Original Article

Reactivation of Cytomegalovirus Infection in A Non-HIV Immunocompromised Patient: A Case Report

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Abstract

Introduction: Cytomegalovirus (CMV) is a double-stranded DNA virus and a member of the Herpesviridae family. Cytomegalovirus infection is one of the important causes of mortality and morbidity in immunocompromised patients. This is a case report of 72 year-old immunocompromised male patient with worsening cough needing an intubation despite previous adequate antibiotic administration. Further examination showed positive CMV infection. The patient showed improvement after administration of ganciclovir.

Keywords: cytomegalovirus, immunocompromised, reactivation, pneumonitis

Abstrak

Cytomegalovirus (CMV) merupakan suatu virus DNA rantai ganda, yang termasuk dalam famili Herpesviridae. Infeksi CMV merupakan salah satu penyebab penting mortalitas dan morbiditas pada pasien-pasien imunokompromais. Tulisan ini melaporkan kasus seorang pasien pria imunokompromais berusia 72 tahun dengan batuk yang semakin memburuk hingga perlu dilakukan intubasi, meskipun sebelumnya telah diberikan terapi antibiotik yang adekuat. Pemeriksaan lebih lanjut menunjukkan adanya positif infeksi CMV. Pasien menunjukkan adanya perbaikan setelah pemberian ganciclovir.

Kata kunci: cytomegalovirus, imunokompromais, reaktivasi, pneumonitis

Introduction

Cytomegalovirus is an important cause of mortality and morbidity in immunocompromised patients. CMV infection in such patients can affect almost every organ in the body.1 In critically ill patients, the most common mechanism for CMV infection is reactivation of the CMV virus. Methods for the diagnosis of CMV infection are viral isolation by viral culture, serology, and a molecular approach for the detection of viral DNA from blood and other clinical specimens.2 Ganciclovir and valganciclovir are the drugs of choice for the treatment of CMV infection.3

Case Report

A 72-year-old male came to the Emergency Department with chief complaint of abdominal discomfort since 4 months before admission. The pain was located at the left upper and central regions of the abdomen, accompanied by burning sensation. There was no radiating pain, and it was not affected by eating. There was no diarrhea, vomiting, fever, blood in stool, stool was not black colored, and no complaints during urination. The patient previously visited another hospital and was told that there is blood thickening in abdominal blood vessel. Then, the patient underwent heparinization. He had a history of hypertension and underwent cardiac stenting two times. He had a history of lymphoma and had undergone chemotherapy six times and radiotherapy. The tumor was in remission. Physical examination revealed patient was compos mentis with stable hemodynamic. Other examinations were within normal limits. Laboratory test showed no significant abnormality.

During hospitalization, the patient had a cough with difficult to expectorate sputum, and shortness of breath, but no fever. Further observations revealed continuous desaturation, thus the patient was sedated and intubation was performed. Further, the hemodynamic parameters were stable with oxygen saturation of 99% via ventilator. On lung examination, there was a vesicular breath sound with bilateral rhales. Bronchoschopy (Fig. 1) and chest x-ray (Fig. 2 and Fig. 3) was conducted. Laboratory examination following bronchoscopy showed elevations in LDH (369 IU/L), procalcitonin (0,78 ng/mL), and CRP (140 mg/L); decrease in the CD4 count (76 cell/mm3); and reactive Anti CMV IgG (from Bronchoalveolar Lavage specimen) (8.3). To control infection, the patient was given intravenous antibiotic (Linezolid and Imipenem) and intravenous antiviral (gancyclovir) 2x250 mg.

