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Case Report Open Access

Cytomegalovirus Retinitis with Multiple Co Infections in a HIV/AIDS Patient having Extreme Low CD4 Count: A Case Report and Review of Literature

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Abstract

Introduction: HIV infection leads to a decrease in the CD4 count ultimately leading to the development of AIDS. Under this condition, within the body of the host several OIs manifest their pathological effects. With progressive decrease in CD4 count and with HIV disease progression, the pathogenic effects of these OIs increase several folds. Under this condition, dissemination of multiple infections is extremely common.

Report of case: A 28 year old male patient presented with complaints of weakness, fever, weight loss, dry cough, respiratory distress and dimness of vision. He was HIV sero positive with CD4 count of 0.1 cells/µl of blood. Indirect opthalmoscopic investigations revealed *Cytomegalovirus* (CMV) retinitis. Treatment with wide spectrum antibiotics could not improve his respiratory distress. Broncoscopy or lung biopsy could not be performed due to his poor general condition. CMV PCR revealed high titre (5.1×10^7 copies of DNA/ml serum). In anticipation that his respiratory distress might be caused due to infiltration of CMV into the lungs and also to combat retinitis, i.e. Ganciclovir was started. On treatment, patient became afebrile and there was significant radiological improvement of *pneuomonitis*. He later developed urinary tract infection of *Pseudomonas aeruginosa* and was treated with Cotrimoxazole (800 mg). With HAART, CD4 increased to 66. Patient's visual acuity improved slightly in left eye.

Discussion: Early detection and prompt treatment of HIV and associated OIs is of utmost importance. The symptoms of *Cytomegalovirus* Retinitis are subtle and nonspecific. So, the clinician must have a high index of suspicion for diagnosing CMV retinitis. At extremely low CD4 counts, a disseminated cytomegalovirus infection should always be considered as a likely etiology of *Pneumonitis*. A CD4 Count of 0.1 cells/µl has made the case more novel. The initiation of HAART at extremely low CD4 counts may boost the immune system with rapid increase in CD4 count.

Keywords: HIV; CD4 counts; Opportunistic infections; CMV; *Pseudomonas aeruginosa*; HAART

Introduction

Since its discovery in 1983 by Barre-Sonoussi [1] and Gallo [2] (first to describe HIV-1) and by Clavel et al. in 1986 [3] (first to describe HIV-2) and its association with AIDS, HIV infection has now taken the status of devastating pandemic. It is being recognized as one of the world's most life threatening public health problems. In this condition, there occurs a progressive reduction in the number of T cells expressing CD4 due to HIV infection, thereby leading to progressive decrease in CD4 count of the infected host. As per CDC USA (Centers for Disease Control and Prevention), a CD4 count below 200 cells/l of blood is one of the important criterion to a HIV infected person to have developed AIDS. Taking advantage of this immunocompromised condition (extreme weak immune system), several opportunistic infections (OIs) manifest their adverse effects. Human *Cytomegalovirus* (CMV) is the very common viral OI which shows their adverse effects under this immunocompromised condition. CMV plays extensive roles for morbidity and mortality [4-6] among this patient group. The different clinical manifestations of CMV diseases include retinitis, pneumonia, colitis, encephalitis, polyradiculopathy, esophagitis, etc. Some rare manifestations include adrenitis and oral ulcers [7]. Multi organ involvement in CMV infection is extremely common particularly amongst this group of patients [8]. Pneumonitis and retinitis caused by CMV are very common amongst the immunocompromised subjects with a high mortality rate [9]. CMV retinitis is especially common amongst the HIV/AIDS patients with a very low CD4 count [10]. Patients with CMV retinitis may develop blind spots, blurring of vision or other visual problems and development of floater, also have a chance of developing retinal detachment causing blindness [10]. Breyer et al. (2011) [11] recently reported that irrespective of age and other risk factors, HIV infected male subjects are often associated with a higher risk of severe lower urinary tract symptoms [11].

Thus the main objective of writing up this case report is to give a clear holistic picture of the detrimental effects of late diagnosis of HIV including complications (or even end-organ diseases) caused by the different OIs in HIV infected hosts. It also highlights the importance of early diagnosis and prompt treatment and regular clinical follow up and monitoring of therapy.

