Online ISSN 2623-2723
Print ISSN: 2338-0373
Jurnal Widya Medika Vol. 8 No 1 April 2022

CITOMEGALOVIRUS (CMV) ENCEPHALITIS: A CASE REPORT

[1] Meryana

DOI: https://doi.org/10.33508/jwm.v8i1.3826

ABSTRACT

Encephalitis results from an inflammatory process in the brain which can be caused by infection, post infection or non-infection processes. The most common etiology is infection, especially by virus. Encephalitis is usually followed by diffuse and or focal neuropsychology dysfunctions of brain and meninges (meningoencephalitis). Symptoms of encephalitis are photophobia, headache or neck stiffness, focal neurological deficits, seizure, decrease of consciousness, behavior disorders, and aphasia. However, some patients may not show predominant neruological deficits or even asymptomatic. Inaccuracy to diagnose the etiology promptly can cause morbidity and mortality due to this disease.

The author reports one case of citomegalovirus (CMV) encephalitis with mild symptoms. In this case, a 36-year old man with symptoms of mild fever and mild headache was consulted by an internist to neurologist, because internal examinations couldn't find the etiology of the patient's symptoms. The results of laboratory examinations of NS-1, Dengue IgM and IgG Dengue, Salmonella IgM and IgD, hepatitis screening tests, and chest X-ray examination showed normal results. Brain MRI with contrast then was performed with normal result. Cerebrospinal fluid (CSF) analysis showed pleiocytosis, predominantly mononuclear cells. Diagnosis of CMV encephalitis was established by examination of CMV PCR (Polymerase Chain Reaction) of CSF that was positive. The patient was then treated with antiviral agent Gansiklovir 5 mg/kg every 12 hours for 14 days. On the third day of therapy, the patients had been free of symptoms. The patient was discharged form the hospital in good condition.

Keywords *: encephalitis, symptoms of encephatilis*

ABSTRAK

Ensefalitis adalah inflamasi pada parenkim otak yang dapat disebabkan oleh karena infeksi, post infeksi, atau non infeksi. Etiologi yang sering dijumpai pada penyakit ini adalah infeksi, terutama infeksi virus. Ensefalitis biasanya diikuti dengan disfungsi neuropsikologis difus dan atau fokal pada otak dan meninges (meningoensefalitis). Gejala ensefalitis antara lain fotofobia, nyeri kepala atau kaku pada leher, defisit neurologi fokal, kejang, penurunan kesadaran, gangguan perilaku dan berbahasa. Akan tetapi, ada juga penderita ensefalitis yang tidak menunjukkan defisit neurologis yang menonjol atau bahkan asimptomatik. Ketidaktepatan dalam mendiagnosis etiologi secara cepat dan tepat dapat berujung pada peningkatan morbiditas dan mortalitas.

Penulis melaporkan satu kasus ensefalitis citomegalovirus (CMV) dengan gejala ringan. Pada kasus ini dilaporkan seorang laki-laki, 36 tahun dengan gejala hanya demam subfebris dan nyeri kepala ringan dikonsulkan oleh departemen penyakit dalam ke departemen neurologi karena di bidang penyakit dalam tidak ditemukan etiologi keluhan pada pasien. Pemeriksaan laboratorium NS-1, IgM dan IgG Dengue, IgM dan IgD Salmonella, skrining hepatitis dan foto thoraks menunjukkan hasil yang normal. Oleh departemen neurologi, dilakukan pemeriksaan MRI kepala dengan kontras yang menunjukkan gambaran normal. Analisis cairan serebrospinalis menunjukkan pleiositosis dengan predominan sel mononuklear. Diagnosis ensefalitis CMV ditegakkan melalui pemeriksaan PCR (*Polymerase Chain Reaction*) CMV dari cairan serebrospinalis yang menunjukkan hasil positif. Pasien kemudian diberi terapi antivirus Gansiklovir 5 mg/kg setiap 12 jam selama 14 hari. Pada hari ketiga terapi pasien sudah bebas keluhan. Pasien keluar RS dalam keadaan yang baik.

