



Case report

Severe cytomegalovirus encephalitis in an immunocompetent healthy young woman: A case report



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ABSTRACT

Cytomegalovirus (CMV) causes a mild illness in immunocompetent patients. Conversely, it can be life-threatening in immunocompromised or critically ill patients. We present a 48-year-old immunocompetent woman presenting primary severe CMV encephalitis. She presented with a headache, fever, and drowsiness. She did not respond to empirical treatment. Her level of consciousness deteriorated, she was put on mechanical ventilation on day two. Bacterial culture, herpes simplex virus, and tuberculosis were negative in cerebrospinal fluid (CSF). After three weeks, the patient was transferred to our center due to financial matters. Brain magnetic resonance imaging (MRI) showed diffuse hydrocephalus, periventricular T2 hyperintensity, patchy basal ganglia, and diffuse leptomeningeal enhancement. CMV polymerase chain reaction (PCR) was positive in cerebrospinal fluid (CSF) specimen. Ganciclovir (5 mg/kg/IV q12h) was initiated. Subsequently, a brain shunt was inserted. Her level of consciousness raised, she was weaned from the ventilator. She was discharged after 52 days in a bedridden state, quadriplegic, and only able to speak words with a minor swallowing problem. She remained in the same condition for one year. She was expired one year later due to aspiration pneumonia after four weeks of hospitalization. Early diagnosis and treatment of severe CMV encephalitis are crucial to prevent neurological sequelae.

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Introduction

Cytomegalovirus (CMV) is a herpes virus with a prevalence rate ranging from 45% to 100% worldwide. Primary infection is asymptomatic or manifests as mononucleosis or influenza in healthy immunocompetent adults [1]. CMV is self-limited in healthy adults and establishes a life-long latent phase within peripheral monocytes and CD34+ myeloid progenitor cells [2].

CMV can cause severe, life-threatening diseases in immunocompromised patients. It is also associated with higher mortality and morbidity in critically ill immunocompetent patients [3,4]. Severe CMV infection is rare in previously healthy immunocompetent adults [5]. Delayed diagnosis of severe CMV in immunocompetent patients may leave severe sequelae. We present a case of primary severe CMV encephalitis in an immunocompetent patient.

Case presentation

A 48-year woman presented to a general hospital, Karaj, Iran, with headache, fever, and drowsiness. A week before the emergency consultation, she had a headache and a reduced appetite. Her vital signs at presentation were as follows: heart rate, 95 beats/min; respiratory rate, 25 breaths/min; blood pressure, 128/77 mmHg; body temperature, 38.5°C; and oxygen saturation of 96% without supplemental oxygen. Neck stiffness, Brudzinski, and Kernig's sign were evident on neurological examination. No focal neurological deficit was present. Nothing was remarkable about her medical or medication history. Laboratory findings are shown in Table 1. Her erythrocyte sediment rate (ESR) level was approximately 100, and the complete cell count revealed a 12,000 leukocytosis.

Her initial brain computed tomography (CT) scan was normal. Cerebrospinal fluid (CSF) analysis showed a lymph-dominant pleocytosis with 1000 cells/mm³ white blood cells, glucose concentration of 56 mg/dL, and protein concentration of 50 mg/dL. CSF was negative for both herpes simplex virus (HSV) DNA and bacterial culture. On the day of admission, the patient was admitted to the intensive care unit (ICU) and started on empirical antibiotic therapy and acyclovir (10 mg/kg/IV q8h).

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Table 1
Laboratory data.

W.B.C	6800/mm ³	ESR	90 mm/h
R.B.C	3.87 Mill/mm ³	CRP	50
Hb	10.8 gm/dl	Urea	15 mg/dl
Hct	31.8%	Creatinine	0.8 mg/dl
M.C.V	82.2 fl	CPK	65 U/L
M.C.H	28 pgm	LDH	604 U/L
M.C.H.C	34 &	Na	135 mEq/L
Platelet	477,000 /mm ³	K	4.3 mEq/L
Total protein	7.7 g/dl	Ca	9.3 mg/dl
Albumin	3 g/dl	P	5.4 mg/dl
Ferritin	234 ng/ml	Mg	2.6 mg/dl

On day 5, a second lumbar puncture was done as there was no response to the treatment. Tuberculosis was negative in CSF.

Her level of consciousness worsened within two days of admission. She only opened her eyes in response to a painful stimulus, and had no verbal or motor response. Due to her comatose condition, she underwent endotracheal intubation and mechanical ventilation. After two weeks, a tracheotomy was performed due to prolonged intubation.

