The Canadian Journal of Neurological Sciences (2023), **50**, 905–906
doi:10.1017/cjn.2022.342

Canadian Journal of Neurological Sciences
Journal Canadien des Sciences Neurologiques

Neuroimaging Highlight

Rhombencephalitis Caused by Cytomegalovirus

Thallys Leal Silva[1], Weydler Campos Hottz Corbiceiro[1] and Diogo Goulart Corrêa[1,2]

[1]Department of Radiology, Federal Fluminense University, Niterói, RJ, Brazil and [2]Department of Radiology, Clínica de Diagnóstico por Imagem (CDPI)/DASA, Rio de Janeiro, RJ, Brazil

Keywords: Rhombencephalitis; HIV; CMV; MRI

(Received 19 August 2022; final revisions submitted 11 November 2022; date of acceptance 7 December 2022; First Published online 16 December 2022)

A 37-year-old man, recently diagnosed with human immunodeficiency virus (HIV) infection, with a viral load of 64 copies/mL and CD4+ lymphocyte count of 204 cells/mm^3, with no antiretroviral treatment, presented with fever, dysarthria, and right hemifacial paresthesia for 2 weeks, evolving with dysphagia and choking. Brain magnetic resonance imaging (MRI) demonstrated a lesion with hyperintense signal on T2-weighted imaging in the right dorsolateral pons extending inferiorly to the medulla, with no gadolinium enhancement (Figure 1). The cerebrospinal fluid (CSF) examination revealed a clear liquid, mild pleocytosis, with 70 white blood cells/mm^3 (85% of lymphocytes), no red blood cells, with normal protein and glucose levels. Polymerase chain reaction (PCR) of the CSF was positive for cytomegalovirus (CMV), with 800 copies/mL (normal range: <500 copies/mL). PCR was performed combined with real-time homogeneous fluorescence detection for CMV DNA quantification, validated for use in the CSF. PCR was negative for herpes simplex viruses, varicella-zoster virus (VZV), Epstein–Barr virus, enterovirus, and *Mycobacterium tuberculosis*. Venereal Disease Research Laboratory was negative. Blood and CSF cultures were negative, including for *Listeria monocytogenes*. Serum and CSF cell-based assay for anti-aquaporin 4 antibodies were negative. The patient was diagnosed with CMV rhombencephalitis and treated with intravenous ganciclovir. Serology for CMV and PCR for CMV in the blood were not performed. Highly active antiretroviral therapy was started, with zidovudine, lamivudine, and efavirenz. One month after the beginning of treatment, the patient was discharged without fever and choking, and partial improvement of the dysarthria, hemifacial paresthesia, and dysphagia.

CMV is a member of the *Herpesviridae* family,[1] commonly infecting humans before their first year of life.[2] It is a neurotropic virus, whose congenital infection is an important health concern. However, neurological manifestations are rare in adults, usually limited to immunosuppressed patients, due to viral reactivation, often characterized by polyradiculomyelitis, retinitis and, less commonly, encephalitis. CMV encephalitis can be a diagnostic challenge, due to atypical clinical and neuroimaging findings. Basal ganglia, diencephalon, and brainstem are the main sites of CMV infection.[3]

A hallmark of herpesviruses family is lifelong latency in specific cells and intermittent reactivations, leading to asymptomatic virus release or recrudescent disease, during periods of relative immunosuppression. Furthermore, neurotropism is other feature of the herpesviruses. After the primary infection, these viruses can remain latent in the neurons, later seeding through the central nervous system (CNS) across endothelial cells or retrogradely along the nerves.[4] VZV is the herpesvirus that most commonly causes rhombencephalitis due to reactivation, with retrograde neural spread. Previous studies reported cases of rhombencephalitis, caused by VZV, with nucleus of the solitary tract, nucleus ambiguus, spinal trigeminal nucleus, and/or vestibular nuclei involvement.[5–7] Although rarely, CMV also causes rhombencephalitis, usually associated with immunosuppression,[8] affecting the dorsal portion of the medulla, in these nuclei regions, similar to our case.[9] Although we did not perform serology and PCR for CMV in the blood, the PCR for CMV was positive in the CSF and negative for the other tested infectious agents. Also, the patient's symptoms improved after treatment.

