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Case illustrated

Metronidazole-induced Encephalopathy

Htay Phyu*, Michael B. Edmond, Takaaki Kobayashi

Division of Infectious Diseases, University of Iowa Hospitals and Clinics, United States

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ABSTRACT

Metronidazole is commonly used in the treatment of anaerobic infections. While neuropathy is known to be associated with metronidazole, encephalopathy has been rarely reported. We herein present a case of metronidazole-induced encephalopathy presenting as frequent falls and slurred speech. Magnetic resonance imaging of the brain demonstrated T2/FLAIR hyperintensity in the dentate nuclei bilaterally. Soon after the discontinuation of metronidazole, dysarthria and dysmetria resolved. Metronidazole-induced encephalopathy should be considered in patients presenting with new neurologic symptoms after the initiation of metronidazole.

Case illustrated

A 69 year-old man presented with perforated appendicitis and *Streptococcus anginosus* bacteremia. He was treated with 17 days of ceftriaxone and metronidazole with a good response. Several days after discontinuing antimicrobials, he developed fever and abdominal pain. Computed tomography (CT) revealed periappendiceal and right upper lobe lung abscesses. He then received 10 days of ceftriaxone and metronidazole, followed by oral amoxicillin/clavulanate and ciprofloxacin for 14 days. Repeat CT showed stable size of the periappendiceal and lung abscesses, and antimicrobials were changed to moxifloxacin and metronidazole. Two months later, while still on these antimicrobials, he presented with a two-week history of numbness and paresthesias of both feet, frequent falls, and one day of slurred speech. Physical examination was significant for dysarthria and mild dysmetria of the right foot. Magnetic resonance imaging (MRI) of the brain demonstrated T2/FLAIR hyperintensity in the dentate nuclei bilaterally (Fig. 1). Metronidazole induced encephalopathy (MIE) and neuropathy were suspected and his antimicrobials were changed to ertapenem. Soon after the discontinuation of metronidazole, dysarthria and dysmetria improved; however, neuropathy continued and gabapentin was started. His lung abscess resolved with ertapenem and he eventually underwent operative drainage of the periappendiceal abscess.

Metronidazole is commonly used in the treatment of anaerobic infections. While neuropathy is known to be associated with metronidazole, encephalopathy has been rarely reported. Neurotoxicity associated with metronidazole can manifest as seizures, dizziness, vertigo, ataxia, confusion, encephalopathy, headache and tremors [1]. The duration of metronidazole treatment before

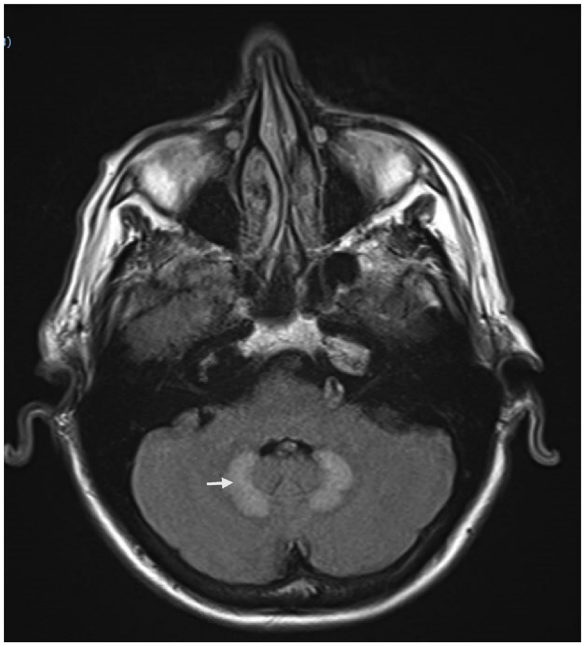

Fig. 1. T2/FLAIR hyperintensity in the dentate nuclei bilaterally associated with metronidazole toxicity.

* Corresponding author at: Division of Infectious Diseases, University of Iowa Hospitals and Clinics, 200 Hawkins Drive, Iowa City, IA, United States.
E-mail address: htay-phyu@uiowa.edu (H. Phyu).

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encephalopathy develops varies between one day to weeks and cumulative doses range from 0.25 to 1,095 g [2]. Typical MRI findings of MIE include T2 hyperintense lesions in the cerebellar dentate nuclei, however, the splenium of the corpus callosum, dorsal pons, medulla, inferior colliculus, subcortical white matter, basal ganglia, thalamus and middle cerebellar peduncles can be affected as well [3]. The differential diagnosis of T2 hyperintense lesions of the bilateral cerebellar dentate nuclei include methyl bromide intoxication, maple syrup urine disease, enteroviral encephalomyelitis and Wernicke encephalopathy [1]. In most cases, MIE is a reversible process that improves within a few weeks after discontinuation of metronidazole. In a recent review of 131 patients, five (4%) patients had persistent neurological deficits, and one remained in a persistent vegetative state [1]. Death was reported in 5 (6%) patients, however MIE was not thought to be the primary cause. MIE should be considered in patients presenting with new neurologic symptoms after the initiation of metronidazole.

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Consent

Obtained.

Author contribution

HP wrote the first draft of the manuscript and TK and ME critically reviewed and revised the manuscript. All authors read and approved the final paper.

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Declaration of Competing Interest

None of the authors has any conflicts of interest to declare.

References

[1] Sorensen CG, Karlsson WK, Amin FM, et al. Metronidazole-induced encephalopathy: a systematic review. J Neurol 2018, doi:http://dx.doi.org/10.1007/s00415-018-9147-6 [published Online First: 2018/12/12].
[2] Hobbs K, Stern-Nezer S, Buckwalter MS, et al. Metronidazole-induced encephalopathy: not always a reversible situation. Neurocrit Care 2015;22(3)429–36, doi:http://dx.doi.org/10.1007/s12028-014-0102-9 [published Online First: 2015/01/07].
[3] Roy U, Panwar A, Pandit A, et al. Clinical and neuroradiological spectrum of Metronidazole induced encephalopathy: our experience and the review of literature. J Clin Diagn Res 2016;10(6)OE01–9, doi:http://dx.doi.org/10.7860/JCDR/2016/19032.8054 [published Online First: 2016/08/10].