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Reversible cerebellar Ataxia: A Rare Manifestation of Metronidazole Toxicity

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Abstract

Metronidazole is a cost-effective and widely used antibiotic against bacteria and protozoan infections. Metronidazole use is associated with adverse effects like neurotoxicity such as cerebellar toxicity, optic neuropathy, peripheral neuropathy and encephalopathy. We here-by present a 28 years old male who had unsteadiness of gait and dysarthria for ten days duration along with positive cerebellar signs following metronidazole therapy for two months in a case of liver abscess. After stopping metronidazole, his symptoms improved.

Introduction

Metronidazole is a 5-nitroimidazole antibiotic, which is a commonly used and cost-effective treatment for parasitic and anaerobic infections. It is generally safe and well tolerated but has minor side effects like nausea, metallic taste and abdominal cramps. Neurological adverse effects are rare but may include headache, confusion, vertigo and peripheral neuropathy etc. Metronidazole-induced encephalopathy (MIE) is a serious adverse effect which includes cerebellar ataxia, seizure and altered sensorium1.

Case Report

A 28 years male presented to us with unsteadiness of gait and dysarthria of ten days duration. Two months ago, he was diagnosed with amoebic liver abscess and prescribed 400 mg of oral metronidazole three times a day. Cerebellar examination revealed horizontal nystagmus on lateral gaze and a wide based gait.MRI brain showed bilateral symmetric T2 and FLAIR hyperintense lesions involving dentate nucleus of cerebellum, dorsal pos and splenium of corpus callosum with diffusion restriction of splenium of corpus callosum [Figure-1]. The patient's neurologic and radiological characteristics improved two weeks after the medication was stopped.

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Discussion:

Metronidazole is used to treat anaerobic or microaerophilic microorganisms such as Entamoeba histolytica, Giardia lamblia, Clostridium difficile etc. Metronidazole is associated with mild to moderate side effects such as nausea, abdominal pain and diarrhea. Neurotoxicity such as cerebellar dysfunction is a rare severe adverse side reported due to metronidazole use[2]. Our patient took metronidazole for two months and presented with unsteadiness of gait and dysarthria with cerebellar signs.

Kalia V et al reported a case of 43-year-old male who presented with slurring of speech, generalized weakness, vertigo, and ataxia for 4 days following metronidazole use for 2 months. The patient symptoms were resolved after discontinuation of metronidazole. MRI of the brain showed symmetrical areas of altered signal intensity in the corpus callosum, dentate nuclei, dorsal pons, and splenium, which were hyperintense on T2W and fluid-attenuated inversion-recovery images.[3]

Chandak et al. reported a 45-year-old case who presented with sudden onset cerebellar symptoms since 2 days after receiving metronidazole for 1 month for liver abscess. MRI Brain showed symmetrical hyperintensities in bilateral dentate nuclei and tectum on T2W & FLAIR sequences[4]. Gupta et al reported a case of a 50 year old male who developed acute ataxia, disorientation, distal symmetrical sensory and proximal motor neuropathy following prolonged intake of metronidazole for treatment of liver abscess[5].

Ahmed et al. first described the imaging findings of metronidazole toxicity. They reported a 45-year-old female who presented with nausea, vomiting, dizziness, confusion,

ataxia, and peripheral neuropathy, and her MRI brain showed symmetrical, bilateral, abnormal hyperintense signal in the supratentorial white matter, corpus callosum, and within the cerebellum and deep cerebellar nuclei on T2W images[6]. They suggested "axonal swelling with increased water content" due to toxic injury as the possible mechanism or, alternatively, localized reversible ischemia due to vascular spasm. Other theories that have been put forward include: (a) interstitial edema and ischemia manifesting as increased signal intensity on diffusion-weighted and apparent diffusion coefficient mapping or (b) Purkinje cell damage after high dose of metronidazole due to binding of the drug to neuronal RNA, causing inhibition of protein synthesis and resulting in axonal degeneration[6].

Multiple sclerosis and acute disseminated encephalomyelitis may present with similar MRI findings, but involvement of the gray matter, a normal CSF, and the temporal profile make these possibilities unlikely. Wernicke encephalopathy is another differential diagnosis, but the involvement is predominantly of the diencephalon and midbrain[6].

The characteristic MRI feature of MIE is the T2W and FLAIR symmetric hyperintensity of the cerebellar dentate nuclei mimicking a headphone, also known as headphone sign[7]. Other usual locations of lesion are brainstem and splenium of corpus callosum which are always bilateral and symmetric[8]. The differentials for dentate nuclei involvement are Wernicke's encephalopathy, drugs (isoniazid and cycloserine), infectious and neurodegenerative disease [9].

Conclusion

Cerebellar toxicity should be considered in any patient on prolong use of metronidazole who presents with ataxia and/or dysarthria. This case also highlights the importance of knowing the classical MRI brain pattern of metronidazole induced neurotoxicity, because discontinuing the medication leads to complete resolution of neurological symptoms.

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