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ORNIDAZOLE INDUCED ATAXIA IN AN INDIAN MAN : A VERY RARE CASE REPORT

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ABSTRACT The ornnidazole is nitroimidazole group of antibiotics which cause cerebellar ataxia as a rare side effect. Ornidazole has a long half life and is very rarely known to cause cerebellar ataxia. Here, we report a 25-year-old patient who developed ataxia due to ornidazole to highlight an unusual adverse event that improved rapidly after discontinuation of the offending drug.

KEYWORDS :

Introduction:

Ornidazole is commonly used for treating amoebiasis, giardiasis, trichomonal and anaerobic bacterial infections. Although adverse events are usually mild and transient with short-duration use, the nitroimidazole antibiotics, especially metronidazole, have been associated with serious adverse events like ataxia when prescribed for prolonged periods of time.(1). We have described the case details of a 25-year-old Indian man who developed disabling cerebellar ataxia following long-term use of a combination tablet of ornidazole and cefixime that improved remarkably following drug cessation.

Case report:

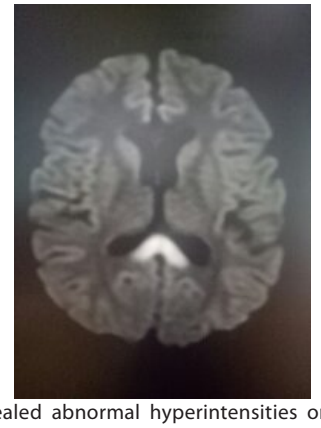

figure 1: revealed abnormal hyperintensities on T2 and fluid attenuated inversion recovery images (FLAIR) involving splenium of corpus callosum and bilateral dentate nuclei of cerebellum.

A 25-year-old Indian man presented to our hospital on 24 october 2016 with progressively worsening walking difficulty, slurring of speech, tremor , sad feelings associated with difficulty in swallowing and frequent arousals from sleep since 4 days. There was no symptoms suggestive of proximal limb/truncal weakness and the ataxia was present only while attempting to walk .He had no sensory deficits or cognitive decline ,behavioural abnormalities and cranial nerve involvement. .He had significant drug abuse as described below.

He took corex syrup (for 1.5 years and stopped it before 7 days of admission. Each 5 ml contains 8 mg alcohol,4mg chlorpheniramine maleate ,10 mg codeine phosphate). He took English liquor on irregular basis since 7-8 years but had no drink since last 1 month. He took lorazepam for some days 6 months back. He had taken heroin only once in life.

On review of his current medications, he reported that 1.5 year ago, he had been prescribed a 5-day course of a combination tablet consisting of ornidazole 500mg and cefixime 200 mg (Tab. MAHACEF-OZ) for treatment of gastroenteris. Even after resolution of his symptoms, he continued using the medication to treat further intermittent episodes of diarrhoea on a daily basis by himself.

On examination, he had normal vitals fully conscious well oriented with marked gait ataxia and prominent bilateral cerebellar signs, including past pointing, dysdiadochokinesia, dysmetria, dysarthria, broad-based gait, broken pursuits and hypermetric saccades. Cranial nerve , sensory system, reflexes, motor systems were normal . All other systemic examination were normal .

The differentials considered were ornidazole-induced cerebellar

ataxia and paraneoplastic cerebellar syndrome, alcohol withdrawal syndrome and cerebellar stroke.

Routine blood tests including CBC, renal, thyroid and liver function were normal. Chest X-ray, ultrasound abdomen was normal.

Magnetic resonance imaging (MRI) of brain with contrast revealed abnormal hyperintensities on T2 and fluid attenuated inversion recovery images (FLAIR) involving splenium of corpus callosum and bilateral dentate nuclei of cerebellum. the spleniul lesion showed restricted diffusion. A neurologist's opinion concurred with our diagnosis of ornidazole toxicity.

The combination tablet was stopped on the first day of admission to the hospital. he underwent intensive physiotherapy focussing on gait and balance training with which he made rapid improvement.

During the outpatient visit, he had made substantial improvement and was walking independently after 2 weeks of tablet stoppage.

Discussion

The temporal association of ataxia with the medication, rapid resolution with drug cessation and absence of other precipitating causes strongly suggested the likelihood of ornidazole toxicity. On the Naranjo adverse drug reaction scale(2),he scored 6 points (5–8, probable), indicating that his symptoms were probably due to ornidazole. Cefixime is not known to cause gait disturbance. Neuropsychiatric manifestation have been documented with use of cefepime and ceftazidime and in patients with renal failure (9). Ataxia is seen with acute alcohol intoxication not alcohol withdrawal and patient had his last drink 1 month back.one case study has shown no significant association between concomitant use of alcohol and imidazoles and development of disulfiram like reactions (10)

The radiological findings in this patient were similar to the changes noted on brain MRI imaging in previous patients with nitroimidazole toxicity. Common adverse events with the nitroimidazoles are mild and include a metallic taste and nausea. However, prolonged use of nitroimidazole has been associated with peripheral neuropathy, seizures, reversible ataxia, optic neuropathy and encephalopathy. Cases of cerebellar ataxia have been reported with a cumulative metronidazole dose of as little as 25 g and up to a maximum of 1080g.(3) Our patient had ingested a cumulative dose of approximately 270g of ornidazole prior to admission

Typical MRI abnormalities reported in the literature with nitroimidazole toxicity include hyperintensities on T2 and FLAIR images in the dentate nuclei, midbrain, dorsal pons, medulla, corpus callosum, globus pallidus, putamen and caudate nuclei and frontal white matter ,(4,5). methyl bromide toxicity can cause same clinical and radiological features(6) . The exact pathophysiology of the neuroimaging changes and the resultant clinical features due to imidazoles is not clear. Direct neuronal toxicity, GABA modulation, nucleic acid binding of intermediate metabolites of metronidazole affecting neuronal protein synthesis and mitochondrial function are Possible toxic mechanisms (7,8)

Awareness of this toxicity and a complete drug review will facilitate an early diagnosis as well as help limit investigations for other causes. Ataxia can occur with all the nitroimidazole antibiotics including the newer drugs. Patient education while prescribing may help to avoid this adverse drug event.

Declaration of conflicting interests

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Ethics approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed consent

Verbal informed consent was obtained from the patient for their anonymized information to be published in this article.

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