IJAER/ June-July 2012/Volume-1/Issue-1/Article No-29/ 168-170 ISSN: 2278-9677

International Journal of Arts & Education Research

# CYTOMEGALOVIRUS-RELATED CORNEAL ENDOTHELIITIS

**Dr. Himanshu Sharma**
Research Supervisor
Deptt. of Chemistry
C.M.J.University
Shillong
Meghalaya

**Anil Kumar**
Research Scholar
Deptt. of Chemistry
C.M.J. University
Shillong
Meghalaya

## ABSTRACT
Cytomegalovirus related corneal endotheliitis is an inflammation of the corneal endothelium caused by Cytomegalovirus. It typically presents as coin-shaped keratic precipitates with or without corneal edema, in otherwise healthy individuals. It may be associated with anterior uveitis and raised intraocular pressure. Patients with Cytomegalovirus related corneal endotheliitis respond to systemic and topical ganciclovir with the use of topical steroid. Making an accurate early diagnosis is crucial in preventing loss of corneal endothelial cells and unnecessary treatment resulting from misdiagnosis in these patients.
**Keywords:** Endotheliitis, Corneal endothelium, Cytomegalovirus, Ganciclovir

## INTRODUCTION-
Corneal endotheliitis, an inflammation of the corneal endothelium, is characterized by corneal edema; keratic precipitates and mild to moderate anterior chamber inflammation. This clinical entity can be attributed to various causes, all of which share a common site of inflammation-corneal endothelial cells. Hence, inflammatory entities (epithelial keratitis and interstitial keratitis) that involve other parts of the cornea-namely, the epithelium and the stroma do not fit the criterion of this disease. Corneal endotheliitis is caused by a variety of mechanisms, including immune-related mechanisms without any known causative organisms (graft rejection following penetrating kerato-plasty) and infectious mechanisms, such as those caused by viruses. Re-search has shown that corneal endotheliitis can be caused by herpes simplex virus, cytomegalovirus, and vermicelli zoster virus and mumps infection.

Human Cytomegalovirus a ubiquitous lymph tropic herpes virus causes various systemic and ocular clinical entities, including retinitis in immune compromised hosts. Ocular Cytomegalovirus manifestations range from corneal endotheliitis, episodic anterior uveitis, sector iris atrophy with iritis, chronic anterior uveitis, and, ultimately, to retinitis. A few cases of Cytomegalovirus related corneal stromal, and endothelial changes, have been reported in immune compromised patients. Recent research has shown an increasing number of cases of Cytomegalovirus associated anterior segment inflammation with a different range of clinical presentations (including anterior uveitis, corneal endotheliitis, or both) in otherwise healthy individuals. This is a review article that discusses the pathology, diagnosis, and management of Cytomegalovirus related endotheliitis.

## PATHOPHYSIOLOGY:
The exact mechanism of corneal endotheliitis is not yet clear. Research initially suggested that the mechanism of corneal endotheliitis was autoimmune related, based on its similarity with graft rejection and good response to topical corticosteroid treatment. However, with advances in diagnostic procedures, more recent research has indicated that this clinical entity may be caused by viruses like Cytomegalovirus. One possible explanation is that corneal endotheliitis is an autoimmune entity that is triggered by microorganisms like viruses. Suzuki and Ohashi proposed that corneal endotheliitis is an anterior chamber associated immune deviation related disease. They posited that a varied dose of virus is shed into the anterior chamber whenever the virus that has established a latent infection becomes intermittently re-activated. Repeated shedding of virus particles leads to the induction of anterior chamber associated immune deviation related disease against viral antigens. Infection occurs when the pre-existing antibodies are incapable of neutralizing the reactivated virus. This mechanism could explain

why some patients respond to topical anti-inflammatory treatment but experience a relapse or recurrence after stopping the treatment. By contrast, if the treatment regimen includes anti-virus medication, patients with cytomegalovirus related corneal endotheliitis respond nicely.

Research has shown that murine cytomegalovirus in immune-competent mice causes a transient, self limited infection mainly in the anterior segment, with only minimal involvement of the posterior segment. This finding could explain why most cytomegalovirus related corneal endotheliitis and uveitis cases occur in immunocompetent patients. The range of ocular manifestations of cytomegalovirus and the variation between immune-competent and immune-deficient patients may depend on the ocular immune response and/or the viral load. Hence, the anterior segment entities being the main mode of expression of infection in relatively competent immune systems and posterior segment involvement in immune compromised subjects.

**CLINICAL FEATURES-**

The clinical features of corneal endotheliitis consist of keratic precipitates and a corneal edema without the involvement of the other corneal layers. Typically, cytomegalovirus related corneal endotheliitis occurs in immunocompetent patients who are not afflicted with any other diseases. Inflammation of the corneal endothelium may or may not be associated with anterior uveitis. High intraocular pressure can occur in patients with cytomegalovirus related corneal endotheliitis; its occurrence may be related to inflammation of the trabecular meshwork. Koizumi et al. found that 7 of 8 (87%) of their patients with high intraocular pressure responded nicely after treatment specific for cytomegalovirus. In addition, cytomegalovirus related corneal endotheliitis can mimic other clinical entities. In some patients, it may present as chronic anterior uveitis and recurrent episodic iritis with raised intraocular pressure, resembling Posner-Schloss man syndrome and in others, it may present with anterior chamber cells and endothelial keratic precipitates, resembling Fuchs' hetero-chromic iridocyclitis.