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Introduction

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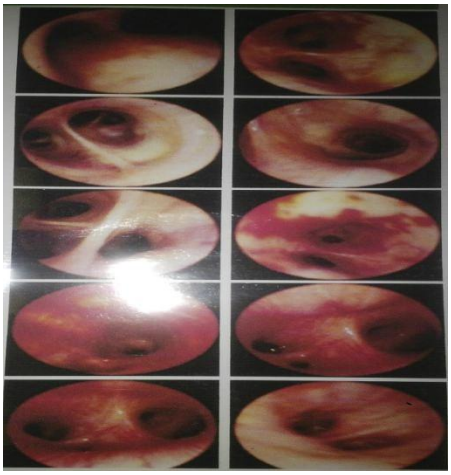
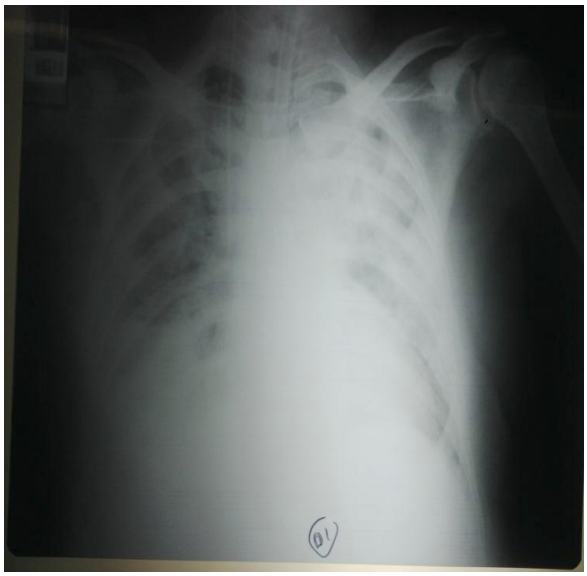
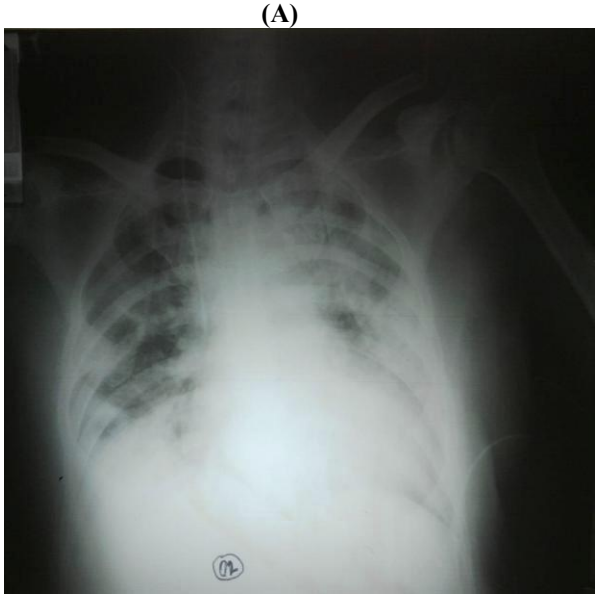


Figure. 1. Bronchoscopy result showed infection and sectional trauma at the lower respiratory tract



(A)



(B)

Figure. 2A. pre-Bronchoscopy. Showed right pleural effusion with infiltrates in both lung fields **2B. post-Bronchoscopy.** Improvement in right pleural effusion and infiltrates.

Discussion

Cytomegalovirus (CMV), a double-stranded DNA virus and a member of the Herpesviridae family, is an important cause of mortality and morbidity in immunocompromised patients. The manifestation of CMV infection is variable, but it usually causes an asymptomatic infection or only mild flu-like symptoms. In immunocompromised patients, CMV infection can affect almost every organ of the body, manifesting as fever of unknown origin, pneumonia, hepatitis, encephalitis, myelitis, colitis, uveitis, retinitis, and neuropathy. Some rare manifestations of CMV infections include Guillian-Barré syndrome, meningoencephalitis, pericarditis, myocarditis, thrombocytopenia, and hemolytic anemia.[1]

In critically ill patients, the most common mechanism for CMV infection is the reactivation of CMV virus, not due to primary infection. CMV has the ability to become latent in various types of cells, like monocytes, CD34+ haematopoietic progenitor cells, and endothelial cells. CMV has a longer replication cycle and it encodes three sequential genes, which encode for immediate early (IE), early, and late proteins, respectively. Activation of the IE region is seen as the first crucial step for reactivation of CMV. These IE sequences contain various nuclear factor kappa B (NF-κB) consensus sequences which are normally inactive. Activation of NF-κB by any mediator could trigger CMV reactivation. These mediators include proinflammatory cytokines, chemokines, adhesion molecules, inflammatory enzymes, and receptors which are released during sepsis, burns, surgery, trauma, multiple organ failure syndrome, allogeneic blood transfusions, or organ and bone marrow transplants. In addition, replication of CMV causes tissue injury, which leads to the release of more proinflammatory cytokines that further causes low-grade chronic inflammatory changes or even exacerbation of certain preexisting diseases.[2]

The patient is an immunocompromised patient with history of lymphoma and had undergone multiple chemotherapy and radiotherapy regiments, with low CD4+ level. It is suspected that the patient had latent CMV infection which was reactivated during hospital admission. Laboratory results confirmed systemic inflammation and infection as seen from the elevated LDH, CRP, and procalcitonin levels which may trigger CMV reactivation by the activation of NF-κB by inflammatory mediators. Continuous replication of CMV causes further tissue injury, resulting in the exacerbation of pneumonia.

Methods for diagnosing CMV infection include viral isolation by viral culture, serology which includes CMV specific antigen and antibody detection, and molecular procedures for the detection of viral DNA from blood and other clinical specimens.[2]

In this patient, reactive Anti CMV IgG was obtained from the BAL sample, which confirmed active CMV infection in the lungs. Ganciclovir and valganciclovir are the drugs of choice for the treatment of CMV disease. Recommended ganciclovir dose is 5mg/BW/day intravenous route, as an induction dose for 2-3 weeks, followed by another 3-4 weeks maintenance dose via the oral route. Recommended valganciclovir dose is 900mg, every 12 hours.[3] Treatment of choice for CMV infection is ganciclovir, but it requires intravenous administration, which affects the feasibility for long term-use. Valganciclovir has an oral bioavailability of 60%, proven to be useful and safe for the prophylaxis and treatment of CMV infection.[4]

conclusion

In immunocompromised critically ill patient with non-resolving pneumonia, CMV pneumonitis should be one of the differential diagnosis.

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