

# **Rapid Onset Peripheral Neuropathy in a patient with Amoebic Liver abscess on Metronidazole - A rare complication**

**AUTHORS-** Mohit Gupta<sup>(1)</sup>, Chandan Kumar<sup>(2)</sup>, Ujjwal Kumar<sup>(3)</sup>, Pranay Swarnkar<sup>(4)</sup>

1,2,3,4- Department of Internal Medicine, Saraswathi Institute of Medical Sciences, Hapur (U.P), India

**Keywords-** Liver Abscess, Metronidazole, Peripheral Neuropathy

## **ABSTRACT**

### **Aim**

We report here a case where the patient developed peripheral neuropathy during a short course of metronidazole treatment at a low cumulative dose which has been rarely reported. This case thus highlights the importance for a treating medical professional to keep in mind that peripheral neuropathy may develop in a patient on metronidazole even on a short duration of it. This peripheral neuropathy is reversible

### **Presentation of Case**

A 40 year old male patient with no past history of alcohol habit or diabetes was admitted with right side chest pain. Ultrasound and CECT abdomen revealed Amoebic Liver Abscess. He was treated with Metronidazole. After one week of therapy (cumulative dose -16.8 gms) he developed severe burning pain in bilateral lower limbs with **Nerve Conduction Velocity (NCV)** study confirming mixed neuropathy. His symptoms resolved after stopping Metronidazole.

### **Discussion**

The exact mechanism of Metronidazole induced peripheral neuropathy is unknown. It is believed to be secondary to axonal degeneration. It binds to neuronal RNA and inhibits protein synthesis. This results in axonal degeneration.

### **Conclusion**

Metronidazole is a widely prescribed drug for treatment of amoebic liver abscess. It can cause peripheral neuropathy in patients even on a short course of treatment. Thus it is important to detect this early and discontinue the medication to prevent development of persistent neuropathy.

## **INTRODUCTION**

Metronidazole is a 5-nitroimidazole derivative. It is generally well tolerated . Its common side effects include mild abdominal pain, headache, nausea and a persistent metallic taste. It may cause peripheral neuropathy at high cumulative doses and during long course treatment <sup>(1,2,3,4,5)</sup>. We report here a case where the patient developed peripheral neuropathy during a short course of metronidazole treatment at a low cumulative dose which has been rarely reported.

## PRESENTATION OF CASE

A 40 year old non diabetic, non smoker and non alcoholic male patient presented with fever and right sided chest pain for 20 days. Fever was of high grade, intermittent type and associated with chills and rigors. There was history of right sided chest pain which was dull in nature .There was decrease in appetite. There was no past history of hypertension or tuberculosis.

On examination, liver was enlarged (span 18 cm) and tender without ascites. Breath sounds, Vocal fremitus and Vocal resonance were decreased on right side of thorax. Percussion note was dull in right lower chest. Rest of the systemic examination was normal. On Investigation - Complete Blood Count levels were normal except for **Total Leukocyte Count** (TLC) - 19,700/ul . **Kidney Function Test and Liver Function Test** were within normal limits. Ultrasound whole abdomen showed a well defined hypoechoic lesion of size 8.3\*7.8\*7.2 cm in segment VIII of liver without vascularity suggestive of liver abscess. **Contrast Enhanced CT** chest and whole abdomen study revealed a large capsulated thick walled rim enhancing fluid density lesion of size 9.7\*7.6\*9.6 cm in right lobe of liver predominantly involving segment VIII. The medial wall had discontinuity suggesting intra pleural rupture and right sided pleural effusion. Amoebic Serology IgG levels were - 6.07 (positive being level > 1.1). Diagnosis of Amoebic Liver Abscess was made. He was started on Ceftriaxone and Metronidazole for treatment. An Inter costal tube was placed for drainage of pus from pleural space. The patient started showing improvement in all symptoms after starting treatment.His lab reports also improved ( TLC- 8900/ul after 7 days of treatment). He complained of new onset burning sensation in bilateral lower limbs after 7 days of treatment which worsened over the next 2 days. Neurological examination showed loss of all sensory modalities in bilateral lower limbs . Serum levels of Vitamin B12 and Thyroid Function Test were within normal range. Nerve conduction velocity (NCV) study was done which showed evidence of mixed neuropathy affecting the lower limbs and suggesting axonal neuropathy. Diagnosis of peripheral neuropathy was made. After excluding all other causes of peripheral neuropathy, metronidazole was considered to be responsible for it . **Metronidazole was thus stopped and the patient was started on Chloroquine for amoebic liver abscess treatment** . The patient's peripheral neuropathy symptoms improved after metronidazole was stopped and completely resolved after 3 weeks of stopping it.

## CONCLUSION

The Patient 's clinical features of Peripheral neuropathy was diagnosed to caused by Metronidazole and was treated by stopping Metronidazole .

## DISCUSSION

Metronidazole is commonly used drug to treat anaerobic and amoebic infection. It is usually well tolerated. . Its common side effects include mild abdominal pain, headache, nausea and a persistent metallic taste. Prolonged use of this drug is associated with peripheral neuropathy .

