



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijidINTERNATIONAL
SOCIETY
FOR INFECTIOUS
DISEASES

Medical Imagery

Metronidazole-induced encephalopathy and cytotoxic lesion of the corpus callosum in a patient with diabetic foot infection



ARTICLE INFO

Article history:

Received 13 August 2019

Received in revised form 25 September 2019

Accepted 25 September 2019

Corresponding Editor: Eskild Petersen,
Aarhus, Denmark

Keywords:
Metronidazole
Encephalopathy

A 39-year-old man with uncontrolled type 2 diabetes mellitus was treated with ceftriaxone 2 g intravenously daily and oral metronidazole 500 mg three times daily for a bilateral diabetic foot infection. Four weeks later, he presented to our clinic with 4 days of dizziness, dysarthria, and difficulty walking. On admission, his Glasgow Coma Scale was E4V2M6 and he had an abnormal finger-to-nose test and gait disturbance. Magnetic resonance imaging (MRI) revealed symmetric T2-FLAIR hyperintensity of the bilateral cerebellar dentate nuclei (Figure 1A) and the corpus callosum (Figure 1C), which were consistent with metronidazole-induced encephalopathy (MIE) and a cytotoxic lesion of the corpus callosum (CLOCC) (Starkey et al., 2017). Three days after the discontinuation of metronidazole, the patient's

ataxia gradually improved. Follow-up MRI 10 days later also demonstrated a marked improvement in the abnormal T2-FLAIR signal (Figure 2A, C).

The risk of MIE is known to be associated with high cumulative doses of metronidazole (Patel et al., 2008) or high peak plasma concentrations (Hobbs et al., 2015). In this case, the cumulative dose of metronidazole was 42 g in total. Bilateral cerebellar dentate nuclei involvement is characteristic (Kim et al., 2007). Although MIE is reversible in most cases, there are sporadic reports of irreversible, devastating complications — especially if left untreated (Sørensen et al., 2018; Hobbs et al., 2015). MIE should be considered if a patient undergoing metronidazole therapy complains of difficulty speaking, difficulty walking, or confusion.