Kata Kunci : encefalitis, gejala encefalitis

1) Neurology Department, Faculty of Medicine of Widya Mandala Catholic University

INTRODUCTION

Encephalitis results from an inflammatory process in the brain which can be caused by infection, post infection or non-infection processes. About 50% cases are

because of infections. The agents of the infection in encephalitis are virus, bacteria, or other infections.[1] The most common etiology is infection, especially by virus. Encephalitis is usually followed by neurological dysfunctions, and is an emergency. Inaccuracy to diagnose the etiology promptly can cause morbidity and mortality due to this disease.[2]

Symptoms and signs of encephalitis arise as diffuse and or focal neuropsychology dysfunctions of brain and meninges (meningoencephalitis), usually marked by inflammation in meninges as photophobia, headache or neck stiffness. It can also appear as focal neurological deficits, seizure, decrease of consciousness, behavior disorders, and aphasia.[1] However, some patients may not show predominant neurological deficits or even asymptomatic.[3] Inaccuracy to diagnose the etiology promptly can cause morbidity and mortality due to this disease. Following, we report a case of citomegalovirus (CMV) encephalitis in a 36-year old young male patient with mild symptoms of mild fever dan mild headache, along with diagnosis establishment and the managements.

CASE

A 36-year old young male patient with mild symptoms of mild fever dan mild headache was consulted by an internist to neurologist, because internal examinations couldn't find the etiology of the patient's symptoms. The symptoms had been experienced for 5 days. Previously, the patient didn't pay attention because the symptoms are relative mild and he could still do daily activities. But then he started to worry because the mild fever and the headache disapperaed only for a while with routine paracetamol, and would re-appear some hours after taking the medicine. He then decided to see an internist. He had no other complaints. In the physical examinations, we found the body temperature was 37,5 °C, other vital signs were normal. Internal examinations were within normal limit. In the neurological examinations, we found GCS was 456, and the pain scale NRS (*numeric rating scale*) of the headache was 3-4. There were no meningeal signs or other neurological deficits. The previous laboratory examinations of

NS-1, Dengue IgM and IgG Dengue, Salmonella IgM and IgD, hepatitis screening tests, and chest X-ray examination showed normal results. Brain MRI with contrast then was performed with normal result. Complete blood examination showed the leukocytes were 10.000/uL with normal diff. count; and trombocytosis 551.000/uL. D-dimer was normal 250 ug/L. CRP increased 90,44mg/L. *Liver Function Test* increased: SGOT 45,8 U/L and SGPT 87,2 U/L. Ureum and serum creatinine were normal. Then we performed brain MRI with contrast which showed no intracranial pathological lesion. Analysis of cerebrospinal fluid (CSF) after lumbar puncture showed it was macroscopic clear, nonne pandy tests were negative. There was mild pleiositosis 55 cells/mm^3, predominantly mononuclear cells (90%). CSF protein was within normal limit (17,2 mg/dL). CSF glucose was within normal limit 66 mg/dl (random blood glucose when lumbar puncture was performed was 90 mg/dl). Gram staining and acid-fast bacilli staining showed negative results. Besides the CSF analysis, we also performed *polymerase chain reaction* (PCR) tests for Micobacterium Tuberculosis (MTB), Herpes Simplex Virus HSV-1, HSV-2, Varicella zooster, Epstein-Barr Virus (EBV) Enterovirus, Citomegalovirus (CMV) of CSF. CSF CMV PCR test showed positive result, on the other hand all other PCR tests were negative.

According to the examinations, we established the diagnosis as citomegalovirus (CMV) encephalitis. With his body weight of 70 kg, the patient got antiviral agent gancyclovir injection, 350 mg/12 hours intravenously. On the third day of gancyclovir treatment, he was completely free from any complaints of fever and headache. The treatment of gancyclovir injection was continued into 14 days of treatment, then the patient was discharged from the hospital. We didnt't performed post therapy CSF analysis re-evaluation because the patient refused to get the second lumbar puncture. Post therapy complete blood examination showed reduction of the leukocytes into 6.900/uL with normal diff count, and the reduction of the trombocytes into 503.000/uL. CRP dropped into 4,31 mg/L. The SGOT

increased into 48,9 U/L, and SGPT into 94,5 U/L. The internist then gave hepatoprotector to the patient.

