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Magnetic resonance imaging of metronidazole induced encephalopathy

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Abstract

We describe a case demonstrating Magnetic Resonance (MR) imaging findings in association with Metronidazole (Flagyl) toxicity. MRI brain showed abnormal signal intensity involving dentate nuclei of cerebellum bilaterally symmetrical. The diagnosis of metronidazole toxicity was made by the MR imaging findings and supported clinically. In hospital, course of treatment drug was discontinued. Patient improved clinically with discontinuation of metronidazole. No follow-up MR imaging was obtained. In this report, we present a case depicting MR imaging changes within the dentate nuclei of cerebellum.

Keywords: Central Nervous System, Metronidazole Toxicity, Magnetic Resonance Imaging.

Introduction

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. Metronidazole is believed to penetrate Cerebro Spinal Fluid (CSF) and the central nervous system (CNS) easily.1 The incidence of MIE is unknown.2 Metronidazole toxicity can involve central and peripheral nervous system especially at dosages exceeding 2g/day for prolonged periods.2,3

Ahmed et al first described the imaging findings of metronidazole toxicity in a 45 year old patient who developed nausea, vomiting, vertigo, dysarthria, and confusion after consuming 35g metronidazole over a 30 day course of therapy. MR imaging of the brain at this point showed symmetric abnormal signal intensity within supratentorial white matter including the corpus callosum and within the cerebellum and cerebellar deep nuclei. Following discontinuation of metronidazole, the patient's symptoms resolved rapidly. Repeat MR imaging of the brain demonstrated near complete resolution of findings 6 weeks after discontinuation of metronidazole.4

Case Report

A 41 year old male patient with addiction of hashish, charas, alcohol and cigarettes was referred for MRI of the brain after complaints of difficulty in walking for 1 week, vertigo and dizziness for 1 day, history of fall 1 day back. According to patient he was in his usual state of health 10 days back when he developed numbness in feet below

Figure: (a) T1-weighted Axial MR image show hypointense signal in bilateral dentate nuclei of cerebellum. (b) T2- weighted Axial MR image show symmetric hyperintense signal in dentate nuclei. (c) FLAIR image demonstrate hyperintense signal. (d) Post contrast T1-weighted Axial image show no abnormal enhancement. (e) Diffusion weighted image demonstrate hyperintense signal in dentate nuclei of cerebellum bilaterally.
ankles and was unable to maintain a balance. Then he developed slurred speech. He had history of Metronidazole use for chronic loose motions. He took 1200 mg/day metronidazole for 4 months. On examination Romberg sign was positive, with slurring of speech and upgoing plantars bilaterally. Bulk, tone, power and reflexes were normal. His Electromyography and nerve conduction studies were abnormal. The findings were suggestive of mild sensory, motor predominantly sensory axonal neuropathy.

His MRI brain was done which showed abnormal signal intensity involving dentate nuclei of cerebellum bilaterally symmetrical. The signal intensity was hypointense on T1-and hyperintense on T2 and FLAIR sequences. After administration of intravenous Gadolinium, there was no enhancement, as seen in Figure-1. Based on these findings the differential diagnosis of metabolic encephalopathy (eg Metronidazole encephalopathy (eg West Nile) was suggested. In hospital treatment drug was discontinued. Patient improved clinically with discontinuation of metronidazole. No follow-up MR imaging was obtained.

Discussion

Serious neurological side effects of metronidazole toxicity include peripheral neuropathy, ataxic gait, dysarthric speech, convulsive seizures and encephalopathy. The mechanism of metronidazole toxicity has not been elucidated. The signal intensity changes observed on the diffusion weighted images most likely represent interstitial edema. Ahmed et al speculated that, because of the reversibility of the MR imaging changes, the cause of the changes associated with acute toxic insult were most likely due to "axonal swelling with increased water content." not demyelination. The typical locations of lesions by MR imaging in patients with MIE are the cerebellar dentate nuclei, midbrain (tectum, red nucleus, tegmentum around periaqueductal gray matter), dorsal pons, dorsal medulla, and corpus callosum (splenium); and these were always bilateral and symmetric. Uncommon locations were the inferior olivary nucleus and the white matter of the cerebral hemispheres. Although MR imaging findings of bilateral involvement of the dentate nuclei are a very characteristic feature of MIE, 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 enteroviral encephalomyelitis.

Horlen et al reported imaging findings of presumed metronidazole toxicity in a 35 year old male patient with liver cirrhosis who had consumed greater than 60 gram metronidazole over a 55 day period and developed ataxia, disorientation and peripheral neuropathy. MR imaging of the brain demonstrated abnormal symmetric hyperintense T2 signal intensity involving the dentate nuclei and inferior basal ganglia. This patient's symptoms also resolved with discontinuation of metronidazole. No follow-up imaging was obtained.

In our case, there was symmetrically increased T2 signal intensity in the dentate nuclei of cerebellum. Patient improved clinically with discontinuation of metronidazole. No follow-up MR imaging was obtained.

Conclusion

This case helps to characterize the changes associated with metronidazole toxicity. MR imaging is suggestive of metronidazole toxicity in clinically suspected cases by demonstrating the presence of increased T2 signal intensity in the deep nuclei.

References