therapeutic effect of topical ganciclovir should be discussed. To identify the clinical features and long-term prognosis of Posner-Schlossman syndrome patients with CMV-positive eyes, their demographic data and clinical manifestations were compared with those of Posner-Schlossman syndrome patients with CMV-negative eyes.

In this report, we investigated the efficacy of a topical ganciclovir treatment on CMV-related Posner-Schlossman syndrome. The long-term changes in the corneal endothelial count and IOP of Posner-Schlossman syndrome patients with CMV-positive eyes were compared with those of Posner-Schlossman syndrome patients with CMV-negative eyes.

MATERIALS AND METHODS

• **PATIENTS:** From January 1, 2005 to June 30, 2013, aqueous tapping for viral polymerase chain reaction (PCR) was routinely performed in patients diagnosed as having Posner-Schlossman syndrome at the Uveitis Clinic of the National Taiwan University Hospital. The National Taiwan University Hospital is the main tertiary referral center in Taiwan. All cases were aqueous PCR-negative for herpes simplex virus (HSV) and varicella zoster virus (VZV) and positive for CMV. The eligible diagnostic criteria of Posner-Schlossman syndrome were as follows: (1) unilateral, recurrent episodes of mild anterior chamber inflammation; (2) the presence of corneal edema and endothelial keratic precipitates; (3) elevated IOP during the attack; (4) the absence of posterior synechiae or posterior inflammation; (5) a duration of attack lasting from a few days to a few weeks; and (6) normal eye examinations between attacks. Aqueous taps were performed in the presence of active inflammation during attack upon presentation. Patients with negative PCR results who presented with persistent anterior chamber inflammation, corneal edema, elevated IOP for more than 2 weeks, or progressive endothelial loss during the follow-up period underwent repeated AC taps for PCR. Among the 126 Posner-Schlossman syndrome patients who were HSV-negative and VZV-negative according to PCR diagnosis, 68 consecutive patients (68 eyes) were CMV-positive and were treated with topical ganciclovir. Another 58 consecutive patients (58 eyes) who were CMV-negative according to PCR diagnosis during the same period were selected as the control group.

The medical records of the CMV-positive and CMV-negative Posner-Schlossman syndrome patients were reviewed. The demographics and clinical findings of each patient were recorded, including their age, sex, duration of disease, best-corrected visual acuity, IOP, and crystalline lens status. The anterior chamber reaction was recorded using slit-lamp microscopy. Changes in the anterior chamber cells were observed after the treatment and accompanied steroid use. The IOP and number of antiglaucomatous medications prescribed at each visit were also compiled. Any glaucoma filtering surgery was highlighted and indicated as poor IOP control. Any self-reported recurrence of uveitis or unexpected IOP was indicated. Corneal endothelial cell density was examined by using confocal microscopy of both the diseased eyes and healthy eyes, and the observations during each visit were recorded. This research protocol was approved by the Ethics Review Board of the National Taiwan University Hospital.

• **TOPICAL GANCICLOVIR TREATMENT OF PATIENTS WITH CYTOMEGALOVIRUS-POSITIVE POSNER-SCHLOSSMAN SYNDROME:** All patients were treated with a topical 2% ganciclovir solution after receiving a CMV-positive diagnosis according to the results of PCR of aqueous humor taps. The 2% ganciclovir solution was prepared by dissolving 500 mg of Cymevene lyophilized IV powder (Roche, Basel, Switzerland) in 25 mL of distilled water.[10] The treatment was applied every 2–3 hours daily as an induction therapy, and every 4 hours as a long-term maintenance therapy, as previously reported.[10] After the continual administration of topical ganciclovir for 3 months, all patients underwent another aqueous humor tap to perform a PCR test for detecting the presence of CMV. Topical ganciclovir was prescribed as a long-term antiviral therapy, without discontinuation. Once the conditions of high IOP and corneal edema occurred during the follow-up period, repeated aqueous taps were performed to determine the CMV viral load.

