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Systemic CMV Infection in Acquired Immunodeficiency Syndrome (AIDS) Patient: A Case Report

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Abstract: **Cytomegalovirus (CMV) is a common pathogen in the general population with reported seroprevelance of 40-100% in general population. Primary infection in immune competent people is usually asymptomatic or results in infectious mononucleosis syndrome. However; it is a major cause of morbidity and mortality in patients with Acquired Immunodeficiency Syndrome (AIDS). It can result in retinitis, esophagitis, colitis, pneumonia, and central nervous system disease.This usually results from reactivation of primary infection. With the advent of effective antiretroviral treatment (ART), there has been a dramatic decline in the occurrence of CMV disease in AIDS patients.**

This is a case report of a 36 years old lady who was admitted to the hospital with convulsions. She was found to be HIV positive. During the course of her hospital stay, she developed bloody diarrhea. The patient was suspected to have systemic CMV infection when CMV was detected in the blood, endotracheal secretion and the cerebrospinal fluid (CSF). Valgancyclovir was started in combination with intravenous immunoglobulin (IVIG).This resulted in a significant improvement of the patient's condition. Early initiation of Anti-retroviral treatment (ART) was avoided to prevent the development of immune reconstitution syndrome.

Keywords: **Acquired Immunodeficiency Syndrome (AIDS), CMV disease.**

1. INTRODUCTION

Cytomegalovirus (CMV) is a double stranded DNA virus that belongs to Herpesvirinae family. It is an important pathogen in immune compromised hosts, especially in patients with AIDS [1, 10]. As with other Herpes viruses, CMV remains latent in the infected host throughout life and rarely reactivates to cause clinical illness except in immune compromised individuals [1, 10].

This is a case report of a 36 years old HIV positive lady who was admitted to the hospital with convulsions. Before admission, the patient had progressive muscular weakness. She was found to be positive for HIV. During the course of her hospital stay, she developed symptoms of encephalitis, pneumonitis and colitis due to CMV infection and was treated with Valgancyclovir.

2. CASE REPORT

A 36 years old lady brought to the emergency room after developing lateral gaze of the eyes, frothing of the mouth and tonic-clonic seizure. A 10 mg of valium given rectally to stop the convulsion and was immediately intubated and mechanically ventilated. Prior to her admission, she had history of progressive muscular weakness and was started on prednislone which she stopped taking on her own.

On examination the patient had a Glasgow Coma Scale of 4/15. Blood pressure 100/60 mmHg, Pulse 110 beats/min and temperature of 38.5°C. Her initial complete blood count revealed: WBC count $8x10^9$/L, hemoglobin of 6.3g/L and platelet count of $80x10^9$/L. She received blood transfusion to correct the hemoglobin level. Liver function test showed GGT of 309 IU/l, AST of 58 IU/l and ALT of 103IU/l. Computed Tomography of the head showed evidence of right basal ganglia

infarct and chronic white matter disease which left the patient quadriplegic. Her troponin level was elevated and she was placed on full anti-ischemic treatment.

During her stay in the hospital, the patient continued to deteriorate despite the full medical support. She continued to spike fever. Testing for Human immune deficiency virus (HIV) was suggested by a virologist and was found to be positive with a viral load of $6.6x10^5$ copies/ml. The patient had no known risk factors. The CD4 count was undetectable throughout the entire hospital stay of the patient. CMV was also detected in the blood, endotracheal secretion (ETT) and cerebrospinal fluid (CSF) with a viral load of $6.5x10^4$, $1.5x10^3$and 2150 copies/ml respectively. Systemic CMV infection was suspected at this point and the patients was started on valgancyclovir 900 mg twice daily course. The ETT was also positive for Streptococcus Pneumoniae and the patient was started on Vancomycin. The patient was on prophylactic Co-Trimoxazole for Pneumocystis Jirovecii. During her hospital stay, the patient developed bloody diarrhea and her hemoglobin level started to drop. She was suspected to have CMV colitis. After stabilizing the patient with blood transfusion, colonoscopy was preformed revealing diffused inflammation and mucosal ulceration with two actively bleeding ulcers. Bleeding was controlled by injecting the vessels with epinephrine. Unfortunately, a biopsy was not taken during colonoscopy.The bleeding was stopped following colonoscopy but the patient continued to have diarrhea. A five days course of intravenous immunoglobulin (IVIG) was given at a dose of 0.4g/Kg. This resulted in significant improvement. Valgancyclovir was continued for 42 days until CMV was no longer detected in the blood. Early initiation of Anti-retroviral (ART) combination therapy was avoided to prevent triggering an immune reconstitution syndrome.The patient was started on Reltigravir and boosted Darunavir after sensitivity testing. The classic ART regimen was avoided as the patient was on multiple drugs (eg. anti-ischemic treatment) to avoid drug interaction. HIV viral load continued to drop after commencing ART. Unfortunately, the patient died seven months after diagnosis due to complications of AIDs.

