International Journal of Basic & Clinical Pharmacology
Azad AK et al. Int J Basic Clin Pharmacol. 2023 Jul;12(4):594-596
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20231897

Case Report

Metronidazole induced neurotoxicity: a case report

Abul K. Azad[1]*, Rohit K. Singh[1], Rani I. Sinha[1], Keshav K. Sinha[1], Munish Kumar[2]

[1]Department of Pharmacology, [2]Department of Neurology, Patna Medical College, Patna, Bihar, India

Received: 17 April 2023
Accepted: 10 May 2023

***Correspondence:**
Dr. Abul K. Azad,
Email: akazad2806@gmail.com

ABSTRACT

Metronidazole is a well-known antimicrobial agent, used for the treatment of anaerobic bacterial and protozoal infections. It is generally well tolerated with common side effects like nausea, dizziness, headache and metallic taste in the mouth. But prolonged use of metronidazole can cause neurotoxicity like ataxic gait, dysarthria, seizures and encephalopathy. Here, we are reporting a case of a 60 years old male patient who was a chronic alcoholic with liver abscess and he developed acute ataxia and dysarthria after four weeks use of metronidazole. The causality of metronidazole in this case was "probable" with score 7 as per Naranjo scale. The patient was managed by discontinuing the metronidazole and there was considerable improvement in his gait and speech after that. The case was recorded properly in adverse drug reaction reporting form and was sent to nearby adverse drug reaction (ADR) monitoring centre.

Keywords: Metronidazole, Neurotoxicity, Adverse drug reaction

INTRODUCTION

Nervous system toxicity is a rare complication of metronidazole leading to neuropathy, ataxic gait, dysarthria, seizures and encephalopathy. These symptoms may occur from short- or long-term metronidazole use. The mechanism of neurotoxicity induced by metronidazole is unclear, and neuroimaging is the foundation of diagnosis. Reaching the appropriate diagnosis is contingent upon a high clinical index of suspicion, prompt brain imaging to identify specific imaging abnormalities, and improvement after prompt withdrawal of metronidazole. Clinical improvements typically occur after discontinuing metronidazole, but in some cases, comprehensive rehabilitation is needed to optimize mobility and activities of daily living (ADLs).[1]

Metronidazole is a nitroimidazole derivative. It has broad spectrum cidal activity against protozoa and most anaerobic bacteria. It is a commonly prescribed drug for amoebiasis, giardiasis, trichomoniasis and anaerobic bacterial infections such as brain abscess and puerperal sepsis.[2] Its use is considered relatively safe. Common side effects are nausea, headache and metallic taste in the mouth. Metronidazole easily penetrates the blood brain barrier and can accumulate, leading to CNS toxicity. The duration of treatment with metronidazole before encephalopathy develops varies between days to weeks and the cumulative dose. The occurrence of encephalopathy with toxic peripheral neuropathy is in fact a rare event.[3]

Here, we are reporting a case of a 60 years old male patient who was a chronic alcoholic with liver abscess and he developed acute ataxia and dysarthria after four weeks use of metronidazole.

CASE REPORT

A 60 years old male patient came to the emergency department of Patna Medical College and Hospital, Patna with complain of fever, pain abdomen and yellowish discoloration of urine for 10 days. He had history of daily alcohol consumption approximately 400 ml for 10 years. There was no drug history. On general physical examination of the patient, he was febrile with temperature

of 38.5 ºC, pulse rate- 110/min and icterus present. Systemic examination was unremarkable except for tender hepatomegaly (liver was palpable 4 cm below the right costal margin). In complete blood count (CBC) report: (WBC -18670/µl). On blood investigation, leukocytosis (WBC -18670/µl). Liver function test (LFT) was deranged: total bilirubin - 2.9 mg/dl, direct bilirubin- 1.76 mg/dl, alanine transaminase- 241 U/l, and aspartate transaminase – 238 U/l. Renal function test (RFT) was also deranged: blood urea -114.8 mg/dl and serum creatinine - 1.41 mg/dl. HIV, hepatitis B and hepatitis C were negative. Ultrasonographic examination revealed one large liver abscess of size 12.4×12.6 cm in right lobe of liver with hepatomegaly (liver size-17.4 cm).