Based on the distribution of the keratic precipitates and configuration of the overlying stromal and epithelial edema, corneal endotheliitis can be classified into four forms: linear, sectorial, disci-form, and diffuse. In both the linear and sectorial forms, the corneal edema is localized; however, the distribution of keratic precipitates differs that is, it is linear in the former but is disseminated to involve the area of the edema in the latter form. In disci form corneal endotheliitis, a round or discshaped stromaledema is present in the central or paracentral region of the cornea and numerous keratic precipitates form inside the corneal edema. In diffuse corneal endotheliitis, the edema is spread over the entire cornea and fine keratic precipitates are scattered within the lesion. Cytomegalovirus related corneal endotheliitis rarely presents in the diffuse form.

**DIAGNOSIS-**

In general, corneal endotheliitis is a clinical diagnosis. Corneal endotheliitis associated with specific coin-shaped keratic precipitates could be used as a screening tool for cytomegalovirus related anterior segment infection, especially if it is associated with high intraocular pressure and corticosteroid-recalcitrant inflammation. In cases of cytomegalovirus related corneal endotheliitis, isolation of the virus from the anterior chamber is necessary before starting the required treatment. Because the aqueous humour is generally free from any pathogens, a positive result obtained by polymerase chain reaction should be considered reliable provided that contamination from the technique itself is excluded. Anterior chamber fluid can be tested for the presence of viral deoxyribonucleic acid and local antibody production. A combination of these tests is preferred because test results can vary during the course of the disease. Testing for deoxyribonucleic acid tends to be positive at the onset (and/or early at reactivation), and antibody testing can be positive at any point in time. In general, the aqueous humour should be analyzed by polymerase chain reaction for herpes simplex virus, varicella zoster virus, and cytomegalovirus deoxyribonucleic acid.

The Goldman Witmer coefficient can also be calculated for aqueous fluid so as to exclude the possibility of passive diffusion from the patient serum. The Goldman Witmer coefficient is defined as titer of antibody in aqueous of antibody in serum X total serum globulins: total aqueous globulins. A Goldman

Witmer coefficient can be considered positive (suggestive of intra ocularanti body production) when the value exceeds. Detection of corneal endothelial pathology (pseudoguttata orowl's eye) can sometimes be performed with in vivo confocalmicroscopy.

**TREATMENT-**

The treatment of cytomegalovirus related corneal endotheliitis should target both its infectious and inflammatory components. One rational strategy is appropriate systemic and antiviral treatment with topical corticosteroids. Most current treatment regimens are drawn from knowledge of cytomegalovirus related retinitis in immune compromised patients. Ganciclovir, a potent anti-viral medication used to treat or prevent cytomegalovirus infections and other members of the herpes virus family, has been widely used in its systemic form to treat cytomegalovirus related retinitis. By inhibiting viral deoxyribonucleic acid polymerase, ganciclovir terminates the elongation of viral deoxyribonucleic acid which in turn arrests viral replication. Topical ganciclovir 0.15% gel has also been shown to be effective in the treatment of active herpetic epithelial keratitis, in the prophylaxis against herpetic keratitis following kerato-plasty, and in the treatment of cytomegalovirus related uveitis. Corneal penetration of topical ganciclovir is good and can reach therapeutic levels in the aqueous humour. Ganciclovir given in gel form is easy to apply and seems to be a safe alternative to the more toxic systemic form.

When Koizumi et al. used systemic ganciclovir to treat patients with cytomegalovirus induced corneal endotheliitis; all patients exhibited a quick clinical response to the treatment. In their study, patients received IV ganciclovir (5–10 mg/kg) and 1 patient received oral form valacyclovir (1500 mg/day). All patients received topical corticosteroids; patients received 0.3% topical acyclovir, 3–5 times per day, and the other patients received 0.5% topical ganciclovir, 6–8 times per day. In another study, Anshu et al. 1 treated 4 patients who had been diagnosed with cytomegalovirus related endotheliitis following Descemet's stripping automated endothelial kerato-plasty with oral valganciclovir 900 mg twice daily for 6 weeks, followed by 900 mg once daily for a further 6 weeks. Patients also received topical steroids, topical anti-glaucoma medications, and topical ganciclovir as needed. All patients responded to treatment and grafts remained clear in 3 of the 4 patients. After completion of treat 2 patient shad recurrence of inflammation, with mean time to recurrence of 8 months. Thus, cytomegalovirus related corneal endotheliitis responds nicely to ganciclovir but can recur after discontinuation of the treatment. Physicians should inform patients about the potential for hematologic toxicity secondary to systemic administration of ganciclovir and, consequently, monitor patients periodically. If myelo suppression or pancytopenia occurs, the treatment should be discontinued.

**CONCLUSIONS**

Cytomegalovirus related corneal endotheliitis is manifested by cornealedema in various locations, the presence of keratic precipitates and a mildanterior chamber reaction, and is usually associated with raised intraocular pressure. Misdiagnoses and delays in treatment may occur because cytomegalovirus related cornea endotheliitis can mimic other clinical diagnoses. Further study is needed to investigateother aspects of the disease, such as pathogenesis, ways of prevention, and efficient treatment modalities.

**REFERENCES**

1. Anshu, A. (2009) 'Cytomegalovirus endotheliitis in Descemet's stripping endothelial kerato-plasty'. Ophthalmology, 116(4): 624–30.
2. Colin, J. (2007) 'Ganciclovir ophthalmic gel, 0.15%: a valuable tool for treating ocular herpes'. Clin. Ophthalmol. 1(4): 441–53.
3. Singh K, (2004) 'Mumps-induced corneal endotheliitis'. Cornea 23:400–2.
4. Suzuki T, (2008) 'Corneal endotheliitis'. Semin. Ophthalmol. 23(4):235–40.