• **CONTROL OF INTRAOCULAR PRESSURE AND NEED FOR GLAUCOMA SURGERY:** Before referral, the duration of disease exposure, number of antiglaucomatous agents used, and number of eyes that received glaucoma filtering surgery were compared between the 2 groups. During the follow-up period, the occurrence of an IOP spike (IOP $>$ 30 mm Hg) and need for glaucoma filtering surgery were evaluated in the 2 groups. For both groups, the Kaplan-Meier survival analysis was used to estimate the probability of not requiring glaucoma filtering surgery in the diseased eye during the follow-up period.

Response to therapy was defined as remission of anterior chamber inflammation, resolution of corneal edema, and good IOP control with or without antiglaucomatous

medications after topical ganciclovir had been received for 1 month. *Early treatment failure* was defined as persistence of anterior chamber inflammation, corneal edema, or poor IOP control despite the use of antiglaucomatous medications within the first 3 months of treatment. *Late treatment failure* was defined as relapse of anterior chamber inflammation, the presence of corneal edema, or elevated IOP after 3 months of treatment. *Recurrence* of CMV-positive Posner-Schlossman syndrome was defined as the presence of active inflammation, corneal edema, endothelial KPs, and elevated IOP with a positive CMV viral load after repeated taps during treatment. *Recurrence* of CMV-negative Posner-Schlossman syndrome was defined as the presence of active inflammation, corneal edema, endothelial KPs, and elevated IOP with a negative CMV viral load after repeated taps during treatment. These definitions were adapted from a previous study of CMV anterior uveitis.[8]

• **EVALUATION OF CORNEAL ENDOTHELIAL CELL DENSITY:** The corneal endothelial cell density was examined in both the diseased eye and the healthy eye during each visit, and the observations were recorded. The initial corneal endothelial cell loss of the diseased eye was measured upon diagnosis. The corneal endothelial cell loss was calculated according to the formula: corneal endothelial cell loss (%) = (1 − endothelial cell density in the diseased eye/endothelial cell density in the healthy eye) × 100%. The initial corneal endothelial cell loss of the CMV-positive Posner-Schlossman syndrome patients and CMV-negative Posner-Schlossman syndrome patients was compared. Progressive endothelial cell loss was defined as a 20% decrease in the initial endothelial cell count in the diseased eye. For both groups, the Kaplan-Meier survival analysis was used to estimate the probability of progressive endothelial cell loss in the diseased eye during the follow-up period.

• **STATISTICS:** Data were reported as means ± standard deviation (SD). To compare the differences between the 2 groups, a statistical analysis of age, visual acuity, duration of disease, number of antiglaucomatous agents, endothelial cell density, endothelial cell loss, and follow-up time was performed using the Student *t* test. All other categorical variables, including sex, lens status, and eyes receiving glaucoma surgery, were analyzed using the χ^2 test (the Fisher exact test was used if $n < 5$); $P < .05$ was considered to be statistically significant.

RESULTS

• **CLINICAL MANIFESTATIONS OF PATIENTS IN THE 2 GROUPS:** The demographic data and initial clinical manifestations of the CMV-positive and CMV-negative Posner-Schlossman syndrome patients are listed in Table 1.

The mean ages of the CMV-positive Posner-Schlossman syndrome patients and CMV-negative Posner-Schlossman syndrome patients were not significantly different (57.69 and 54.05 years, respectively; $P = .08$). The proportion of pseudophakia was also similar between the CMV-positive and CMV-negative Posner-Schlossman syndrome patients ($P = .633$). The 2 groups did not differ in sex composition ($P = .486$). Five eyes (5/68; 7.35%) in patients who were CMV-positive and 2 eyes (2/58; 3.45%) in patients who were CMV-negative exhibited diffuse iris atrophy.