Rhombencephalitis encompasses any inflammatory disease affecting the hindbrain, which in turn is composed of the pons, medulla, and cerebellum. The etiology of rhombencephalitis can be classified as infectious or inflammatory.[8] The most common causes of infectious rhomboencephalitis are *Listeria monocytogenes* and *Mycobacterium tuberculosis*. Other important causes of infectious rhombencephalitis are Enterovirus 71, and *Mycoplasma pneumonia*, in addition to the *Herpesviridae* family. Although brain MRI alone cannot determine the responsible infectious agent, infectious rhombencephalitis demonstrates hyperintense signal on T2-weighted imaging and FLAIR, as in our case, which may be associated with leptomeningeal enhancement and mass effect. In addition, other diseases that should be considered with this imaging aspect are demyelinating disease, such as neuromyelitis optica spectrum disorders, vasculitis, such as Behçet's disease, and neoplasms, mainly glioma and lymphoma. However, demyelinating diseases may present lesions in other parts of the CNS and optic nerves; vasculitis may present typical clinical manifestations, such as oral and genital ulcers in Behçet's disease; tumors usually demonstrate a greater expansive effect, with diffuse

Corresponding author: Thallys Leal Silva, Department of Radiology, Federal Fluminense University, Avenida Marquês de Paraná, 303, Centro, Niterói, RJ, 24070-035, Brazil. Email: thallys_leal@id.uff.br

Cite this article: Silva TL, Corbiceiro WCH, and Corrêa DG. (2023) Rhombencephalitis Caused by Cytomegalovirus. *The Canadian Journal of Neurological Sciences* **50**: 905–906, https://doi.org/10.1017/cjn.2022.342

© The Author(s), 2022. Published by Cambridge University Press on behalf of Canadian Neurological Sciences Federation

https://doi.org/10.1017/cjn.2022.342 Published online by Cambridge University Press