After three weeks, her condition remained unchanged. She was transferred to our center due to financial matters. At presentation to our hospital, she was on mechanical ventilation with tracheotomy on synchronized intermittent mandatory ventilation (SIMV) mode. No verbal and motor response was detected. She opened her eyes in response to painful stimuli.

Brain magnetic resonance imaging (MRI) showed diffused hydrocephalus, Patchy bilateral basal ganglia enhancement, bilateral confluent periventricular white matter T2 hyperintensity, Bilateral frontal gyral enhancement, and diffuse leptomeningeal enhancement suggestive of meningitis (Figs. 1 and 2). The magnetic

resonance venography and angiography were unremarkable. On repeated CSF examination, protein, glucose, and cell count remained unchanged, and cytomegalovirus (CMV) DNA polymerase chain reaction (PCR) was positive.

Ganciclovir (5 mg/kg/IV q12h) was initiated. Her level of consciousness started to rise within one week. She established eye contact and flexor response to pain; however, she had no verbal response. As the hydrocephalus was apparent in brain imaging, a neurosurgical consult advised brain shunt insertion. The patient was transferred to a neurosurgical center, and the brain shunt was inserted. Her hydrocephalus improved within one week. The patient was managed by a therapist-implemented patient-specific (TIPS) ventilator weaning protocol. She was weaned from the ventilator within two weeks as she established spontaneous breathing and was subsequently transferred to the ward.

After two weeks of ganciclovir therapy, CMV DNA was negative on CSF, and initial enhancements resolved on subsequent brain MRI. Her level of consciousness improved within three weeks of weaning from the ventilator; she established eye contact, obeyed commands, and was able to speak words. She did not develop convulsion. Her deglutition function was impaired, but it was improved after two weeks.

As CMV encephalitis is mainly found in immunocompromised patients, a full assessment of occult malignancies, rheumatologic diseases, and human immunodeficiency virus (HIV) was done. Breast ultrasound, stool occult blood, CSF cytology, and chest and abdominal computed tomography (CT) scan were unremarkable. The rheumatologic investigation was negative, the anti-HIV antibody was negative by enzyme-linked immunosorbent assay (ELISA) method and HIV viral load was undetectable.

On day 52, she was discharged in a bedridden state with spastic quadriplegia, she obeyed commands, and she was able to speak

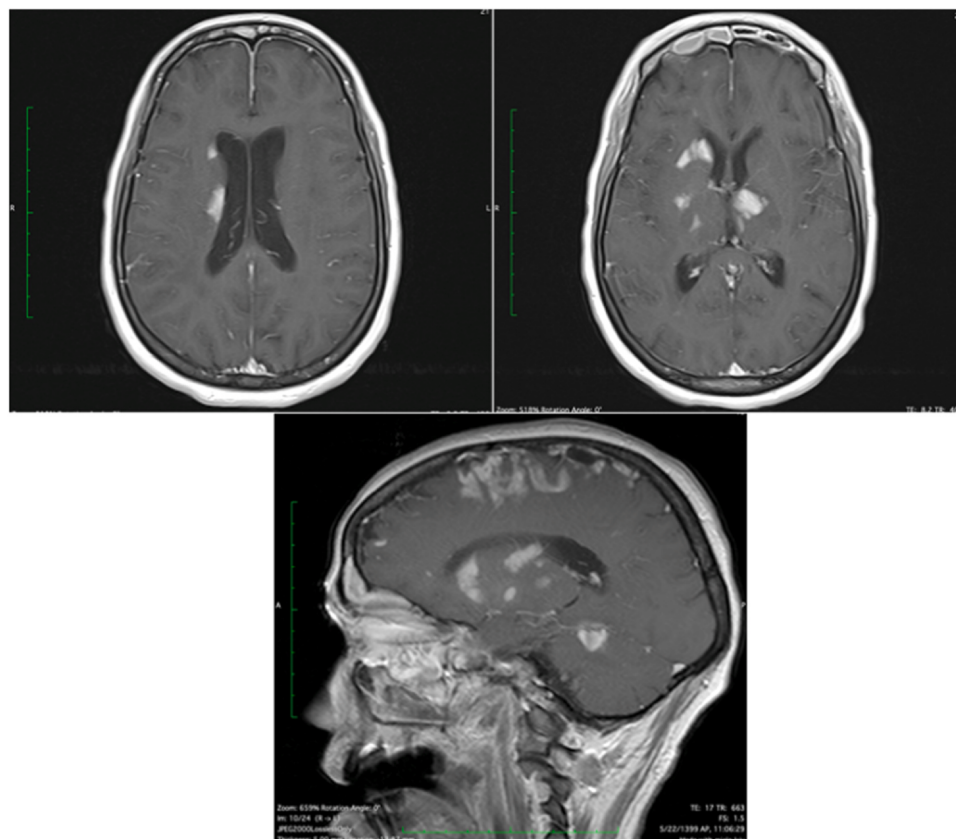


Fig. 1. T1-weighted brain MRI with gadolinium: Diffuse leptomeningeal and patchy bilateral basal ganglia and cerebral peduncles enhancement. Bilateral frontal gyral enhancement.

