Cytomegalovirus Retinitis in an Immunocompetent Patient: A Case Report

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Abstract- A 25-year-old female known case of end-stage renal disease was admitted with chief complaints of headache, dizziness, and vomiting after undergoing her last dialysis seven days prior to her admission and gradual vision loss from 2 days after the onset of her headache. Ocular examination on admission revealed white conjunctiva in the left eye without a pupillary response to light. The ophthalmologic evaluation showed severe retinitis with no fundus change in the left eye. The high intraocular pressure was documented on multiple occasions reaching a peak of 45 mm/Hg. Based on the imaging of the left eye and the clinical presentation of retinitis, the patient was diagnosed with Cytomegalovirus (CMV) retinitis.

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Introduction

The majority of the human population ranging from an estimated 40% to 100%, is a carrier of the cytomegalovirus (CMV) (1). People with acquired immune deficiency syndromes and those taking immune suppressive medications are susceptible to a systemic spread of CMV which may manifest in the retina and cause a sight-threatening condition termed CMV retinitis. The presentation of CMV retinitis in an immunocompetent subject is an extremely rare phenomenon (2). Inhere, we report an immunocompetent case of CMV retinitis and review previous cases.

Case Report

A 25-year-old woman, known case of end-stage renal disease (ESRD) of unknown etiology was admitted to our center with chief complaints of headache, vomiting, and dizziness from 7 days, plus a gradual vision loss of the left eye from 2 days prior to admission. She was diagnosed with ESRD 16 months earlier and was on the waiting list for kidney transplantation. The patient was on routine dialysis of 3 times a week, and her last dialysis was 7 days prior to her current admission (the day her disease course started).

Regarding drug history, she only used acetaminophen and mefenamic acid from the time her kidney failure was diagnosed. Family history revealed cataract in both parents and rheumatic arthritis in one of the siblings (brother).

On admission her vital signs were normal, and she was afebrile. Physical examination was as followed: the left eye had whitish conjunctiva. The pupil was dilated, unresponsive to light. However, patient expressed a vision of light, ruling out complete blindness. The ocular movement was normal. Right eye vision, movements, and pupillary response were normal. Other physical examinations were unremarkable. Slit lamp examination showed severe retinitis of the left eye.

Lab data on admission revealed an elevated white blood cell (WBC) count of 11400/mm3 which was neutrophil dominant (61%), elevated C reactive protein (25 mg/l), blood urea nitrogen (54 mg), creatinine (12.2 mg) and potassium levels (6.3 mEq/l). Urinalysis showed elevated protein and glucose levels (3+ for each) and was 3+ for blood with red blood cell (RBC) count of 12-14 per high power field (HPF), WBC count of 8-10 per HPF, many bacteria, few yeasts, and pseudohyphae. Cultures obtained from blood and urine were negative for any type of growth. Stool examination was normal. Patient's serum was tested for CMV immunoglobulins (Ig), results came back positive for IgG (>250AU/ml) and negative for IgM (0.11AU/ml). Other viral markers including HIV

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antibody, HBs antigen, and HCV antibody were negative. CD4 and the CD4/CD8 ratio were in the normal range.

PCR of cerebrospinal fluid was negative for herpes simplex virus after the lumbar tap.

Brain MRI did not show any abnormalities other than a minimal mucosal thickening in bilateral ethmoid air cells and in the maxillary sinuses which were in favor of mild sinusitis. The high intraocular pressure was documented on multiple occasions reaching a peak of 45 mm/Hg. Fundus photography of the left eye showed opacification of the retina with areas of hemorrhage, exudate, necrosis, and periphlebitis in the form of frosted branch angiitis (Figure 1). The patient did not give consent for biopsy of the vitreous fluid for PCR testing, based on imaging of the left eye and clinical presentation of retinitis, the patient was diagnosed with CMV retinitis (3).

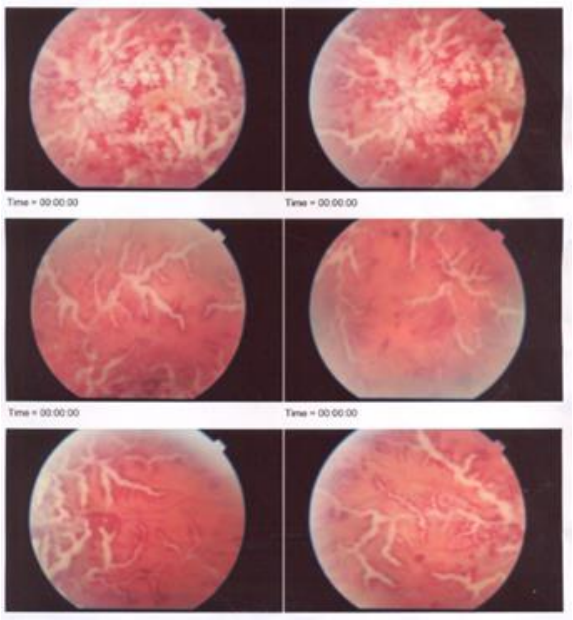

Figure 1. Fundus photography of the left eye

With a diagnosis of CMV retinitis, treatment was started. Treatment included intravenous (IV) gancyclovir (75 mg every 48 hours), prednisolone and atropine eye drops (1 drop of each every 8 hours) and two intraocular injections of gancyclovir.

