LETTER TO THE EDITOR

Metronidazole-induced vertigo

To the Editor,

A 57-year-old female patient was treated with metronidazole due to paralytic ileus. Two weeks later, she presented with vertigo after being given a cumulative dose of 25 g. On physical examination, she revealed gaze-induced bidirectional nystagmus without other neurologic finding. Laboratory findings, including white blood cell count and cerebrospinal fluid (CSF) test, were all normal. Facial nerve stimulation studies show decreased compound muscle action potentials on both sides. Blink reflex studies, auditory brainstem response, and pure tone audiometry were within normal limits. Videonystagmography and vestibular function revealed central vestibulopathy.

Brain magnetic resonance imaging (MRI) demonstrated symmetric high signal intensity in dorsal medulla (Fig. 1A) and inferior colliculus (Fig. 1B) on T2-weighted fluid-attenuated inversion recovery imaging (T2WFLAIR). Her vertigo resolved in 2 weeks after cessation of metronidazole. Follow-up of brain MRI showed no previous brain lesions (Fig. 1C and D).

Metronidazole, a 5-nitroimidazole compound, is a good choice for treating anaerobic and protozoa-related infections. However, in rare cases, it can adversely induce peripheral neuropathy or encephalopathy [1] due to its cellular penetration to CSF. Metronidazole-induced encephalopathy (MIE) is one serious but rare side effect. The exact mechanism of the neurotoxicity is yet to be clarified. Rao and Mason [2] reported that catecholamine neurotransmitters can induce 5-nitroimidazole drugs to produce semiquinone radicals and nitro anion radicals, which may contribute to neural damage.

Graves et al.’s [3] study stated that MIE will occur if a daily dose of 1.6 g is used for an average duration of 79 days. However, our patient received 1.5 g daily for 14 days, which was originally considered to be within the safety range. Most reported initial symptoms of MIE were gait disturbance, dysarthria, altered consciousness, and weakness of extremities. Vertigo, which presented as the first symptom in our patient, is extremely rare. Because of the occurrence of gaze-induced bidirectional nystagmus, central vertigo was highly suspected. It indicated that the lesion could be at brain stem, cerebellum, and brain stem–cerebellum axis [4]. Her vertigo could be explained by lesions of medulla and inferior colliculus found on the MRI study. Furthermore, her vertigo and MRI lesion recovered soon after cessation of metronidazole intake. The characteristic brain lesions of MIE can appear as abnormal high signal intensity on diffusion-weighted imaging, T2W, and FLAIR MRI images. In descending order of frequency, the previously reported lesions were at cerebellar dentate nuclei, midbrain, corpus callosum, pons, medulla, cerebral white matter, and basal ganglia [5]. To our knowledge, our patient’s lesions were present in both dorsal medulla and inferior colliculus, meaning that these were the first reported combination lesions of the central nervous system.

The symptoms and signs of MIE can resolve completely by an average of 37 days after termination of metronidazole usage, as reported in Graves et al.’s study [3]. Our patient showed a good prognosis in 14 days. However, Kim et al. described an irreversible MIE case. Special low apparent diffusion coefficient lesions in MRI study may indicate a poor prognosis. Groothoff et al. reported a fatal case probably due to long exposure to a high dose of metronidazole.

Vertigo is a commonly encountered complaint associated with otolaryngologists and neurologists. Usually, to differentiate between peripheral and central types is a challenge. Central vertigo due to MIE should be considered in the differential diagnosis when central type of nystagmus and a history of metronidazole usage are identified. Close
monitoring of side effects during metronidazole usage, even in the case of a safe dosage, is essential, and it must be discontinued immediately after MIE is confirmed by brain MRI.

References


Figure 1. Fluid-attenuated inversion recovery magnetic resonance imaging revealed symmetric high signal intensity in both (A) dorsal medulla (arrowheads) and (B) inferior colliculus (arrows). (C, arrowheads; D, arrows). The signal disappeared completely after cessation of metronidazole.