Although the duration of the glaucomatocyclitic crisis was longer in CMV-positive eyes than in CMV-negative eyes, this difference was not significant. (5.44 ± 4.74 years in CMV-positive eyes and 3.72 ± 3.79 years in CMV-negative eyes; $P = .054$). Upon diagnosis, significantly more CMV-positive Posner-Schlossman syndrome patients received glaucoma filtering surgery than did CMV-negative Posner-Schlossman syndrome patients because of uncontrollable IOP (13.24% and 1.72%, respectively; $P = .017$). However, the number of antiglaucomatous agents used was similar for both groups ($P = .17$).

The corneal endothelial cell density of the diseased eye in CMV-positive and CMV-negative Posner-Schlossman syndrome patients exhibited significant differences (1498 ± 743 cells/mm^2 and 2040 ± 593 cells/mm^2, respectively; $P < .001$). Endothelial cell loss in the diseased eye relative to the healthy eye was significantly higher in CMV-positive patients than in CMV-negative patients (45.24% and 18.48%, respectively; $P < .001$).

The best-corrected visual acuity at diagnosis was slightly lower for CMV-positive eyes than for CMV-negative eyes (0.33 and 0.18 in logMAR, respectively; $P = .023$). The follow-up time from diagnosis to the final visit was similar in CMV-positive and CMV-negative patients (39.79 ± 14.96 months and 36.81 ± 11.32 months, respectively; $P = .17$).

• **CLINICAL OUTCOMES AFTER TOPICAL GANCICLOVIR TREATMENT:** The clinical outcomes of CMV-positive and CMV-negative Posner-Schlossman syndrome patients are listed in Table 2.

Among the 68 eyes that were treated topically with ganciclovir, the Posner-Schlossman syndrome patients with CMV-positive eyes received long-term topical 2% ganciclovir treatment, without discontinuation. All 68 eyes (100%) responded positively to treatment, exhibiting anterior chamber inflammation remission, resolution of corneal edema, and good IOP control within 1 month of topical ganciclovir treatment. Topical steroid use was reduced after anterior chamber inflammation decreased gradually. The average number of antiglaucomatous agents decreased from 1.78 to 0.88 in CMV-positive patients after they had received topical ganciclovir treatment for 1 month. After the continual administration of topical ganciclovir for 3 months, all eyes exhibited an undetectable level of CMV DNA at repeated taps. No patient

TABLE 1. Demographic Data and Initial Clinical Manifestations of Patients With Cytomegalovirus-Positive Posner-Schlossman Syndrome and Patients With Cytomegalovirus-Negative Posner-Schlossman Syndrome

Characteristics	CMV-Positive Patients (N = 68)	CMV-Negative Patients (N = 58)	*P* Value
Number of diseased eyes (n)	68	58	
Age at diagnosis (mean ± SD) (y)	57.69 ± 10.55	54.05 ± 12.59	.08
Male sex (n)	38	36	.486
Lens status of the diseased eye (n)			.633
Phakic	54	44	
Pseudophakic	14	14	
Duration of disease (mean ± SD) (y)	5.44 ± 4.74	3.72 ± 3.79	.054
Endothelial cell density of the diseased eye (mean ± SD) (cell/mm^2)	1498 ± 743	2040 ± 593	<.001
Endothelial cell density of the healthy eye (mean ± SD) (cell/mm^2)	2664 ± 449	2524 ± 509	.103
Corneal endothelial cell loss of the diseased eye (mean ± SD) (%)	45.24 ± 25.38	18.48 ±18.19	<.001
Number of antiglaucomatous agents used for the diseased eye at diagnosis (mean ± SD) (n)	1.78 ± 1.13	1.73 ± 1.13	.17
Eyes receiving filtering surgery (n)	9	1	.017
Corrected visual acuity in the diseased eye at diagnosis (mean ± SD) (logMAR)	0.33 ± 0.29	0.18 ± 0.12	.023
Follow-up time (mean ± SD) (mo)	39.79 ± 14.96	36.81 ± 11.32	.17

CMV = cytomegalovirus; logMAR = logarithm of the minimal angle of resolution.