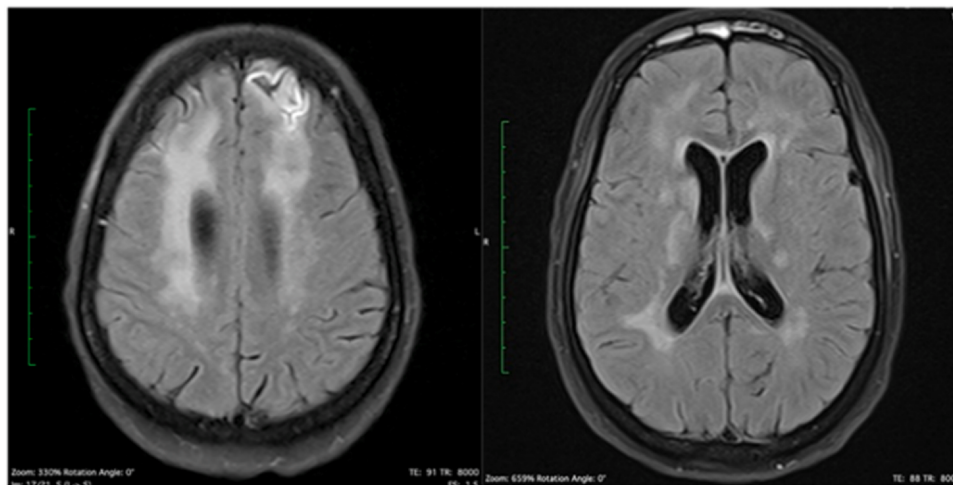


Fig. 2. T2-weighted FLAIR sequence of brain MRI: Periventricular hyperintensity.

words. She had minimal swallowing problems. Due to delayed ganciclovir treatment, she remained bedridden and quadriplegic without any further improvement. The patient was referred to home care facilities and the rehabilitation unit. She was followed up as an outpatient. No improvement was evident during the outpatient follow-up.

Approximately one year later, she was readmitted due to aspiration pneumonia. Subsequently, the patient expired within four weeks of admission due to sepsis.

Discussion

We presented an immunocompetent patient diagnosed with primary cytomegalovirus (CMV) encephalitis. CMV has a seroprevalence of 30–100% within different populations. It manifests as a self-limited nonspecific viral syndrome or mononucleosis-like illness [5]. CMV can establish a life-long latency period in the host cells. It can be reverted to productive infection if the host becomes immunocompromised, as in organ transplant recipients, HIV-infected patients, or patients with hematologic malignancies [6].

CMV infection in immunocompetent hosts has a benign, self-limited course. There are rare cases of severe CMV infection in immunocompetent adults [7]. There are reports of severe CMV infection like encephalitis in immunocompetent patients [8]. Our patient was diagnosed with CMV encephalitis based on MRI findings and positive CMV PCR in the CSF. Ventriculitis, ependymitis, or periventricular enhancement may be evident in brain MRI [9]. However, brain CT scan and MRI might be normal in CMV encephalitis [10].

There are reports of self-limited CMV encephalitis in immunocompetent, that resolved without specific antiviral therapy [11]. On the contrary, Early diagnosis and initiation of specific antiviral treatment (i.e., ganciclovir) are the mainstays of improving outcomes; however, the overall prognosis of CMV encephalitis is poor in immunodeficiency [10].

Our patient did not fully recover from CMV encephalitis. It may be due to delayed diagnosis and specific antiviral therapy. So, CMV should be considered even in an immunocompetent patient presented with encephalitis, especially in the case of poor response to the empirical treatment, preventing delayed diagnosis and specific treatment [12]. Even in the case of positive HSV encephalitis, CMV should be considered as there are reports on simultaneous CMV and HSV encephalitis [13].

Consent

Written informed consent was obtained from the patient's guardian for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contributions

NK and MHM, collected the data. All authors drafted the paper and critically revised the manuscript for important intellectual content and gave final approval for the version to be published.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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