3. LITERATURE REVIEW

Cases of CMV infection in HIV infected patients were identified through a search of the literature in Google Scholar search engine and PubMed data base using the term "CMV infection in HIV patients". Most of the case reports described a single CMV manifestation in HIV infected patients. To our knowledge this is one of the first cases describing systemic CMV in an HIV patient with an undetectable CD4 count. Some cases described CMV infection in HIV patients with relatively preserved CD4 count and even immuocompetent patients. Most of cases that were reviewed were concerned with the clinical presentation and management of CMV infection.

4. DISCUSSION

CMV infection is one of the most common opportunistic infections in people with human immunodeficiency virus (HIV) [4] with clinical CMV disease seen in up to 40% of patients with acquired immunodeficiency syndrome (AIDS) [6].This is most frequently seen in patients with CD4-T lymphocytes count of less than 100 cells/µl [4,9,10]. However; it can also occur in HIV patients with relatively preserved CD4 count [3,8]. Our patient had an undetectable level of CD 4 count which persisted for several months even after the initiation of ART. CMV disease in HIV patients almost exclusively occurs as a result of reactivation of the latent virus in a previously infected host [6]. It can manifest as retinitis in 85% , esophagitis in 2.7% [6] and colitis in 7.3% [4,6] of patients with AIDS. Other manifestations of CMV include pneumonia and central nervous system disease [1]. Colitis is the most common extra ocular manifestation of CMV disease in HIV infected patients [6]. Diarrhea in association with abdominal pain are the most frequent symptoms complex in patients with CMV colitis and should raise the clinical index of suspension for such diagnosis [2,6]. Other symptoms include fever, weight loss and cachexia or even extensive gastrointestinal hemorrhage [6].

During the course of her hospital stay, the patient started developing symptoms of colitis (bloody diarrhea), pneumonitis and encephalitis. CMV was detected in the blood, endotracheal aspirate (ETT) and cerebrospinal fluid (CSF) with a viral load of $6.5x10^4$, $1.5x10^3$ and 2150 copies/ml respectively. At this point, the patient was suspected to have systemic CMV infection. There was even an evidence of hepatitis with elevated liver enzymes.

The diagnosis of CMV disease requires evidence of the virus in end organ tissue, CSF or blood using histopathology, cytology, culture or PCR [10]. However; Immunocompromised patients present a challenge because reactivation of a latent virus is common [10]. Other microbiological, parasitic and fungal causes must be excluded [3,8]. The diagnosis of CMV colitis should be established by colonoscopic examination, revealing characteristic ulceration of the gut mucosa, and histologic confirmation on biopsy which shows the classic intracytoplasmic "owl's eye" inclusions [2,3,5]. Common

colonoscopy findings include diffused inflammation and mucosal ulceration [3,5]. Histological examination of biopsy may reveal enlarged cells with the characteristic CMV inclusions [2,3,5,6,7], however; the histopathology is not always diagnostic [3]. Culture of CMV from biopsy samples has been shown to be unreliable as a diagnostic tool in immunosuppressed individuals as they may shed the virus asymptomatically [9]. Our patient's colonoscopy revealed diffused inflammation and mucosal ulceration with actively bleeding ulcers. The ulcers were controlled by injecting the vessels with epinephrine. Unfortunately, a biopsy was not taken. However; the diagnosis of CMV colitis can be established by correlating the presence of CMV in the blood in a patient with a suggestive clinical picture. Diagnosis of encephalitis and pneumonia was established by demonstrating CMV in CSF and endotracheal aspirate by PCR, respectively.

For the treatment of CMV disease, intravenous Gancyclovir (5 mg/kg twice daily), Foscarnet (90 mg/kg twice daily), or Cidofovir (5 mg/kg/week) are considered as effective regimen [2,3,4,9,10]. If symptoms are not severe enough to alter absorption, oral Valgancyclovir (900 mg twice daily) may also be used effectively [9,10]. Data from the Valgancyclovir Study Group sways opinion towards the use of oral Valgancyclovir, a prodrug of Gancyclovir with excellent oral bioavailability, which has been demonstrated to maintain patients in remission for longer than intravenous Gancyclovir and is therefore normally used as first-line treatment [9].Our patient was started on oral Valgancyclovir of 900 mg twice daily in addition to a five days course of intravenous immunoglobulin (IVIG) at a dose of 0.4g/Kg. This resulted in significant improvement in patient's condition. The CMV viral load was slowly decreasing and treatment was continued for 50 days until the CMV viral load was no longer detected in the blood.Up to 40% of patients on Gancyclovir will experience bone marrow suppression [10]. Our patient had continuous drop in hemoglobin level even after colitis was cleared due to being on Valgancyclovir. This was controlled by multiple blood transfusions until CMV was cleared and Valgancyclovir was finally stooped.

This case report highlights the importance of CMV as a potential pathogen causing systemic infection in HIV patients, especially when the CD4 count is less than 100/µl. It should be noted that an episode of CMV colitis in HIV patients is an evidence of advanced HIV infection and thus an indication for the initiation of anti-retroviral treatment. It is clinically important not to miss the diagnosis of CMV infection in HIV patients as effective treatment is available for both HIV and CMV and can save the life of the patient.

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