To compare the difference in 2 groups, statistical analysis of age, endothelial cell density, corneal endothelial cell loss, number of antiglaucomatous agents use at diagnosis, corrected visual acuity, and follow-up time were performed with Student *t* test. The categorical variables of lens status and eyes receiving filtering surgery were performed using χ^2 test. $P < .05$ was considered statistically significant.

TABLE 2. Clinical Outcomes of Patients With Cytomegalovirus-Positive Posner-Schlossman Syndrome and Patients With Cytomegalovirus-Negative Posner-Schlossman Syndrome at the Final Visit

Characteristics	CMV-Positive Patients (N = 68)	CMV-Negative Patients (N = 58)	*P* Value
Number of diseased eyes	68	58	
Endothelial cell density of the diseased eye (mean ± SD) (cell/mm^2)	1445 ± 705	2000 ± 583	<.001
Endothelial cell density of the healthy eye (mean ± SD) (cell/mm^2)	2636 ± 450	2482 ± 517	.077
Decrease of endothelial cell density of the diseased eye (mean ± SD) (cell/mm^2)	53 ± 21	40 ± 19	.243
Number of antiglaucomatous agents use at the final visit (mean ± SD) (n)	0.75 ± 0.5[a]	0.68 ± 0.4	.258
Eyes on no antiglaucomatous medication (n)	29	34	.074
IOP crisis higher than 30 mm Hg (n)	25	26	.358
Eyes receiving filtering surgery during the follow-up period (n)	8	0	.007
Follow-up time (mean ± SD) (mo)	39.79 ± 14.96	36.81 ± 11.32	.17

CMV = cytomegalovirus; IOP = intraocular pressure.

To compare the difference in 2 groups, statistical analysis of endothelial cell density, endothelial cell density decrease, and number of antiglaucomatous agents used at the final visit and follow-up time were performed with Student *t* test. The categorical variables of eyes receiving filtering surgery, eyes on no antiglaucomatous medication, and eyes with IOP crisis were performed using χ^2 test. $P < .05$ was considered statistically significant.

[a]The average number of antiglaucomatous agents for CMV-positive patients at the final visit, excluding 8 cases receiving filtering surgery.

with CMV-positive eyes who received topical ganciclovir treatment experienced early treatment failure.

• **TRABECULITIS AND INTRAOCULAR PRESSURE CONTROL:** Among the 68 CMV-positive eyes, 29 eyes (42.65%) were on no antiglaucomatous medication at the final visit. Among the 58 CMV-negative eyes, 34 eyes (58.62%) were on no antiglaucomatous medication at the final visit ($P = .074$). Twenty-five CMV-positive eyes (36.76%) exhibited IOP spikes and late treatment failure during the follow-up period. Among these eyes, 5 (20%) exhibited recurrence of CMV-positive Posner-Schlossman syndrome and active

inflammation with a detectable CMV viral load after repeated aqueous taps during the attack. Self-discontinuation of topical ganciclovir use was reported in these 5 cases. The remaining 20 eyes exhibited neither anterior inflammation nor a positive CMV viral load at repeated taps. Twenty-six CMV-negative eyes (44.83%) exhibited IOP spikes during the follow-up period. All of these eyes exhibited a negative CMV viral load at repeated taps and recurrence of CMV-negative Posner-Schlossman syndrome. Recurrence of IOP spike (IOP > 30 mm Hg) was observed in 25 of 68 CMV-positive eyes (36.76%) and 26 of 58 CMV-negative eyes (44.83%) during the follow-up period ($P = .358$).

