Case Report

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A Case Report of CMV-Associated Encephalitis

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ABSTRACT

Cytomegalovirus (CMV) infection is not common in immunocompetent patient. This study is a case report of a 60-year-old man with no evidence of immunocompromised history, who died from CMV-associated encephalitis. The patient presented with a 5-month headache whose pattern and severity changed in the past few days, coffee ground vomiting, and three times seizure. The condition caused his level of consciousness to decrease, he didn't respond to the primary empirical treatment, and the primary paraclinical work up had no specific findings. Magnetic resonance imaging (MRI) showed normal pressure hydrocephalus, and cerebrospinal fluid (CSF) analysis had aseptic pattern, blood culture was negative, and CSF culture was negative too. After that multiplex polymerase chain reaction (PCR) was done on the CSF, which was positive for CMV. Foscarnet therapy was initiated for the patient, but it was too late, and the patient did not respond to these treatments. Finally, the patient died. It is too important to diagnose these conditions and initiate therapy as soon as possible.

Keywords: PCR, Cytomegalovirus, Encephalitis

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Introduction

Cytomegalovirus (CMV) is a member of the *Herpesviridae* family and is frequently associated with an infection that is self-limiting in immunocompetent individuals **(1)**. In patients with profoundly-immunocompromised conditions, the virus could cause more severe diseases, including colitis, pneumonia, and less commonly encephalitis. Early initiation of antiviral therapy is crucial for achieving an overall positive outcome. We present a case pertaining to a hospital visit where a patient had headaches and seizure attacks within the past 40 days with no history of epilepsy or immunocompromised state. The patient's mental status changed during hospitalization. The importance of this case is due to multiple points. The presentation was somewhat difficult and different from typical forms. The patient had no history of immunocompromised status. The patient was not hospitalized, and the source of infection was unknown.
CMV is a herpesvirus that results in lifelong latent infection after primary infection. In the event of immunosuppression, it is able to be reactivated. CMV is associated with encephalitis, a syndrome that is less common but more devastating **(2, 3)**. CMV-associated encephalitis is a common viral infection that is rarely reported in immunocompromised patients with CD4 (cluster of differentiation four) cell counts greater than 50 **(4).** In this report, we discuss an immunocompetent person infected with CMV causing encephalopathy. Encephalitis is a syndrome that is less common but more devastating, and CMV is associated with encephalitis **(5).** Immune dysfunction is a common occurrence during CMV infection, which includes autoimmune phenomena.

In people with profoundly immunocompromised conditions, CMV could lead to severe diseases, such as colitis, pneumonia, and less frequently encephalitis. Diagnosis is made by detecting CMV in cerebrospinal fluid (CSF) through PCR (polymerase chain reaction) testing or cell culture, as central nervous system (CNS)

imaging findings are not specific. An overall positive outcome could be achieved by early initiation of antiviral therapy.

Case Presentation

The patient was a 60-year-old man with a history of CVA (cerebral vascular accident) for five months ago as well as a history of diabetes mellitus and CABG (coronary artery bypass graft surgery) for ten years ago, who complained of nausea and vomiting, headache, and seizures. The patient complained of headache in the frontal area during 40 days before admission, and five days before admission, the headache pattern changed, and its severity increased. To relieve his headaches, he used painkillers, which caused nausea and coffee-ground vomiting several times, the patient also experienced three seizures within 24 hours before admission. The patient had a history of hospitalization 20 days before admission due to headache and dizziness, and in the previous hospitalization, he was diagnosed with hypertensive crisis and chronic kidney disease (CKD). The patient also complained of dizziness, abdominal pain, and constipation upon arrival. Physical examination showed decreased respiratory sounds in the base of both lungs. In the neurological examination, it was not possible to perform sensory examinations due to the decrease in the patient's mental status. There was no cervical redor, reflexes were bilateral and symmetrical, and Babinski's reflex was bilateral and downward, other examinations had no abnormal findings (Table 1).

