Metronidazole-induced encephalopathy: an uncommon scenario

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Abstract

Metronidazole can produce neurological complications although it is not a common scenario. We present a case where a patient developed features of encephalopathy following prolonged metronidazole intake. Magnetic resonance imaging (MRI) brain showed abnormal signal intensity involving both dentate nuclei of cerebellum and splenium of corpus callosum. The diagnosis of metronidazole toxicity was made by the MRI findings and supported clinically.

Metronidazole is a common antimicrobial agent used in the treatment of anaerobic and protozoal infections. Metronidazole-induced encephalopathy (MIE) is a rare toxic encephalopathy caused by the drug metronidazole. MRI brain usually clinches the diagnosis.

Case report

A 42-year-old male patient presented with complaints of difficulty in walking for 1 week, vertigo, and dizziness and slurred speech for 3 days. He had a history of taking 750 mg/day metronidazole for last 9 months duration for chronic diarrhoea.

On examination, Romberg sign was positive, with slurring of speech, dysarthria, dysmetria on finger-to-nose examination, and an ataxic wide-based gait. Hypotonia and pendular knee jerks were noted. Rest of the examination was non-contributory.

Computed tomography (CT) performed on admission showed no evidence of acute stroke and routine laboratory analysis (including complete blood counts, electrolytes, glucose, renal and liver function tests) was unremarkable.

His MRI brain showed bilaterally symmetrical abnormal signal intensity involving dentate nuclei of cerebellum (Figure 1) and splenium of corpus callosum (Figure 2). The signal intensity was hypointense on T1- and hyperintense on T2-weighted and fluid attenuated inversion recovery (FLAIR) sequences.

The patient's clinical presentation and MRI images were found to be consistent with metronidazole-induced encephalopathy (MIE). Discontinuation of metronidazole led to gradual improvement in the patient's condition. Typical pattern and location of lesions and reversibility of symptoms following withdrawal of metronidazole confirmed the case as metronidazole-induced encephalopathy.
Figure 1. Hyperintensity of bilateral dentate nuclei on T2 weighted image in MRI brain

Figure 2. Hyperintensity of splenium of corpus callosum on T2-weighted image in MRI brain
Discussion

Metronidazole may produce a number of neurologic side effects, such as cerebellar syndrome, encephalopathy, seizure, autonomic neuropathy, optic neuropathy, and peripheral neuropathy.\(^1,2\) The exact incidence of this rare event is not yet ascertained.\(^3\)

The duration of treatment with metronidazole before cerebellar symptoms manifest is variable, and cumulative doses range from 25 g to 110 g.\(^1\) In our case, total dose of metronidazole was more than 200 g. Most lesions induced by metronidazole toxicity are reversible.

The signal intensity changes observed on the diffusion weighted images most likely represents interstitial oedema. Ahmed et al postulated that, because of the reversibility of the MRI changes, the cause of the changes associated with acute toxic insult was most likely due to axonal swelling with increased water content and not demyelination.\(^4\)

In MRI of patients with MIE, T2 hyperintense lesions in the cerebellar dentate nuclei are most common.\(^5\) The midbrain, dorsal pons, dorsal medulla, and corpus callosum can also be affected. Uncommon locations include the inferior olivary nucleus and the white matter of the cerebral hemispheres.\(^4,6\)

The differential diagnosis of T2 hyperintense lesions of the bilateral cerebellar dentate nuclei in patients with symptoms of acute encephalopathy includes methyl bromide intoxication, maple syrup urine disease and other metabolic encephalopathy.\(^7\)

However, a clear temporal relationship with metronidazole intake and reversibility of symptoms on its discontinuation along with normal metabolic profile as well as no clinical evidence of maple syrup urine disease make the diagnosis of MIE undisputable in this case.

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