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Clinical Features, Diagnosis and Treatment Outcomes of Cytomegalovirus Endotheliitis in Hong Kong

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Corneal endotheliitis refers to the specific inflammation of corneal endothelium. (Khodadoust & Attarzadeh 1982) The clinical features include corneal edema, keratic precipitates, trace to moderate anterior chamber reaction and destruction of corneal endothelium. (Alfawaz 2013) Cytomegalovirus has been detected using polymerase chain reaction (PCR) and southern blot techniques in patients with corneal endotheliitis. (Koizumi et al. 2006), (Jhanji et al. 2013) We reviewed the data of patients who were diagnosed with CMV endotheliitis in the past 3 years in our hospital. Patients were identified from the Clinical Data And Reporting System of the Hospital Authority of Hong Kong using prescription history of ganciclovir ointment or valganciclovir tablet. Overall, 17 eyes of 16 patients (9 males, 7 females) were included. The median age at presentation was 57.5 years (Range: 23-79 years), and the median age at diagnosis was 61.5 years (Range: 34-80 years). The median duration between initial presentations to diagnosis of CMV endotheliitis was 1986 days (range: 19—4270 days). All patients were immunocompetent throughout the period of study. Prior to PCR confirmation of CMV endotheliitis, 12 eyes (70.6%) were labeled as anterior uveitis, and 7 eyes (41.2%) were diagnosed as Posner Schlossmann Syndrome. Overall, 14 eyes (82.4%) were treated for uveitic glaucoma. Before a diagnosis of CMV endotheliitis, all patients had received topical corticosteroid therapy (prednisolone acetate 1% ophthalmic suspension), 9 eyes (52.9%) underwent cataract surgery with implantation of intraocular lens, and 10 eyes (58.8%) underwent trabeculectomy or needling.

About three-fourths of cases in our series (13 eyes, 76.5%) were categorized as atypical CMV endotheliitis based on the diagnostic criteria proposed by the Japanese Corneal Endotheliitis Study Group. (Koizumi et al. 2015) Clinical signs observed on slit lamp examination included, localized corneal edema (10 eyes, 58.8%), iris atrophy (5 eyes, 29.4%), coin-shaped keratic precipitates (3 eyes, 17.7%), linear keratic precipitates (1 eye, 5.9%) and diffuse bullous keratopathy (1 eye, 5.9%). During treatment, 4 eyes (23.5%) developed cataract. The mean LogMAR visual acuity was 0.38 ± 0.54 at presentation and 0.70 ± 0.62 at diagnosis ($p=0.093$). The median intraocular pressure was 26mmHg (Range: 12–58 mmHg) at presentation and 18mmHg (Range: 8–47 mmHg) at the time of diagnosis ($p=0.138$). Initial treatment was started in the form of topical ganciclovir ointment (every 2 hours) in 13 eyes (81.2%) and oral valganciclovir (900 mg twice daily) in 4 eyes (23.5%). However, both topical and oral treatments were required during later stages of the disease.

Overall, ganciclovir ointment was used in all (100%) patients whereas oral valganciclovir was used in 13 (81.2%) patients. The mean duration of anti-CMV treatment was 12.4 ± 6.7 months.

The median follow-up period from time of diagnosis was 17 months (Range: 5-29 months). The anterior chamber inflammation was controlled in 15 out of 17 (88.2%) eyes at final follow-up with the addition of anti-CMV treatment to topical corticosteroids. One patient (5.8%) continued to develop bullous keratopathy despite treatment, and another patient (5.8%) underwent combined penetrating keratoplasty and phacoemulsification with intended aphakia after the diagnosis of CMV endotheliitis. The median intraocular pressure was significantly lower at final visit at 15mmHg (Range: 9–29 mmHg) as compared to the median intraocular pressure at presentation ($p = 0.001$). The mean number of anti-glaucoma medications was reduced from 3.71 ± 1.69 to 1.65 ± 1.17 between diagnosis and final follow-up after treatment ($p=0.001$). However, there was no statistically significant difference between the final mean visual acuity (0.68 ± 0.60) and mean visual acuity at presentation ($p = 0.171$) or diagnosis ($p = 0.240$).

Our case series reflected a very wide range in the time-lapse between symptomatic onset and final diagnosis of CMV endotheliitis. This was further suggested by the facts that our patients had a poor visual acuity at presentation, high rate of cataracts and history of glaucoma surgery at the time of diagnosis. Visual acuity at termination was partly affected by glaucomatous damage. The mean available Visual Field Index at baseline was 95.5% and dropped to 88.8% at termination of study. The mean deviation (MD) was -3.77 at baseline and dropped to -6.15 at conclusion of study. Mild to moderate corneal haze may also have contributed to the poor visual acuity at the end of the study in our patients. Unfortunately we did not have the optical coherence tomography data for determining the macular status.

We observed from our series that during the initial years, a significant proportion of these patients presented with brief episodes of hypertensive anterior uveitis, which showed rapid response to topical corticosteroids in the beginning. However, in later years the condition became chronic anterior uveitis with trace inflammation in the anterior chamber despite prolonged use of topical corticosteroids. The initiation of ganciclovir gel or oral valganciclovir often successfully controlled these inflammatory reactions that had not responded to topical corticosteroids alone.

Up to this moment, there is no consensus on the treatment of CMV endotheliitis. Valganciclovir and ganciclovir are commonly used agents for treatment of CMV endotheliitis. (Pavan-Langston et al. 2012) In our clinic, ganciclovir ointment is the preferred initial treatment for CMV endotheliitis. This choice is attributed to the absence of systemic adverse effects and low cost of ganciclovir ointment, as compared to oral valganciclovir.

In summary, our study showed that CMV endotheliitis remains a rare yet important differential diagnosis for cases with hypertensive anterior uveitis. Care should be taken to examine the status of endothelium and/or presence of clinical signs of endotheliitis in patients who are referred for management of hypertensive anterior uveitis.

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