Based upon above findings diagnosis of Amoebic liver abscess was done. Patient was prescribed broad spectrum antibiotic and intravenous Metronidazole 2 gram/day in divided doses and ultrasound guided liver abscess aspiration was done, which showed anchovy sauce pus. Repeat ultrasonography (USG) was done after two weeks, which showed persistence of large abscess of volume 1160 ml. Once again USG guided liver abscess aspiration was done and Metronidazole therapy was continued. During the course of treatment, after one month, he presented with sudden onset of ataxia and slurring of speech (dysarthria) as shown in Figure 1. Cumulative dose of metronidazole was 60 gram.

Figure 1: Patient with complains of ataxia and slurring of speech.

On CNS examination, higher mental function was intact and all cranial nerves were intact. There was no motor weakness and sensory systems were intact. There was impaired coordination bilaterally. He exhibited positive past-pointing test or finger-nose test. There was a scanning speech. He was severely ataxic and was unable to walk unassisted. Rest of the CNS examination was normal. All routine investigations were repeated after the development of ataxia. Complete blood count (CBC), LFT, RFT, serum electrolytes, random blood sugar, routine examination of urine were normal. Vitamin B_{12} and thyroid function test were normal. Cerebrospinal fluid (CSF) examination was normal. Magnetic resonance imaging (MRI) brain was done on the day of presentation of ataxia and dysarthria, that showed bilateral symmetrical hyperintense signal on FLAIR and T2W images and restriction on DWI in the dentate nuclei of the cerebellum, a finding that was consistent with Metronidazole induced neurotoxicity (Figures 2-4).

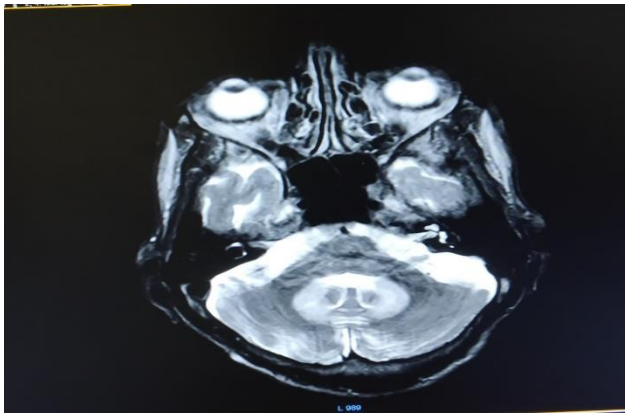

Figure 2: The T2W magnetic resonance image showing bilateral symmetrical hyperintense signal in dentate nuclei of cerebellum.

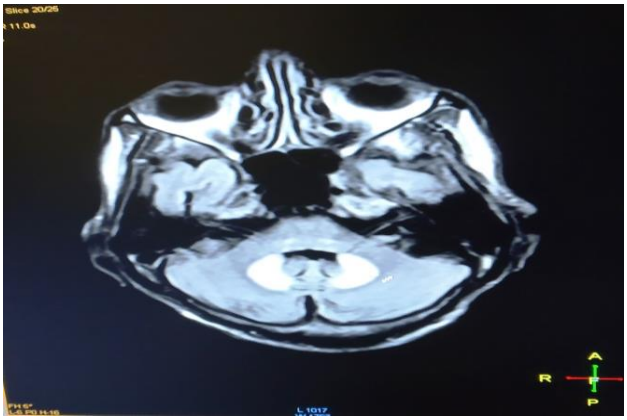

Figure 3: The FLAIR magnetic resonance image showing bilateral symmetrical hyperintense signal in dentate nuclei of cerebellum.

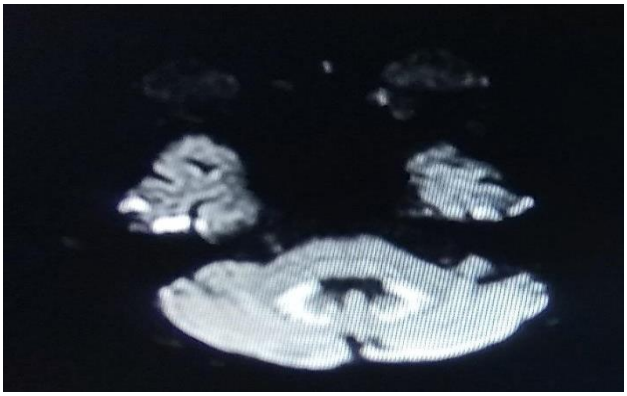

Figure 4: The DWI magnetic resonance image showing restriction in dentate nuclei of cerebellum.