DISCUSSION

Viral Encephalitis is a inflammatory disease of the brain parenchyme that caused by virus infection.(4) The epidemiology data are very various between countries. In USA, it is estimated that there are about 20.000 new cases each year, with the most common cause is *Herpes Simplex Virus* (HSV). But international data are not the same in the developing countries because of the difficulty to detect the pathogen agents.(1) Pathogen viruses as the etiology of encephalitis are *Varisella Zooster Virus* (VZV), measles virus, rabies, *Japanese Encephalitis*, mumps, influenza virus, *Human Herpes Virus* (HHV), Citomegalovirus (CMV).(1,4) For the recurrence rate, the most common cause is HSV, which is around 25%. Children and young adults are the most common age groups, but severe cases are more common in infants and geriatric patients.(1) In this case, the patinet was a young adult, in accordance with the most common age group.

There is virus receptor in the cell wall where the virus adheres and starts to replicate. The most common way to spread to the central nervous system (CNS) is hematogenously, and then neural *retrograde*. Rabies virus spreads to CNS *retrogradely* from the peripheral nerves to the temporal lobe. HSV, through the olfactory nerve, goes into temporal lobe and pons, expands to other brain area.(1) Cytomegalovirus (CMV) is a double-stranded DNA virus in the herpes virus family that can cause disseminated or localized end-organ disease especially in HIV-infected patients with advanced immunosuppression. Neurologic manifestations of CMV infection include encephalitis, ventriculitis, myelitis, retinitis, radiculoganglionitis, and peripheral neuropathies. These infections usually occur in patients with severe immunodeficiency:

$CD4^+$ lymphocyte counts typically are lower than 50/µL. Other risk factors for CMV encephalitis include prior history of opportunistic infections, high levels of plasma HIV RNA (>100,000 copies/mL), and high levels of CMV as measured by

polymearase chain reaction (PCR). Most infections occur in the setting of prior CMV disease (seropositive), reactiviation of latent CMV virus, or infection with a novel strain. [3]

Clinical manifestations of viral encephalitis are usually marked by acute fever, headache, decrease of consciuosness, behavior changes, aphasia, or seizure. Neck stiffness or focal neurological deficits can be found such as parese, tremor, ataxia, hypotonia, hypereflexia, and diplopia. Encephalitis can cause increase of intracranial pressure, papil edema, and cranial nerves paresis.[1,4] But encephalitis can be also asymptomatic.[3] In this patient, the symptoms were very mild (mild fever and mild headache). It can be because the patient was in young adult age with the excellent general health status.

Differential diagnoses of CMV encephalitis are herpes simplex encephalitis, CNS criptococcosis, and other viral encephalitis, CNS toxoplasmosis, CNS lymphoma, and metabolic encephalopathy.[3] Other differential diagnoses are bacterial and TBC meningoencephalitis.[4]

The diagnosis of encephalitis, especially those caused by viruses, can be carried out through clinical approaches and further examination like complete blood count, serological test, radiology, and CSF examinations.[4] Laboratory examinations include complete blood examinations, complete blood count (CBC), serum electrolyte levels, serum glucose level, blood urea nitrogen (BUN) and creatinine levels, in some case also urine electrolyte levels and urine or serum toxicology screening.[5] Computed tomography (CT) and magnetic resonance imaging (MRI) can aid in the diagnosis and can exclude other diagnostic considerations (eg, absence of parenchymal enhancement, evidence of increased intracranial pressure). MRI is preferred to CT in the diagnosis of CMV encephalitis. MRI findings are typically non-specific and demonstrate T2 FLAIR hyperintensities in the periventricular white matter. The presence of enhancement suggests ventriculitis, which can occur in CMV encephalitis. Mass lesions due to CMV have been reported but are rare.

T2-weighted MRI may show diffuse white matter hyperintensity similar to that seen in HIV encephalopathy and other HIV-associated central nervous system (CNS) disorders. Contrast MRI may reveal meningeal and ependymal enhancement, as well as ring enhancing lesions. Cerebrospinal fluid (CSF) analysis not only can point to the correct diagnosis but also permits exclusion of other diagnostic considerations. CMV PCR in the CSF is the recommended method to diagnose and confirm CMV with neurologic involvement. CSF analysis will typically show low glucose, elevated protein, and can have mononuclear pleocytosis. In patients with seizure, we should perform EEG examination. [3,4] In this patient, brain MRI with contrast showed normal result without contrast enhancement. In CSF analysis, we got mild pleiocytosis 55 cells/mm3, predominantly mononuclear cells (90%). CSF glukose and protein were normal. Gram and acid-fast bacilli stainings were negative. Diagnosis of CMV encephalitis was established by the positive result of CSF CMV PCR; on the other hand, PCR tests for Micobacterium Tuberculosis (MTB), Herpes Simplex Virus HSV-1, HSV-2, Varicella zooster, Epstein-Barr Virus (EBV) Enterovirus, Citomegalovirus (CMV) were all negative.