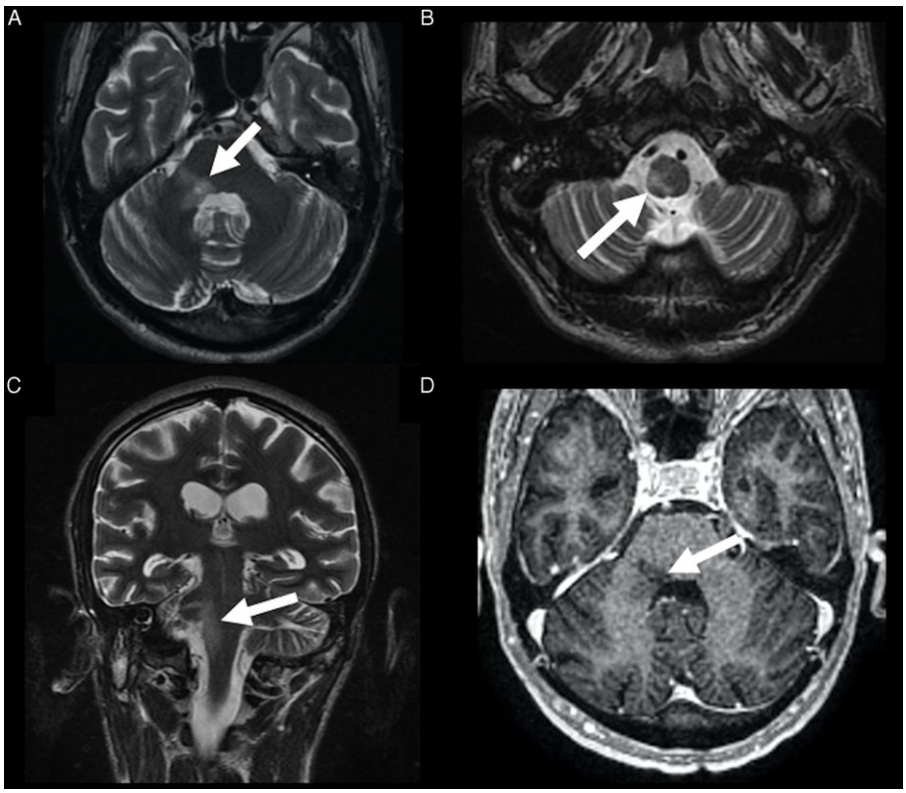


Figure 1: Rhombencephalitis caused by CMV. Brain MRI demonstrated a hyperintense lesion on T2-weighted imaging, in the right dorsolateral pons (arrow in A), extending through the medulla (arrow in B), in the axial (A and B) and coronal planes (arrow in C), with no gadolinium enhancement (arrow in D).

enlargement of the brainstem, which may be associated with parenchymal enhancement, signs of hyperperfusion or restricted diffusion.[10]

Therefore, it is important to consider CMV rhombencephalitis in the differential diagnosis of brainstem lesions, especially in immunosuppressed patients.

Statement of Authorship. TLS undertook conception, drafted the article, and had final approval of the last version.

WCHC collected the patient data, edited the article, and had final approval of the last version.

DGC edited the article, provided direct supervision, and had final approval of the last version.

Disclosures. The authors do not have anything to disclose.

References

1. Andreula C. Cranial viral infections in the adult. Eur Radiol. 2004; 14 Suppl 3:E132–44. DOI 10.1007/s00330-003-2040-3.
2. Studahl M, Lindquist L, Eriksson BM, et al. Acute viral infections of the central nervous system in immunocompetent adults: diagnosis and management. Drugs. 2013;73:131–58. DOI 10.1007/s40265-013-0007-5.
3. Ludlow M, Kortekaas J, Herden C, et al. Neurotropic virus infections as the cause of immediate and delayed neuropathology. Acta Neuropathol. 2016;131:159–84. DOI 10.1007/s00401-015-1511-3.
4. Baskin HJ, Hedlund G. Neuroimaging of herpesvirus infections in children. Pediatr Radiol. 2007;37:949–63. DOI 10.1007/s00247-007-0506-1.
5. Kim JH, Chung PW, Oh S, et al. Ramsay Hunt syndrome complicated by a brainstem lesion. J Clin Virol. 2007;39:322–5. DOI 10.1016/j.jcv.2007.05.002.
6. Kaski D, Davies N, Seemungal BM. Varicella-zoster virus meningo-rhombencephalitis presenting as Ramsey Hunt. Neurology. 2012;79:2291–2. DOI 10.1212/WNL.0b013e31827689c2.
7. Inagaki A, Toyoda T, Mutou M, Murakami S. Ramsay Hunt syndrome associated with solitary nucleus, spinal trigeminal nucleus and tract, and vestibular nucleus involvement on sequential magnetic resonance imaging. J Neurovirol. 2018;24:776–9. DOI 10.1007/s13365-018-0673-x.
8. Jubelt B, Mihai C, Li TM, Veerapaneni P. Rhombencephalitis/brainstem encephalitis. Curr Neurol Neurosci Rep. 2011;11:543–52. DOI 10.1007/s11910-011-0228-5.
9. Katchanov J, Branding G, Stocker H. Combined CMV- and HSV-1 brainstem encephalitis restricted to medulla oblongata. J Neurol Sci. 2014;339:229–30. DOI 10.1016/j.jns.2014.02.009.
10. Renard D, Guillamo JS, Ion I, Thouvenot E. Brainstem lesions: MRI review of standard morphological sequences. Acta Neurol Belg. 2022;122:597–613. DOI 10.1007/s13760-022-01943-y.

https://doi.org/10.1017/cjn.2022.342 Published online by Cambridge University Press