In the initial tests, the leukocyte count was 12,000, the percentage of polymorphonuclear leukocytes (PMN) was 85%, the creatinine level was 2.1, the erythrocyte sedimentation rate (ESR) was 31, and other tests were normal. Also, the patient's leukocyte count decreased during hospitalization. Lumbar puncture (LP) CSF analysis was performed twice, each time an infectious pattern was observed (pr:103/glc:32/RBC:180/WBC:500/PMN:80/Lymph:20), but no organisms grew in the culture. Also, due to the endemicity of the area, Brucella tests were performed, which were negative, and the patient's blood culture tests were negative.

The patient underwent endoscopy and was diagnosed with gastritis due to the vomiting mentioned earlier. The patient underwent brain MRI and was diagnosed with normal pressure hydrocephalus, then because of meningoencephalitis findings, HSV (herpes simplex virus) PCR was requested, which was negative, then CSF multiplex PCR of meningoencephalitis germs was requested, which was CMV positive. (Figure 1).

Table 1. Laboratory examination findings in this study

Variable		Variable	
BS	239	ESR	65
BUN	31	CRP	132
Cr	2.1	Alb	2.5
WBC	12	Ca	7.8
HB	13.9	Mg	2.11
PMN	85	P	2.8
LYMPH	11	-	-

BS: Blood sugar; BUN: Blood urea nitrogen; Cr: Creatinine; WBC: White blood cells; HB: Hemoglobin; PMN: Polymorphonuclear leukocytes; LYMPH: Lymphocytes

