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Polyradiculopathy and Gastroparesis due to Cytomegalovirus Infection in AIDS: A Case Report and Review of Literature

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Patient: Female, 46
Final Diagnosis: CMV gastroparesis and radiculopathy
Symptoms: Nausea • paraplegia • urinary retention • vomiting
Medication: —
Clinical Procedure: Lumbar puncture
Specialty: Infectious Diseases

Objective: Unusual clinical course

Background: Cytomegalovirus (CMV) infection has been well described as an opportunistic infection of patients with human immunodeficiency virus (HIV). To the best of our knowledge, this is the first case report of a patient with AIDS and lumbosacral polyradiculopathy, associated with gastroparesis resulting from CMV infection.

Case Report: A 46-year-old Hispanic woman with a history of HIV for 10 years was admitted to our hospital for nausea, vomiting, urinary retention, and generalized weakness. Bilateral lower extremity examination revealed flaccid paraplegia, decreased sensations from the groin downwards, bilateral lower extremity areflexia, and absent plantar reflexes, with enlarged urinary bladder. CMV was detected in CSF by PCR, and cervical and lumbar magnetic resonance imaging (MRI) revealed intense nodular leptomeningeal enhancement from the lower thoracic cord and extending along the conus medullaris/filum terminalis and nerve roots. Gastric emptying scintigraphy revealed severe delayed gastric emptying time. Ganciclovir was initiated and her neurological symptoms and gastrological symptoms gradually improved. Over 8 weeks, nausea and vomiting resolved and the patient was able to walk before being discharged from the hospital.

Conclusions: Polyradiculopathy and gastroparesis can result from CMV infection in AIDS patients. Whether the mechanism is secondary to viral infection or immune systems remains unclear. It is important for physicians to be aware of this uncommon presentation in the antiretroviral therapy (ART) era. CMV treatment should be initiated immediately once diagnosis is confirmed.

MeSH Keywords: Cytomegalovirus • Gastroparesis • HIV

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/894512

Background

Cytomegalovirus (CMV) infection has been well described as an opportunistic infection of patients with human immunodeficiency virus (HIV). The most common presentation was retinitis prior to the ART era, and gastrointestinal infection in the post-ART era, but rarely for polyradiculopathy. We report the first case, to the best of our knowledge, of acquired AIDS with lumbosacral polyradiculopathy, associated with gastroparesis resulting from CMV infection. Early diagnosis with proper management significantly improves outcome in these patients.

Case Report

A 46-year-old Hispanic woman with HIV for 10 years was admitted to our hospital for nausea, vomiting, urinary retention, and generalized weakness. Three months ago, the patient was diagnosed with Pneumocystis jiroveci pneumonia and CMV pneumonitis. After a complete course of trimethoprim-sulfamethoxazole treatment, ganciclovir and ART were started. However, the patient was non-compliant due to severe nausea and vomiting.

Her vital signs were normal and there was no orthostatic hypotension. Mental status was normal. Neurological examination revealed normal cranial nerves and upper extremities strength and sensations, and there was no nuchal rigidity. No evidence of CMV retinitis was found on funduscopic examination. Bilateral lower extremity examination revealed flaccid paraplegia and areflexia, saddle anesthesia, and absence of plantar reflexes. The patient also had neurogenic bladder with Foley drainage.

Laboratory studies showed a white blood cell count of 5.4 k/mcl, hemoglobin of 10.6 g/dl, and a platelet count of 365 K/mcl. Serum chemistry and urinalysis were unremarkable. Glycated hemoglobin was 5.3%. The CD4 count was 6 cells/cumm. The HIV viral load was 8434 copies/mL.

The cerebrospinal fluid contained 24 white blood cells /cu mm (11% polynuclear cell and 80% lymphocyte), 110 red blood cells, 146 mg/dl protein, and 62 mg/dl glucose. VDRL test was negative. Bacterial and fungal cultures were sterile. Epstein Barr virus (EBV), herpes simplex virus (HSV) type 1 and type 2, and mycobacterial DNA PCR were negative. Toxoplasma gondii antibody IgG was negative. CMV was detected in CSF by PCR.