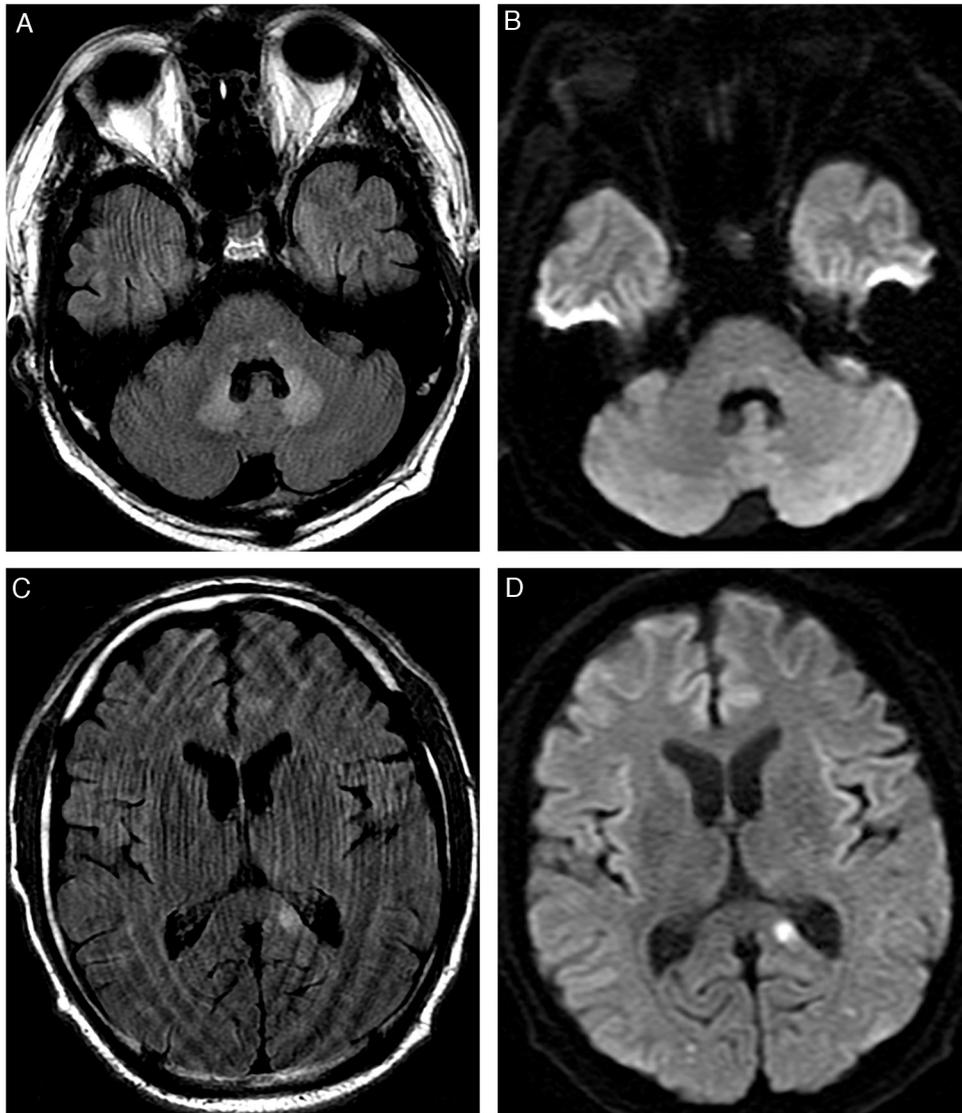


Figure 1. The dentate nuclei demonstrating characteristic hyperintensity on T2-FLAIR (A), without reduced diffusion on DWI (B). There is a cytotoxic lesion of the corpus callosum in the splenium to the left of the midline with T2-FLAIR hyperintensity (C) and diffusion restriction (D) with a low ADC (not shown). (FLAIR, fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient).