Prompt initiation of antiviral drugs is essential for treatment of cytomegalovirus (CMV) encephalitis. These agents inhibit viral replication by competing with deoxyguanosine triphosphate for viral DNA polymerase, inhibiting DNA synthesis. Because the clinical presentation, cerebrospinal fluid (CSF) studies, and imaging studies may not provide a definitive diagnosis, a high level of suspicion is necessary to avoid a delay in proper therapy. Delayed diagnosis and treatment can lead to death.[3] Encephalitis can cause some complications such as seizure, increasing of intracranial pressure, coma, and *SIADH (Syndrome of Inappropriate Secretion of Antidiuretic Hormone).*[5]

Etiological management for CMV encephalitis consists of :[4]

- Induction therapy (2-3 weeks) : Gancyclovir 5 mg/kg every

12 hours + Foscarnet 60 mg/kg every 8 hours

- Maintenance : Gancyclovir 5 mg/kg/day, Foscarnet 60-120 mg/kg/day

In patients with seizure, the management of the seizure is done according to the protocol of status epilepticus. In refractory status epilepticus case, the patient should be admitted to ICU using ventilator and anesthetic drugs. Sedatives can be given if the patient is restless, using clobazam 2x10 mg. Analgetics, for example metamizole 3x1 gram iv can be given if the patient has headache. When there are signs of raised intracranial pressure, we can give mannitol 20%, initial dose is 1-1,5 g/kgBW for 20 minutes, continued with 0,25-0,5 g/kg BW every 4-6 hours, or use hypertonic saline NaCl 3% 2 ml/kgBW for 30 minutes or natrium lactate 1.2 ml/kgBW for 15 minutes. Hemicraniectomy decompression, extraventricular drainage (EVD) or ventriculoperiotneal (VP) shunt may be considered in malignant intracranial hypertension. Giving IVIG (intravenous immunoglobuline) 0,4 mg/kgBW for 5 days can be considered in the patient who has super refracter status epilepticus. [4] To this patient, we gave antiviral agent gancyclovir injection 350mg/12 hours intravenously (body weight 70 kg) for 14 days. At the third day of the treatment, patient had been completely free from fever and headache.

CONCLUSION

Encephalitis results from an inflammatory process in the brain which can be caused by infection, post infection or non-infection processes. The agents of the infection in encephalitis are virus, bacteria, or other infections. The most common etiology is infection, especially by virus. Symptoms and signs of encephalitis arise as diffuse and or focal neuropsychology dysfunctions of brain and meninges (meningoencephalitis), usually marked by inflammation in meninges as photophobia, headache or neck stiffness, focal neurological deficits, seizure, decrease of consciousness, behavior disorders, and aphasia, parese, tremor, ataxia, hypotonia,

hypereflex, and diplopia. However, some patients may not show predominant neurological deficits or even asymptomatic. Inaccuracy to diagnose the etiology promptly can cause morbidity and mortality due to this disease. The earlier the management, the more likey the patient gets better outcome.

REFFERENCES

1. Sugianto P, Ganiem AR, Munir B. Ensefalitis Virus. Modul NeuroInfeksi Kelompok Studi Neuroinfeksi Perhimpunan Dokter Saraf Indonesia 2019. 2019; 137-158.
2. Estiasari R, Imran D, Maharani K, et al. Ensefalitis Antireseptor NMDA: Ensefalitis dengan Gejala Awal Psikosis, Anti- NMDA receptor encephalitis: Encephalitis Presenting with Early Psychosis Symptoms. Neurona. Vol. 35 No. 1 Desember 2017.
3. Krel R, Singh NN, Thomas FP. Cytomegalovirus Encephalitis in HIV. https://emedicine.medscape.com/article/1167229-overview. Updated : Jan 08, 2020.
4. Kurniawan M, Suharjanti I, Pinzon RT. Ensefalitis Viral. Acuan Panduan Praktik Klinis Neurologi. Perhimpunan Dokter Spesialis Saraf Indonesia. Page:211-213. 2016.
5. Howe DS, Lazoff M, Brenner BE. Encephalitis. https://emedicine.medscape.com/article/791896-overview. Updated : Aug 07, 2018