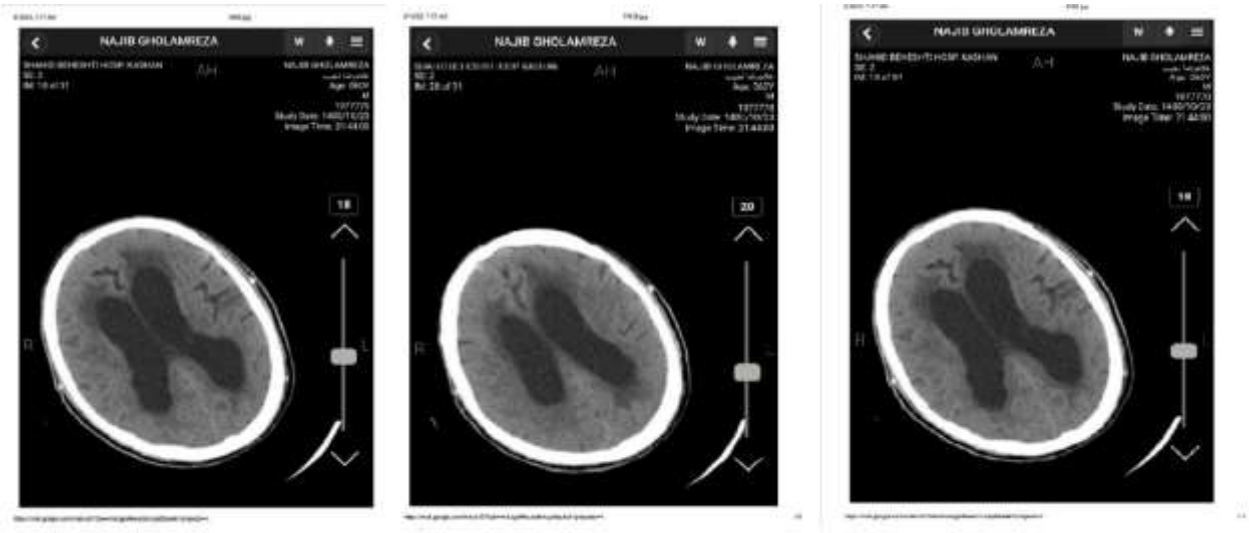


Figure 1. Brain MRI showing normal pressure hydrocephalus

Discussion

According to the findings, this patient was diagnosed with CMV infection and encephalopathy. CMV infection and encephalopathy were diagnosed by taking into account both clinical information and laboratory results. Symptoms such as fever, liver failure, cervical lymphadenopathy, hepatosplenomegaly, etc., which are the main symptoms of CMV infection, are difficult to distinguish from those of primary Epstein-Barr virus (EBV) infection. CMV, a member of the herpesvirus family, is a double-stranded DNA virus that could cause either localized or diffuse end-organ diseases, particularly in severely immunosuppressed HIV-infected individuals. Neurological complications such as encephalitis, ventriculitis, myelitis, retinitis, radiculo-ganglionitis, and peripheral neuropathies are caused by CMV infection. Clinical signs of viral encephalitis are often visible. Ataxia and seizures are common in viral encephalitis. Neck rigidity and specific neurological impairments such paresis, tremor, ataxia, hypotonia, hyperreflexia, and diplopia may also be present. Increased intracranial pressure, papilledema, and paired cranial nerves are all possible complications of encephalitis. Encephalitis, however, may occasionally be asymptomatic **(6, 7).** Noninvasive CMV tests, such as CMV DNAemia and pp65 antigenemia tests, are also widely accessible and provide the prospect of quick findings; if utilized properly, they may aid in early diagnosis. Clinicians should consider severe primary CMV infection as a differential diagnosis in clinical settings given this background. The most frequent causes of encephalitis in children and adolescents are viruses. Diagnosis is very challenging and must be based on imaging results, clinical presentations, and virological markers **(8)**. The exact diagnosis should be established utilizing epidemiological data, clinical presentations, and auxiliary tests whenever feasible.

It is crucial to understand the optimal strategy for gathering samples and choose the appropriate

identification method for each particular virus in order to enhance the chance of obtaining positive findings **(9)**. Immunocompetent people may also develop CMV-associated encephalitis, and it doesn't seem to be linked to any specific clinical condition **(4)**.

In a study, CMV DNA was detected in all specimens collected from AIDS patients, and quantitation of CMV genomes in CSF cells was proved to be a reliable means of detecting CMV infection in AIDS patients **(10)**.

Therefore, the presence of intrathecal HCMV infection is essential for diagnosis. This diagnosis is very challenging due to the limited sensitivity of viral culture methods. Despite the fact that in a small number of cases, a positive PCR could not be linked to an HCMV-associated CNS disease, the highly sensitive PCR detection of HCMV DNA in CSF continues to be a suitable method for antemortem diagnosis of HCMV-related neurological diseases (11).

Conclusion

A viral PCR panel including CMV PCR might be valuable in patients presenting a medical and radiological picture consistent with viral encephalitis.

This report seems to have some problems: 1) the patient was diabetic, and diabetes itself is considered as an immune system disorder; thus, the patient was not immunocompetent. On the other hand, diabetes as an immune system disorder could not be considered as a risk factor for CMV, because due to the high prevalence of diabetes in our country, the prevalence of CMV infection should also be high in the country, which is not the case. 2) There was evidence of infection in both blood and LP CSF. But the question raised here is whether any treatment was prescribed according to the reported LP results. The answer is positive, and according to the evidence of infection, antibiotic treatment was prescribed. 3) Another question raised here is why the combination of cortin, IVIG (intravenous immunoglobulin), and antiviral was not used when CMV infection was diagnosed. The answer is that it is not mandatory to use IVIG in the treatment of CMV infection, and it is recommended only in the treatment of lung involvement.

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Conflict of Interest

The authors declare that they have no conflict of interest.

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Ethics Approval and consent to participate

This study was approved by the Ethics Committee of Kashan University of Medical Sciences (IR.KAUMS.REC.1402.010), all procedures performed in studies involving human participants were in accordance with the ethical standards of the Institutional and National Research Committee.

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