During her hospital stay and after receiving therapy, ocular pressure decreased from 45 mm Hg to 30 mmHg and finally 16 mmHg. The patient also developed a decreased vision of the right eye during hospital stay. Slit lamp examination showed signs of early retinitis. With clinical suspicion of CMV retinitis, the same medication was started for the right eye during hospital admission. During a six month follow-up, the patient regained full vision of both eyes, and ophthalmic examinations did not show any signs of inflammation in both eyes.

Discussion

CMV retinitis is one of the rare presentations of CMV infection. It is mostly seen in patients with HIV, patients under long-term treatment by immunosuppressive medications, infants, and those with low CD4 counts. However, there have been some case reports of CMV retinitis in immunocompetent patients. Previous literature suggests four main risk factors for an immunocompetent individual to acquire CMV retinitis which includes old age, diabetes, intraocular surgeries and intraocular (local) immunosuppression (4).

Systemic manifestations of CMV infections can include multiple organs such as the lung, gastrointestinal system, liver, CNS, kidney, heart, pancreas, and other systems (5). Our patient presented with decreased vision and increased intra ocular pressure, which is two of the most common clinical manifestations of CMV retinitis (6).

The most common site for the virus to establish in is inside the monocytes, and the mechanism by which the virus spreads to the retina is believed to be through a hematogenous route (4). Once the patient develops some form of immunosuppression, either systemic (in old age and diabetes) or local (with intraocular injection of steroids), the virus reactivates in the retina, and clinical symptoms manifest (7). In patients with diabetes aside to the systemic immunosuppression caused by the disease, it is believed that a decrease in retinal blood supply causes entrapment of virus-carrying leukocytes and consequently increases the risk of CMV retinitis (4). Our patient had advanced kidney disease which is associated with vascular dysfunction, and perhaps the same mechanism may have had a role in the pathogenesis of CMV retinitis. Another issue with our patient relates to the immune system, as end-stage kidney disease itself is associated with dysfunctional immune system function (8) and this may have made the patient susceptible to CMV retinitis, although our patient was not uremic.

To the best of the authors' knowledge less than 25 cases of CMV retinitis has been reported in patients without any type of systemic immunosuppression (the use of immunosuppressive medications, pregnancy, leukemia, and infancy). Other than our case who was a 25-year-old female and another case reported by Furukawa *et al*., (9) (54-year-old female), all immunocompetent cases reported to date have been in patients older than 60-years-old. Sixteen out of the 22

cases were diabetic, and all cases had at least one of the four major risk factors documented for CMV retinitis and were either old age, diabetic, had intraocular surgeries or intraocular (local) immunosuppression (Table 1).

Table 1. Review of immunocompetent cases of CMV retinitis*

Study		Age-sex	DM	IOS	Local immunosuppression	other
Saidel et al. (11)	1	75 - M	+			
Hsu et al. (12)	2	77 - M	+	+		
Furukawa et al. (9)	3	54 - F	+		+	
Delyfer et al. (13)	4	77 - M	+		+	
	5	69 - M	+	+	+	
Sekiryu et al. (6)	6	63 - M	+	+	+	
Park et al. (14)	7	77 - F			+	HTN
Toyokawa et al. (7)	8	83 - M	+		+	
Vertes et al. (15)	9	78 - F		+	+	
Toriyama et al. (16)	10	74 - M		+		
Schneider et al. (17)	11	83 - F	+			HTN, CAD, Anemia
	12	78 - M	+			
Radwan et al. (1)	13	61 - M				HTN, AR, MVP
Takayama et al. (18)	14	69 - M	+			PDR
Yamamato et al. (4)	15	74 - M	+		+	Colon cancer Metastatic liver cancer
	16	61 - F	+		+	
	17	71 - M	+		+	HTN
Bae et al.(2)	18	81 - M	+			MS, CVA, HLP
Davis et al. (10)	19	61 - M	+			CHF, HTN, Aortic Aneurysm
	20	80 - F				HTN
	21	75 - M	+			CAD
Karkhaneh et al. (19)	22	61 - F			+	
This study	23	25 - F				ESRD

M: Male; F: Female; DM: Diabetes mellitus; IOS: Intraocular surgery; HTN: Hypertension; CAD: Coronary artery disease; AR: Aortic regurgitation; MVP: Mitral valve prolapse; PDR: Proliferative diabetic retinopathy; MS: Multiple sclerosis; CVA: Cerebrovascular accident; HLP: Hyperlipidemia; CHF: Congestive heart failure.

* Any study that included patients with systemic immunosuppression such as the use of immunosuppressive medications, pregnancy, leukemia, and infancy were not considered as immunocompetent cases for inclusion in our review of the literature

The early diagnosis of CMV retinitis and prompt treatment is of paramount importance as it can eventually lead to necrotizing retinitis. The complications associated with CMV retinitis in the immunocompetent individual can be magnified compared to an immunosuppressed one. This is due to the disproportionate immune response to the activity of the virus in the retina in the immunocompetent individual in comparison to the immunosuppressed individual (10). As seen in our patient, all immunocompetent cases of CMV retinitis may not be old age, diabetic, locally immunosuppressed or have a history of previous ocular surgery, this points to the significance of clinical suspicion for the diagnosis of CMV retinitis.

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