Metronidazole therapy was discontinued following which there was a considerable improvement in his gait and speech. After 5 days, he was able to walk some steps independently. Then patient was discharged and advised to come for follow up after 10 days. When he came after 10 days, there was no complain in walking and speech. He was advised for repeat MRI of brain. The causality of metronidazole in this case was "probable" with score 7 as per Naranjo scale. The case was recorded properly in adverse drug reaction reporting form and was sent to nearby adverse drug reaction (ADR) monitoring centre.

DISCUSSION

Metronidazole is available for the treatment of anaerobic and protozoal infections. Sometimes, it may produce acute neurological side effects, particularly after prolonged use, such as cerebellar involvement, encephalopathy, seizures, and peripheral neuropathy. Patients who already having risk factors like alcoholism and uremia, are more prone to develop metronidazole toxicity.[4] The duration of treatment with Metronidazole for the appearance of CNS toxicity is variable (1 week to 6 months), and cumulative doses range from 25 g to 110 g.[5] Patients with severe hepatic dysfunction are at an increased risk of accumulation and may be at an increased risk of metronidazole induced neurotoxicity, even with short-course therapy. In our case, total dose of metronidazole that the patient received was 60 g and total duration was of 30 days. Although, the mechanism of metronidazole neurotoxicity remains unclear, but most of the lesions induced by Metronidazole neurotoxicity may be reversible. Characteristic MRI brain findings are symmetrical hyperintense signal on T2 weighted and FLAIR images, most commonly in the areas of cerebellar dentate nuclei. Lesions are always bilaterally symmetrical, a pattern typical of metabolic neurological toxicity. Discontinuation of metronidazole and supportive measures are the primary treatment.

In our case, on the basis of history of chronic alcoholism, differential diagnosis of Wernicke's encephalopathy was considered. However, MRI brain findings and absence of ophthalmoplegia were not in favour of Wernicke's encephalopathy. Other causes of acute ataxia like lithium and phenytoin toxicity were excluded, as there was no history of these drugs.

CONCLUSION

Metronidazole induced neurotoxicity or encephalopathy should be considered in any patient who presents with seizure, cerebellar features, altered sensorium, and is receiving prolonged therapy of metronidazole. MRI should be performed for definitive diagnosis and reversibility of lesion should be looked in follow up MRI. Metronidazole should be immediately discontinued in these conditions. Increased awareness among physicians may enable early recognition of potentially reversible neurotoxicity and unwarranted prescription of such medicines.

ACKNOWLEDGMENTS

Authors would like to thanks Dr. Pankaj Hans, Associate Professor, Department of Medicine, Patna Medical College and Hospital, Patna for immense support throughout the case study.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Hillaker, Emily DO, Lau, James MD, Boomgaardt, Jacob DO, Weppner, Justin DO. Metronidazole-induced neurotoxicity: A case report. Medicine: Case Reports and Study Protocols. 2023;4(1):e0268.
2. Kumari P, Porwal YC, Arora A, Kumar M, Kumar D. Metronidazole induced neurotoxicity in a case of liver abscess. Int J Hepatobiliary Pancreat Dis. 2016;6:96-9.
3. Damodaran A, Nayak D, Khan F, Majid S, Hamad I, Ibrahim M. Metronidazole-induced Neurotoxicity: A Case Report. Bengal Physician J. 2022;9(1):19-21.
4. Thakkar N, Bhaarat, Chand R, Sharma R, Mahavar S, Srivastava S, et al. Metronidazole Induced Encephalopathy. J Assoc Physicians India. 2016;64(11):72-4.
5. Chandak S, Agarwal A, Shukla A, Joon P. A Case Report of Metronidazole Induced Neurotoxicity in Liver Abscess Patient and the Usefulness of MRI for its Diagnosis. J Clin Diagn Res JCDR. 2016;10(1):TD06-7.

Cite this article as: Azad AK, Singh RK, Sinha RI, Sinha KK, Kumar M. Metronidazole induced neurotoxicity: a case report. Int J Basic Clin Pharmacol 2023;12:594-6.