Clogging of the trabecular meshwork with pigments and peripheral anterior synechiae were widely identified in these 25 cases. The average duration of symptoms for these 25 cases was 7.24 years (range of 3–23 years). The IOP of 17 eyes could be controlled after treatment with antiglaucomatous agents. Eight eyes (32%) received additional glaucoma filtering surgery to alleviate advanced glaucoma; these 8 eyes exhibited a negative CMV viral load at repeated taps during the attack. Certain features were observed in these 8 cases, including advanced glaucomatous cupping, steroid use for longer than 1 year, presence of pigments in the trabecular meshwork, and peripheral anterior synechiae. The mean duration of symptoms in these 8 cases was 8.5 years (range of 4–14 years). After 8 patients who received glaucoma filtering surgery were excluded, the average number of antiglaucomatous agents decreased from 1.2 to 0.75 in patients who were CMV-positive at the final visit.

The Kaplan-Meier analysis results revealed that although CMV-negative patients and CMV-positive patients with disease durations shorter than 5 years did not exhibit differences in the probability of receiving glaucoma filtering surgery ($P = .183$, log-rank test), CMV-positive patients with a disease duration longer than 5 years exhibited a significantly higher probability of receiving surgery ($P = .024$, log-rank test) (Figure 1).

• **ENDOTHELIITIS AND ENDOTHELIAL CELL COUNT:** The initial and final endothelial cell density measurements in CMV-positive eyes undergoing topical ganciclovir treatment were 1498 ± 743 cells/mm^2 and 1445 ± 705 cells/mm^2, respectively. The initial and final endothelial cell density measurements in CMV-negative eyes were 2040 ± 593 cells/mm^2 and 2000 ± 583 cells/mm^2, respectively. The decrease in endothelial cell density in the diseased eyes during the follow-up period was not significantly different between the 2 groups ($P = .243$). None of the 25 eyes that exhibited an IOP spike presented localized corneal edema or keratic precipitates as the clinical representations of endotheliitis before topical ganciclovir treatment.

Figure 2 displays the Kaplan-Meier survival curve based on the definition of progressive endothelial cell loss. The probability of being free of progressive endothelial loss 4 years after diagnosis was 97.3% in CMV-positive eyes and 100% in CMV-negative eyes. No significant differences were observed in the estimated probability between the 2 groups ($P = .219$, log-rank test).

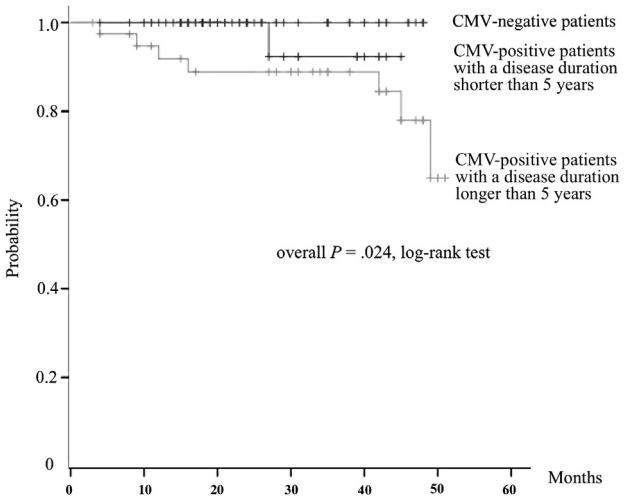

FIGURE 1. Kaplan-Meier survival analysis conducted to estimate the probability that glaucoma filtering surgery was not required in patients with cytomegalovirus-negative Posner-Schlossman syndrome and patients with cytomegalovirus-positive Posner-Schlossman syndrome receiving topical ganciclovir therapy during the follow-up period. The Kaplan-Meier analysis results revealed an overall log-rank of $P = .034$ when all 3 groups were calculated simultaneously; $P = .024$ comparing CMV-negative patients and CMV-positive patients with a disease duration longer than 5 years; $P = .183$ comparing CMV-negative patients and CMV-positive patients with a disease duration shorter than 5 years separately (log-rank test).