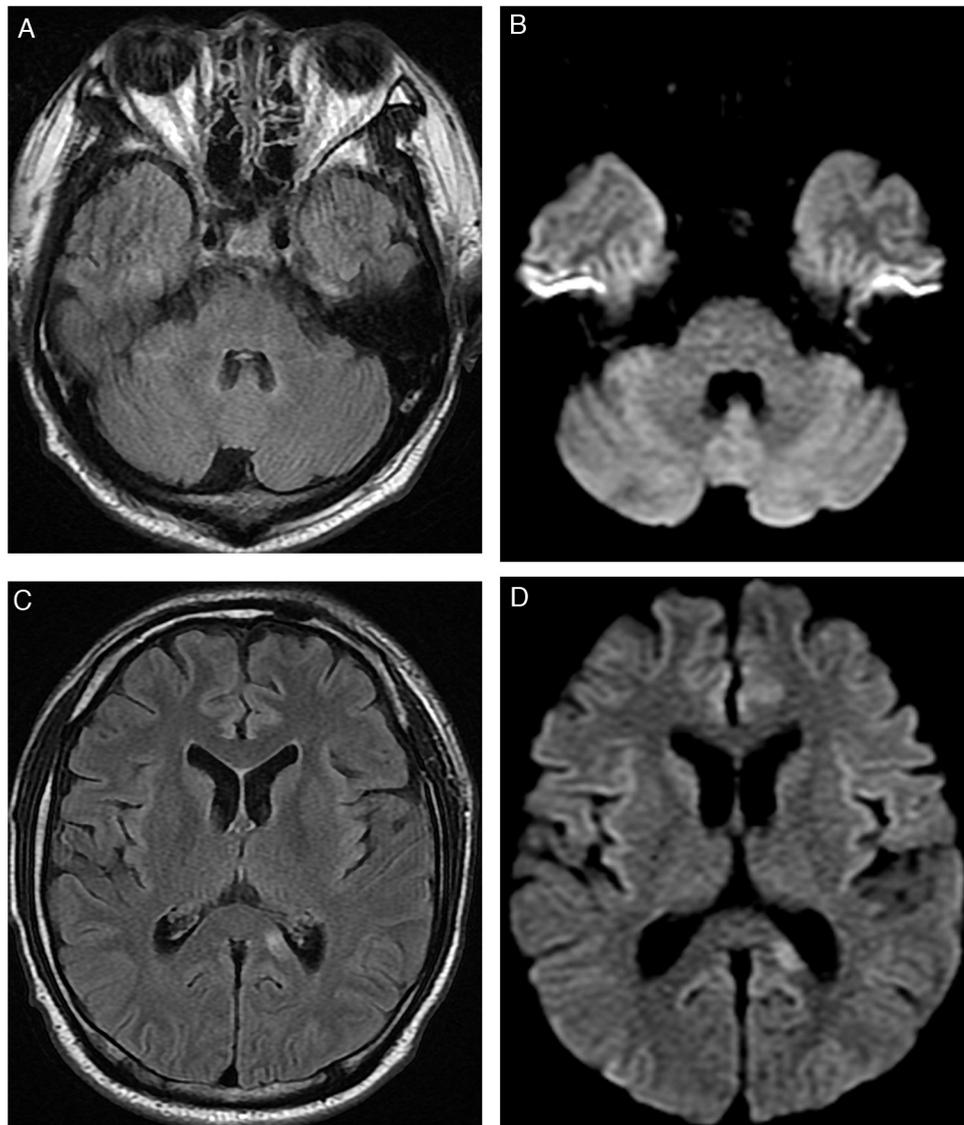


Figure 2. Follow-up MRI at 10 days demonstrating resolution of the dentate T2-FLAIR hyperintensity (A), with continued normal DWI (B). The corpus callosum lesion demonstrating improvement in T2-FLAIR hyperintensity (C) and decreased diffusion signal (D) with near normalization of the ADC (not shown). (FLAIR, fluid-attenuated inversion recovery; DWI, diffusion-weighted imaging; ADC, apparent diffusion coefficient).

Conflict of interest

The authors have no conflict of interest to declare.

Funding/support

No funding received.

Ethical approval

No ethical approval was needed.

References

- Hobbs K, Stern-Nezer S, Buckwalter MS, Fischbein N, Finley Caulfield A. Metronidazole-induced encephalopathy: not always a reversible situation. *Neurocrit Care* 2015;22(June (3)):429–36.
- Kim E, Na DG, Kim EY, Kim JH, Son KR, Chang KH. MR imaging of metronidazole-induced encephalopathy: lesion distribution and diffusion-weighted imaging findings. *Am J Neuroradiol* 2007;28(October (9)):1652–8.
- Patel K, Green-Hopkins I, Lu S, Tunkel AR. Cerebellar ataxia following prolonged use of metronidazole: case report and literature review. *Int J Infect Dis* 2008;12(November (6)):e111–4.
- Sørensen CG, Karlsson WK, Amin FM, Lindelof M. Metronidazole-induced encephalopathy: a systematic review. *J Neurol* 2018;. doi:<http://dx.doi.org/10.1007/s00415-018-9147-6> PMID: 30536109.

Starkey J, Kobayashi N, Numaguchi Y, Moritani T. Cytotoxic lesions of the corpus callosum that show restricted diffusion: mechanisms, causes, and manifestations. *Radiographics* 2017;37(2):562–76 (†image 1A, C, D reprinted with permission, p.567, ©RSNA).

Takahiro Matsuo^{a,*}
Nobuyoshi Mori^a
Aki Sakurai^a
Jay Starkey^b
Keiichi Furukawa^a

^a*Department of Infectious Diseases, St Luke's International Hospital,
Tokyo, Japan*

^b*Department of Diagnostic Radiology, Division of Neuroradiology,
Oregon Health and Science University, Portland, OR, USA*

* Corresponding author at: Department of Infectious Diseases, St. Luke's International Hospital, 9-1, Akashi-cho, Chuo-ku, Tokyo, Japan.

E-mail address: tmatsuo@luke.ac.jp (T. Matsuo).

Corresponding Editor: Eskild Petersen, Aarhus, Denmark

Received 13 August 2019

Received in revised form 25 September 2019

Accepted 25 September 2019