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# METRONIDAZOLE INDUCED CEREBELLAR ATAXIA: A CASE REPORT

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## ABSTRACT

Metronidazole is a very commonly prescribed antibiotic for the treatment of anaerobic bacterial and protozoal infections. The most common adverse effects associated with it are nausea, dry mouth, vomiting, and diarrhea. Neurologic toxicity is very rare and if occur it includes peripheral neuropathy, headache, dizziness, syncope, vertigo, and confusion. Cerebellar toxicity is a very unusual, adverse event associated with its use. We are reporting a case of this very rare side effect, i.e. Reversible Cerebellar toxicity, in a patient who was on prolonged metronidazole therapy for multiple liver abscesses.

**KEYWORDS:** Metronidazole, Cerebellar Ataxia, Multiple liver abscesses.

## INTRODUCTION

Metronidazole is a 5-nitroimidazole and has potent activity against anaerobic bacteria, several protozoa including *Entamoeba*, *Giardia*, *Trichomonas* and *B. coli*, *H. pylori* and *Guinea worm*. It is also often used to eradicate *Helicobacter pylori* along with other drugs and to prevent infection in people recovering from surgery. It inhibits nucleic acid synthesis by disrupting the DNA of microbial cells. This function only occurs when metronidazole is partially reduced, and because this reduction usually happens only in anaerobic cells, it has

relatively little effect upon human cells or aerobic bacteria [1]. Inappropriate usage in excessive doses can give rise to neurological problems such as ataxia, seizures, peripheral neuropathies, cerebellar signs and symptoms, and encephalopathy. The neurological features usually become apparent when the drug is used in a dose exceeding 2 g/day for prolonged periods [2].

**Case Report**

A 45 year old man presented to medical emergency with chief complaints of fever, chills and right hypochondrium pain of 7-8 days duration. On examination, he was febrile with temperature of $39.5^0$C. His pulse rate was 118/min with no icterus or lymphadenopathy. Systemic examination revealed no abnormality except tender hepatomegaly. Liver was palpable 6-7cms below right costal margin. Ultrasonographic examination revealed one large liver abscesses of size 9x9 cm and on the posterior aspect of the right lobe of the liver. USG-guided aspiration of the abscess had been done and serology for *Entamoeba histolytica* had been positive. Patient was put on metronidazole 800 mg TDS orally. Patient started showing improvement in all symptoms within 5 to 6 days and was discharged after about a week. He was advised to continue metronidazole at same doses for another week, and to follow up in OPD. After about 12 weeks of discharge, patient presented with history of dizziness, diplopia, disorientation, inability to walk, slowed speech, incoherence and vomiting of three days duration. Neurological examination showed horizontal nystagmus. There was past-pointing on finger-nose test. There was severe ataxia and patient was not able to stand without support. Liver function tests were mildly deranged (SGOT 63 IU/L, SGPT 69 IU/L, alkaline phosphatase 121 IU/L). Cerebrospinal fluid (CSF) examination showed 5 cell/mm3 with glucose of 47 mg/dL, proteins 32 mg/dL, chloride 117 mmol/L and was negative for cryptococcal antigen. MRI head revealed reveal Bilateral Symmetric semilunar hyper intensities involving deep cerebellar parenchyma. On the basis of history and clinical findings a diagnosis of metronidazole induced cerebellar dysfunction made and patient was advised to stop metronidazole. Within 5to 7 days of stopping metronidazole patient's condition improved. His speech became clear, cerebellar signs were improved, and he could walk unassisted although he remained unsteady. He was discharged after 8th day of admission and came for follow up after two week. He was perfectly well at that time with no neurological deficit [6] [7] [8].

## DISCUSSION

The exact incidence of metronidazole-induced neurotoxicity is not known and the underlying mechanism for brain injury has not been completely understood. It is the suggested mechanism for neurotoxicity is 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 [3].

There are several case reports describing distal symmetrical predominantly sensory peripheral neuropathy with metronidazole and even with another nitroimidazole [4] [5]. Complete or partial resolution may occur after discontinuation of therapy. However symptoms may take upto two years to completely resolve.

MRI plays an important role not only in the diagnosis of this entity but also in the follow-up of these cases, where it may be of use in predicting the outcome after drug discontinuation. The usual sites of involvement are cerebellar dentate nuclei, midbrain, dorsal pons, splenium of the corpus callosum, and the dorsal medulla. The differential diagnosis includes demyelinating diseases, and metabolic, infectious, and inflammatory processes. Multiple sclerosis and acute disseminated encephalomyelitis may present with similar MRI findings. Atypical non-alcoholic Wernicke's encephalopathy can sometimes present with MRI findings of dorsal medulla and cerebellum. Heat stroke can also rarely involve the cerebellum but the predominant involvement is of the thalami and external capsules. The other differential diagnosis includes Marchiafava-Bignami disease, Encephalitis (Demyelinating, Influenza, *Escherichia coli*, Mumps, Adenovirus, Epstein-Barr virus and Rota virus), Osmotic myelinolysis, Acute toxic encephalopathy and Anti-epileptic drugs but these are commonly causes T2 hyperintense lesions in the splenium of the corpus callosum.

## SOURCE OF FUNDING

Nil

## CONFLICT OF INTEREST

Authors declare no conflict of interest.

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