Head computed tomography (CT) was negative. Cervical and lumbar magnetic resonance imaging (MRI) revealed intense nodular leptomeningeal enhancement from the lower thoracic cord and extending along the conus medullaris/filum terminalis and nerve roots, consistent with an infectious or inflammatory process (Figure 1).

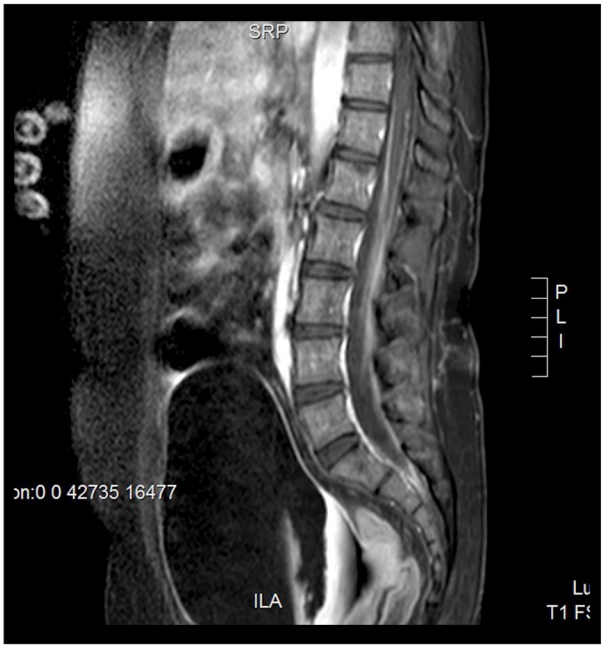

Figure 1. Intense nodular leptomeningeal enhancement from the lower thoracic cord and extending along the conus medullaris/filum terminalis and nerve roots.

Esophagogastroduodenoscopy and colonoscopy were normal. Gastric emptying scintigraphy revealed severe delayed gastric emptying time, with 11% emptied at 90 minutes.

After ruling out other causes of gastroparesis, and in the setting of active systemic CMV infection, the diagnosis of acute inflammatory polyneuropathy and idiopathic severe gastroparesis, likely caused by CMV autonomic neuropathy, was made. The patient received 5 sessions of plasmapheresis on presentation when labs were pending, with mild improvement. After CMV was positive, ganciclovir was initiated and later was switched to foscarnet due to progressive neutropenia. After 3 weeks of treatment, a repeat CSF study for quantitative CMV DNA PCR showed 4130 copies/ml. Her neurological symptoms and gastrological symptoms gradually improved. After 8 weeks of admission, slight weakness and urinary retention still persisted. Nausea and vomiting has been completely resolved and she was able to walk and eat before being discharged from the hospital.

Discussion

Prior to the ART era (prior to 1996), CMV was the most common cause of serious opportunistic viral disease. Almost 90% of HIV patients had CMV infection, with 25% developing life-threatening CMV disease [1]. Common manifestations of CMV in AIDS patients include retinitis, colitis, or encephalitis in up to 40% of patients [1]. Neurological manifestation of CMV,

including myelitis, polyradiculopathy, and mononeuritis multiplex, are less common [2]. There are published case reports, but the incidence rate for each is unknown. Before the ART era, CMV disease decreased dramatically in ART-compliant patients; incidence of CMV retinitis dropped 80% [3]. However, in ART non-compliant patients, CMV infection is still a significant threat.

Pathogenesis of neuropathy in CMV infection may involve both direct cellular infections and/or molecular mimicry. CMV has been shown to infect Schwann cells, macrophages, fibroblasts, and endothelium [4]. CMV infects neuron by direction fusion with the membrane, causing axonal death in its lytic life cycle [5]. Neutrophils then respond to release of cellular components and viral antigens. Typical pathological findings are areas of inflammation with polymorphonuclear cell (PMN) infiltration and necrosis, and CMV infection of endoneurial cells [6]. Another hypothesis is that it occurs through molecular mimicry. During CMV's replication cycle, viral antigen is expressed at the cell surface, which could be recognized by antigen-presenting cells. Once recognized, a predominantly lymphocytic response is triggered, with antibodies produced, and subsequent formation of membrane-attacking complex or macrophage response against cells that produce similar substances, mainly ganglioside (GM2). CMV-infected fibroblasts are known to produce antigen similar to GM-2 and trigger production of anti-GM2 IgM antibody [7].