DISCUSSION

IN THIS STUDY, WE IDENTIFIED 2 CLINICAL DETECTABLE differences between CMV-positive patients and CMV-negative patients with presumed Posner-Schlossman syndrome prior to PCR tests. First, the endothelial cell loss in the infected eyes of CMV-positive Posner-Schlossman syndrome patients was more severe than that of the CMV-negative Posner-Schlossman syndrome patients (45.24% and 18.48%, respectively; $P < .001$). Second, the number of eyes receiving glaucoma filtering surgery was significantly higher in patients with CMV-positive Posner-Schlossman syndrome than in patients with CMV-negative Posner-Schlossman syndrome (13.24% and 1.72%, respectively; $P = .017$). All these cases received glaucoma filtering surgery because of uncontrollable IOP, detected in other hospitals before referral.

In the current study, 14 CMV-positive eyes (20.59%) and 14 CMV-negative eyes (24.14%) underwent cataract surgery before diagnosis. When the eyes that had previous intraocular surgery were excluded from the analysis, the

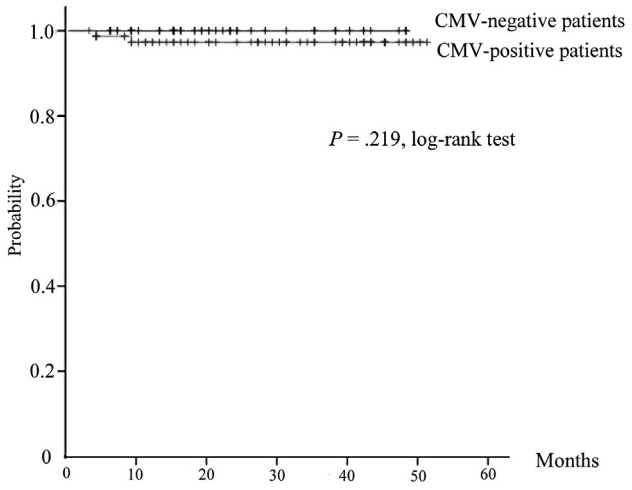

FIGURE 2. Kaplan-Meier survival analysis conducted to estimate the probability that patients with cytomegalovirus-negative Posner-Schlossman syndrome and patients with cytomegalovirus-positive Posner-Schlossman syndrome who received topical ganciclovir therapy during the follow-up period were free of progressive endothelial cell loss. Based on the definition of progressive endothelial cell loss, as a 20% decrease in the initial endothelial cell count in the diseased eye, the probability of being free of progressive endothelial loss 4 years after diagnosis was 97.3% in CMV-positive eyes and 100% in CMV-negative eyes. The Kaplan-Meier analysis results revealed that there was no significant difference in the estimated probability between the 2 groups ($P = .219$, log-rank test).

endothelial cell loss in the diseased eyes of CMV-positive Posner-Schlossman syndrome patients was still significantly higher than that in the CMV-negative Posner-Schlossman syndrome patients (35.23% and 14.21%, respectively; $P < .001$). After topical ganciclovir treatment of CMV-positive eyes, the probability of being free of progressive endothelial loss 4 years after starting the treatment became similar in both groups ($P = .219$, log-rank test).

In a previous study with a median follow-up duration of 27.7 months, the rate of acute CMV anterior uveitis recurrence after systemic and intravitreal ganciclovir therapy was terminated was 84.61%. The rate of acute CMV anterior uveitis recurrence in patients who continually used topical 0.15% ganciclovir gel decreased to 57.14%.[8] In the current study, of which the average follow-up duration was 39.8 months, the rate of CMV-positive Posner-Schlossman syndrome recurrence in patients who continually used 2% ganciclovir eye drops was 7.35%. This considerably lower recurrence rate may be attributed to the higher concentration of topically applied ganciclovir, which increased the higher drug concentration in the anterior chamber.