Case Report

A 28 year old male patient admitted with the complaints of weakness, fever, significant weight loss, dry cough, respiratory distress and dimness of vision in both eyes. The fever was intermittently present for the last 5 months, without any chill or rigor. The patient was primarily diagnosed as seropositve at ART Center, School of Tropical Medicne & College Hospital, Kolkata "a few months back" (no documentation" but he did not comply with the physician's advice and lost to follow up. Rigorous medical interrogation and counselling revealed that the patient had sexual contacts with multiple sex partners (was a frequent visitor in brothels). On examination, the patient was febrile (100.2°F), anaemic, had a blood pressure of 106/60 mm of Hg. Pulse rate was 112/min. He was tachypneic (respiratory rate 31/min) and he was using all his accessory muscles of respiration, however there was no cyanosis. He was cachectic and poor nutrition with a BMI of 17.3. There was no cervical lymphadenopathy. Respiratory system examination revealed bilateral diffuse crepitations. The patient had no oral ulcers or thrush. His visual acuity was 6/18 in right eye, 6/60 in left eye. Indirect ophthalmoscopy revealed evidence of retinal hemorrhage and hard exudates, more of a peripheral lesion, suggestive of CMV retinitis (Figure 1). Test for his HIV seropositivity was done. His HIV serostatus was confirmed by the three ERS (Enzyme Linked Immunosorbent Assay [ELISA], Rapid, Simple), an ELISA (HIV ELISA, Rapid test) and Western Blot as recommended by the National Aids Control Organization (NACO), Ministry of Health and Family Welfare, Government of India. He came out to be positive for HIV-1 and his CD4 count came out to be 0.1 cells/µl of blood.

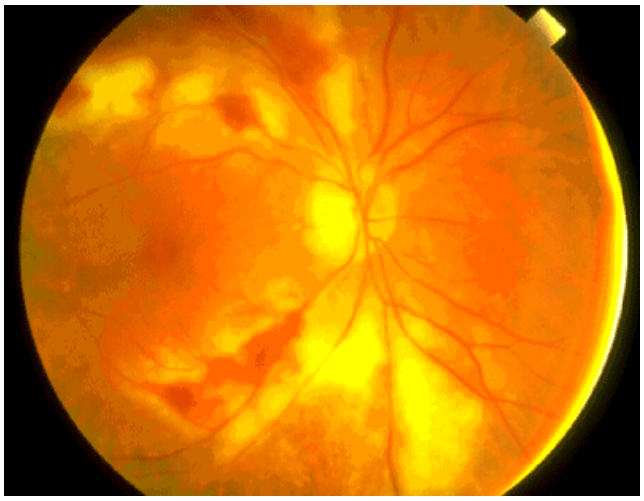

Figure 1: The picture is showing perivascular haemorrhage and exudates characteristic of CMV retinitis. This is often described as "Cottage Cheese with Tomato Ketchup" appearance.

Investigations revealed a total count of 4700/mm, haemoglobin 8.2 gm/ dl, a microcytic hypochromic blood picture. LDH was 110U/L. Mantoux test and sputum for acid fast *bacilli* were negative. X ray showed bilateral chest infiltrates (Figure 2). Routine oral swab was taken for examination.

The patient was not responding to broad-spectrum antibiotic therapy given to combat his respiratory distress. For confirmation of the causative agent for pneumonia, bronchoscopy with broncho alveolar lavage and lung biopsy were planned for cytological and histopathological analysis. However, these tests could not be performed as the patient did not co-operate for bronchoscopy due to respiratory distress and also did not give consent for a lung biopsy.

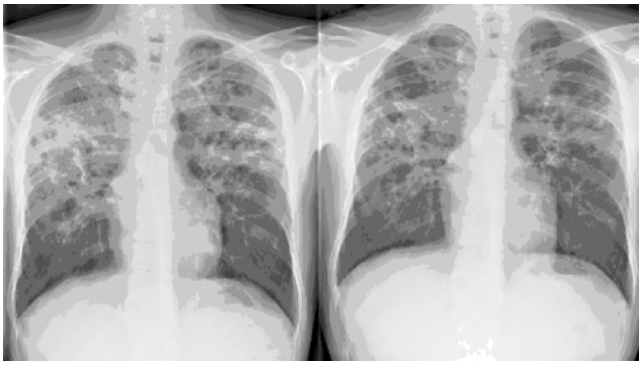

Figure 2: Chest skiagram of the patient showing non specific diffuse interstitial *pneumonitis*.

Indirect ophthalmoscopy done previously was suggestive of cytomegalovirus retinitis. Thus in anticipation of dissemination of CMV infection, CMV PCR was performed to know the titre of CMV viral load in the serum. CMV PCR turned out to be positive with 5.1×10^7 copies of CMV DNA/ml of serum.

Thus, in anticipation that his respiratory distress might have been caused due to CMV *Pneumonitis* (as substantial evidence of CMV Retinitis and a high titre in the blood has already been documented) a Provisional diagnosis of Disseminated CMV infection was made.

Discussion

Early detection and proper treatment is of utmost importance to combat this condition. However, in a developing country like India, subjects belonging to a lower socio-economic strata with no or poor educational background and virtually no knowledge of HIV/AIDS, are often diagnosed late in the course of the disease as is the case of the above subject whose HIV status was detected for the first time when the CD4 value has gone down as low as 0.1 cells/µl of blood. Moreover most of the patients(like our case) also fail to comply with the physicians advice and donot follow up regularly Thus due lack of knowledge, awareness and the prevalent social stigma, many of the subjects are diagnosed late and many are initially apprehensive to come forward and seek for medical advice and attention. The most important cause of mortality in case of patients who have low CD4 count (or have developed AIDS) is the development of several End-organ diseases due to multiple OIs which have been left untreated as a result of late diagnosis leading to progressive failure of the immune system [12].