CMV nervous system infection can manifest as diffuse encephalitis (the most common type), ventriculo-encephalitis, myelitis, polyradiculopathy, or mononeuritis multiplex. CMV encephalitis is progressive over several weeks, affecting memory, attention, concentration, motor, sensory, vision, and cranial nerves. Ventriculo-encephalitis develops rapidly with more focal neurological findings, cranial nerve deficits, nystagmus, and less cognitive impairment. Brain CT or MRI shows periventricular enhancement [8]. CMV myelitis is characterized by mostly lower limb weakness and hyper-reflexia. MRI of spinal cord shows cord enhancement, but CSF analysis usually is unremarkable. CMV radiculopathy typically presents as sensory loss, progressive weakness, urinary incontinence, and/or bowel incontinence [9]. MRI of spinal cord shows leptomeningeal enhancement. CSF study shows predominance of polymorphonuclear neutrophils (PMN) and hypoglycorrhachia [9]. CMV mononeuritis multiplex shows multifocal sensory and motor defect, especially in cranial nerves [10].

Knowledge of the patterns of contrast enhancement facilitates radiologic differential diagnosis. Leptomeningeal (pia-arachnoid) can be diffuse or focal. Diffuse enhancement can be due to carcinomatosis, meningitis, sarcoidosis, or post-surgical. Focal enhancement is present in meningitis (e.g., tuberculous, carcinomatosis, vasculitis, and lymphoma) [11].

Antiviral agents that inhibit viral DNA synthesis that have been studied are Acyclovir, Ganciclovir, Foscarnet, and Valacyclovir. Acyclovir is not indicated for CMV due to inferior response compared to Ganciclovir [12]. Ganciclovir is the first-line treatment, especially in patients with renal dysfunction. Its major adverse effects are neutropenia and thrombocytopenia [13]. Granulocyte colony-stimulating factor or Granulocyte-macrophage colony-stimulating factor can be considered as adjunct. In patients with severe neutropenia or thrombocytopenia, Foscarnet is preferred. However, renal function has to be monitored. IV fluid hydration and electrolyte monitoring (potassium, calcium, and magnesium) are recommended [8]. After completion of treatment course, and with negative CMV PCR in repeat lumbar puncture, Valacyclovir is an effective prophylaxis [14].

Our patient presented with lower extremity sensory and motor loss with areflexia, and urinary retention. These symptoms were consistent with CMV polyradiculopathy as described above. Her MRI was consistent with infection or inflammation of the spinal cord. However, her CSF analysis revealed lymphocytic predominance instead of the typical PMN response. This may suggest that molecular mimicry may play the predominant role in pathogenesis. The patient was initially started on Ganciclovir and her weakness and paresthesia resolved with six weeks of treatment. However, bladder retention persisted. She developed neutropenia, which improved as she was switched to Foscarnet. After four weeks of treatment, repeat CSF analysis still showed positive CMV PCR.

Due to persistence of nausea and vomiting, a gastric motility study was done and revealed gastroparesis with emptying half-time of 550 minutes. The patient was non-diabetic and did not have recent surgery. Medication was reviewed and possible culprits discontinued. There was no evidence of amyloidosis, demyelinating disease, or other neurological disorder. One possible explanation is CMV. Idiopathic gastroparesis is commonly described as an acute and self-limiting episode of nausea and vomiting. After an asymptomatic period, the patient then develops gastroparesis, which could last months to years with no effective treatment [15]. Our patient did not respond to prokinetic agents. However, her symptoms improved near the end of her induction treatment.

Conclusions

We describe a case of AIDS with lumbosacral polyradiculopathy and gastroparesis likely resulting from CMV infection. The mechanism of pathogenesis remains unclear; whether it is secondary to direct viral infection or autoimmunity triggered by molecular mimicry. Incidence of CMV opportunistic infection is greatly reduced in the ART era. However, it is still a possibility,

especially in non-compliant patients, and should be considered in differential diagnosis. Treatment should be initiated immediately once the diagnosis is confirmed.

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Conflict of interest

All authors have no conflict of interest to disclose.