Although many previous studies have reported corneal endothelial cell damage in CMV-related anterior segment infection,[1,2,5,17,19,20] the change in the corneal endothelium after treatment was still poorly understood. Among earlier cases receiving intravitreal and systemic ganciclovir, most patients still suffered from progressive endothelium loss after several treatment courses. Miyanaga and associates suggested that severe corneal endothelial loss was correlated with a high CMV viral load. In their study, 60% of corneal endothelium loss happened within 6 months after the first onset of symptoms.[5] In our series, we also detected cases with severe endothelial cell loss within a short symptomatic duration. We demonstrated the substantial preservation of corneal endothelium as a result of topical ganciclovir treatment. Furthermore, no case of CMV-positive eyes presented corneal edema or keratic precipitates after topical ganciclovir treatment during follow-up. Because the CMV viral load could pose a risk to the corneal endothelium after discontinuing the ganciclovir treatment, we recommend a continual topical ganciclovir application to prevent corneal endothelium loss in this vulnerable group.

Similar to the pathogenesis of the HSV-related glaucoma,[21] we proposed the following mechanism for the pathogenesis of the CMV-related glaucoma, based on our findings: (1) a thick and edematous trabecular band develops as trabeculitis; (2) a steroid-induced glaucoma develops; (3) a trabecular blockage of pigments and chronic inflammatory cells is generated; and (4) a peripheral anterior synechia develops, with secondary angle-closure glaucoma. In cases with a short duration, trabeculitis and steroid-glaucoma were the main reasons for the IOP elevation. In cases with a long duration and sequelae of uveitis, a trabecular blockage containing inflammatory materials, as well as peripheral anterior synechiae, may exist and cause an IOP elevation, even after viral clearance. This may explain the variable prognosis in CMV-positive eyes with different disease durations.

In the current study, none of the patients who were CMV positive and received topical ganciclovir experienced early treatment failure. After receiving topical ganciclovir treatment, all patients exhibited good IOP control regardless of whether they concurrently used antiglaucomatous medications. After topical ganciclovir treatment had been administered for 1 month, the average number of antiglaucomatous agents decreased from 1.78 to 0.88 in patients with CMV-positive eyes. Generally, IOP control was much easier after the topical application of ganciclovir in cases with a short duration of symptoms than in cases with a long duration of symptoms. Twenty-nine patients (42.65%) were on no antiglaucomatous medication at the final visit. Topical ganciclovir, similar to systemic ganciclovir in previous literature, decreased the demand for antiglaucomatous agents in CMV anterior uveitis.[2] The mechanisms of IOP decrease after ganciclovir treatment could be multifactorial. The transient IOP elevation caused by CMV trabeculitis could attain a normal aqueous outflow after viral clearance. Furthermore, a decreased application of topical steroids might also decrease the risk of steroid-induced IOP elevation.

However, 25 CMV-positive eyes (36.76%) exhibited late treatment failure. Most of these failures resulted from poor IOP control rather than recurrence of anterior CMV uveitis. In addition, most of these cases presented with symptoms that persisted for a long duration and sequelae of uveitis. In accordance with a previous study, patients with a longer disease duration may have a higher risk of developing glaucoma as a manifestation of Posner-Schlossman syndrome, and antiglaucomatous surgery is necessary to prevent IOP spikes in patients with glaucomatous damage.[22] Topical ganciclovir use enabled us to infer that the pathogenesis of the IOP spike in these long-lasting cases after viral clearance was attributable to the sequelae of uveitis rather than CMV trabeculitis.

In the current study, none of the 8 eyes that exhibited an uncontrollable IOP rise and received glaucoma filtering surgery had a CMV-positive viral load at repeated taps during the attack. The duration of disease exposure was much longer in these eyes. In addition to the findings of trabecular clogging and peripheral anterior synechiae, all these cases exhibited advanced glaucomatous cupping and profound visual field defects. Because of the critical conditions in these eyes, aggressive treatments were required to normalize the IOP. All eyes exhibited a stable IOP after surgery, and no complications were reported in these cases. No IOP attack was observed in these eyes after surgery during the follow-up period.