Widespread CMV infection and EODs caused by CMV are extremely common in these immunocompromised hosts [4-6]. Amongst the HCMV induced EODs that are common among the HIV/AIDS patients, CMV Pneumonitis has high mortality rate. An autopsy study carried out by McKenzie et al. in 1991 revealed CMV to be the most abundant source of pulmonary diseases amongst the HIV/AIDS patients. The study revealed that out of a total of 75 HIV infected subjects who died of pulmonary diseases, autopsy study

showed that CMV was found in the pulmonary tissue of 44 of them [9].

However, the commonest disease associated with CMV infection is CMV retinitis which is characterized by pain in the eye, blind spots, blurred vision, the appearance of floaters and other visual problems. Without proper treatment the damage to the retina can cause blindness in less than 6 months. The problem usually begins in one eye and will often progress to the other eye [10].

At present, there are four antiviral drugs licensed for the treatment of CMV infections: ganciclovir, valganciclovir, foscarnet and cidofovir. With the advent of antiviral therapy, major advances in the treatment and prevention of CMV infection has been achieved. This has lead to dramatically improved outcomes in case of immunocompromised hosts [12].

Under this immunocompromised condition, Urinary Tract Infection (UTI) may also be very common. Study by Breyer et al. (2011) showed that more HIV-positive men had moderate or severe lower urinary tract symptoms (33.2% and 11.4%, respectively) compared to HIV-negative men (29.2% and 4.2%, respectively). The study further infers that men with HIV were twice as likely to develop severe urinary tract symptoms as men without HIV. Again, HIV infected subjects with a history of AIDS are 2.5 times more likely to report severe urinary tract symptoms [11]. *Pseudomonas aeruginosa* infection in the urinary tract is common. *Pseudomonas* can invade the bloodstream from the urinary tract and is the source of nearly 40 percent of *Pseudomonas* bacteremias and may complicate the scenario by developing systematic diseases like bacteremic pneumonia, sepsis and meningitis which are associated with extremely high mortality rates [13].So proper treatment is of utmost importance.

Also, with the advent of HAART (Highly Active Antiretroviral Therapy), which is a combination of atleast three active antiretroviral agents, a partial recovery of the host immunity occurs as is manifested by a rise in $CD4^+$ T-lymphocytes count which leads to a decrease in AIDS related morbidity and mortality [14-15].

In this article we report one late diagnosed HIV-1 infected patient with baseline CD4 count of 0.1 cells/µl blood who presented with respiratory distress and was subsequently diagnosed to have developed broncopneumonia which was not responding to conventional antibiotics. Indirect opthalmoscopic examination revealed that he had developed CMV retinitis with detectable amount of CMV in the serum. On treatment with Gancyclovir IV, marginal improvement of his clinical condition was observed. Furthur, HAART increased his CD4 count to 66 cells/µl blood. During his follow up, he developed symptomatic *Pseudomonas aeruginosa* infection in the urinary tract. Treatment with Cotrimoxazole resolved his urinary tract infection. Patient was on high flow oxygen, and IV ganciclovir 5mg/kg for 3 weeks, followed by valganciclovir 900 mg qd for 4 months. HAART was initiated with zidovudine, lamivudine and nevirapine.

Conclusion

This is a case of very late diagnosed (diagnosed at CD4 0.1 cells/µl of blood) HIV-1 infection where the subject was suffering from multiple opportunistic infections ranging from bacteria to virus. These include CMV infecting the eye causing retinitis, *Pneumonitis* of unknown etiology (Probably CMV) and *Pseudomonas aeruginosa* infection in the UTI. However, by correct anticipation to consider CMV as the likely etiology of *Pneumonitis* and prompt proper treatment, clinical betterment of the subject could be achieved. Moreover, starting HAART further helped the cause. Patient started improving after 7 days of intensive therapy. Patient became afebrile, his distress resolved and there was significant radiological improvement of *Pneumonitis*. He was discharged from the hospital on termination of his iv ganciclovir treatment. During his follow-up after 10 days, he complained of suffering from a frequent urge to urinate and burning sensation on urination. The urine had an unpleasant odour and often appeared cloudy and occasionally dark. His urine culture report showed presence of *Pseudomonas aeruginosa* (colony count $>10^5$) which was treated effectively with Cotrimoxazole (800 mg) 12 hourly for 14 days based on the culture and sensitivity report. His CD4 count increased to 66 after 2 months and increased to 101 after 4 months.

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