Peripheral Neuropathy can also occur with other nitrimidazole group agents like tinidazole or ornidazole <sup>(1)</sup>.The exact mechanism of Metronidazole induced peripheral neuropathy is unknown. In experimental models, metronidazole or its metabolites were found to bind selectively with neuronal ribonucleic acid (RNA) . After binding, they inhibit protein synthesis and result in axonal degeneration<sup>(5,6,7)</sup> .Other suggested mechanisms include the following : modulation of gamma-amino butyric acid (GABA) by intermediate metabolite of metronidazole in the central nervous system ,or free radical injury to nerve tissue <sup>(5,8)</sup> .

The overall incidence of metronidazole associated peripheral neuropathy is unknown . On reviewing the literature , most cases of metronidazole associated peripheral neuropathy are seen with >42 g of total drug or >4 weeks of treatment as compared to those patients receiving ≤42 g total (17.9% vs. 1.7%) <sup>(1)</sup>. Symptoms resolve after discontinuation of therapy in most patients . On reviewing the literature from India <sup>(9,10,11)</sup> the cumulative dose of metronidazole causing peripheral neuropathy was low (13.2-18 grams) and the latency to symptom onset very short (11 days to 18 days) when compared to patients from the West. This may reflect a genetic susceptibility to the neurotoxic effects of metronidazole or a genetic variation in the metabolism of metronidazole in Indian patients.

The overall incidence of metronidazole associated peripheral neuropathy is unknown . On reviewing the literature , most cases of metronidazole associated peripheral neuropathy are seen with >42 g of total drug or >4 weeks of treatment as compared to those patients receiving ≤42 g total (17.9% vs. 1.7%) <sup>(1)</sup>. Symptoms resolve after discontinuation of therapy in most patients . On reviewing the literature from India <sup>(9,10,11)</sup> the cumulative dose of metronidazole causing peripheral neuropathy was low (13.2-18 grams) and the latency to symptom onset very short (11 days to 18 days) when compared to patients from the West. This may reflect a genetic susceptibility to the neurotoxic effects of metronidazole or a genetic variation in the metabolism of metronidazole in Indian patients.

The treating medical professional should thus keep in mind that peripheral neuropathy may develop in a patient on metronidazole even on a short duration of it .

## ACKNOWLEDGEMENTS

We acknowledge the support of staff in departments of internal medicine and radiology .

## **COMPETING INTEREST**

All authors declare that there were no conflicts of interest.

## **AUTHORS' CONTRIBUTIONS**

Mohit Gupta - Involved in drafting the manuscript. Final approval for publication. Edited the content for critical information. Analysis and interpretation of data.

Chandan Kumar-Involved in drafting the manuscript. Final approval for publication. Edited the content for critical information. Analysis and interpretation of data.

Ujjwal Kumar- Involved in drafting the manuscript. Final approval for publication. Edited the content for critical information. Analysis and interpretation of data.

Pranay Swarnkar- Revised the manuscript for critical information

## **CONSENT**

Written Informed consent was obtained from the patient for this case report

## **REFERENCES**

1. Andersson KE. Pharmacokinetics of nitroimidazoles. Spectrum of adverse reactions. Scand J Infect Dis Suppl 1981;26:60-7.
2. Clinical relevance of metronidazole and peripheral neuropathy: a systematic review of the literature . Goolsby TA (1), Jakeman B (2) , Gaynes RP (3). Int J Antimicrob Agents . 2018 Mar;51(3):319-325. doi:10.1016/j.ijantimicag.2017.08.033. Epub 2017 Sep 5
3. Gupta B S, Baldwa S, Verma S, Gupta J B, Singhal A. Metronidazole induced neuropathy. Neurol India 2000;48:192
4. A Case Report of Metronidazole-Induced Central Nervous System Complications (P4.396) Ning Wu, Joseph Nguyen, Aiesha Ahmed Neurology Apr 2016, 86 (16 Supplement) P4.396
5. Rapid onset peripheral neuropathy:A rare complication of metronidazoleHitender KumarAsha Sharma,SK Attri ,Sumin Kaushik JIACM 2012;13(4):346-8
6. Bradley WG,Karlsson IJ,Rassol CG. Metronidazole neurophy. BrMed J (Clin Res)1977; 2: 610-11.

7. Gupta, AK, Agarwal, MP, Avasthi, R, Bhadoria, DP, Rohatgi, N. Metronidazole-induced neurotoxicity. J Assoc Physicians India. 2003 Jun;51:617-8.
8. Rao DN, Mason RP. Generation of nitro radical anions of some 5-nitrofurans 2- and 5-nitroimidazoles by norepinephrine, dopamine and serotonin: A possible mechanism for neurotoxicity caused by nitroheterocyclic drugs. J Biol Chem 1987;262:1173-6.
9. Sarma G R, Kamath V. Acute painful peripheral neuropathy due to metronidazole. Neurol India 2005;53:372-3
10. Pais P, Balasubramaniam KR Metronidazole-peripheral neuropathy. (Letter to Editor). JAPI 1982;30:918-9.
11. Kapoor K, Chandra M, Nag D, Paliwal JK, Gupta RC, Saxena RC. Evaluation of metronidazole toxicity: a prospective study. Int J Clin Pharmacol Res 1999;19:3:83-8.