The outcomes of IOP control after antiviral treatment have varied in different studies. Hwang and associates reported an excellent serial change in the IOP after an intravitreal loading dose of ganciclovir. No surgical intervention was required in this series. However, the average follow-up time was only 14.7 months.[18] By contrast, van Boxtel and associates determined that 2 out of 5 eyes needed further glaucoma surgery after treatment with systemic antiviral medications.[15] In a recent study, Sobolewska and associates reported the long-term effects of oral valganciclovir therapy in CMV-positive Posner-Schlossman syndrome patients; they reported that 36.4% of patients required surgical treatment in addition to oral valganciclovir administration to stabilize the IOP.[7] In the current study, we determined that the duration of disease exposure influenced the probability of receiving glaucoma filtering surgery in CMV-positive eyes after ganciclovir treatment. A significant higher probability of receiving glaucoma surgery was observed in CMV-positive patients with a disease duration longer than 5 years ($P = .024$, log-rank test) than in CMV-positive patients with shorter disease durations. This may explain the variable prognosis reported in previous studies.

The corneal endothelium and adjacent trabecular endothelium are 2 vulnerable sites in CMV-related infections. The pathology of the CMV-infected cornea–trabecular endothelium has been reported.[4] We determined the endothelial cell density and morphology in the corneal endothelium of the diseased eyes, using confocal microscopy.[20] However, the pathogenesis of CMV-related trabeculitis, as well as the state of the trabecular meshwork after ganciclovir treatments, are poorly understood. The changes in morphology and function in the trabecular meshwork as a result of CMV infection require further investigation.

This study has certain limitations. It was retrospective, considered only a few patients, and lacked adequate controls when assessing various features. Furthermore, the symptoms of IOP spikes may be neglected by patients, and the event could be underestimated. Nonetheless, our study examined the clinical outcomes of topical ganciclovir in CMV-positive Posner-Schlossman syndrome patients in a comprehensive way. We determined that topical ganciclovir treatment can preserve the corneal endothelium and assist in the control of IOP. However, the sequelae of uveitis may cause an IOP spike in long-lasting cases after viral clearance. Early diagnosis and proper treatment could decrease the risk of advanced glaucoma and avert the need for glaucoma surgery. A large prospective study may be warranted to confirm our observations.

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REPORTING VISUAL ACUITIES

The AJO encourages authors to report the visual acuity in the manuscript using the same nomenclature that was used in gathering the data provided they were recorded in one of the methods listed here. This table of equivalent visual acuities is provided to the readers as an aid to interpret visual acuity findings in familiar units.

Table of Equivalent Visual Acuity Measurements

Snellen Visual Acuities				
4 Meters	6 Meters	20 Feet	Decimal Fraction	LogMAR
4/40	6/60	20/200	0.10	+1.0
4/32	6/48	20/160	0.125	+0.9
4/25	6/38	20/125	0.16	+0.8
4/20	6/30	20/100	0.20	+0.7
4/16	6/24	20/80	0.25	+0.6
4/12.6	6/20	20/63	0.32	+0.5
4/10	6/15	20/50	0.40	+0.4
4/8	6/12	20/40	0.50	+0.3
4/6.3	6/10	20/32	0.63	+0.2
4/5	6/7.5	20/25	0.80	+0.1
4/4	6/6	20/20	1.00	0.0
4/3.2	6/5	20/16	1.25	−0.1
4/2.5	6/3.75	20/12.5	1.60	−0.2
4/2	6/3	20/10	2.00	−0.3

From Ferris FL III, Kassoff A, Bresnick GH, Bailey I. New visual acuity charts for clinical research. Am J Ophthalmol 1982;94:91–96.

Biosketch

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Biosketch

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