■ *Case Report*

# Metronidazole induced peripheral neuropathy

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**Abstract**

Metronidazole is a little known cause of drug-induced neuropathy.We report a patient who developed paraesthesia of both limbs after one month course of metronidazole. The electrophysiologic test confirmed a bilateral motor-axonal neuropathy. This neuropathy improved dramatically with cessation of the drug.

**Keywords:** metronidazole, peripheral neuropathy, hepatic amebiasis

## Introduction

Metronidazole, a nitroimidazole antibiotic, has been widely used for treating infections due to anaerobic bacteria, parasitic infections, pseudomembranous colitis, acne rosacea, helicobacter pylori and Crohn's disease.[1] The adverse affects of metronidazole include nausea, anorexia, vomiting, diarrhea, abdominal cramping,neutropenia, metallic taste, urticaria, headache, and disulfiram-like reaction.[1] Peripheral neuropathy is its rare side effect.[2]

We report a 42-year-old male who developed neuropathy during prolonged use of metronidazole and the improvement in the neurological manifestations after cessation of metronidazole. To the best of our knowledge this is the first reported case of metronidazole induced neuropathy from Nepal.

## Case report

A 42-year old gentleman, bus conductor by occupation, reported to the medical OPD with tingling and numbness of both feet for 7 days, which was of insidious onset and gradually progressive over 2 days to involve both the hands. From the beginning it was associated with unsteady gait with frequent tendency to fall towards any side while walking. He was a diagnosed case of liver abscess for last one month and was on pig tail catheter drainage on arrival. He was on tablet metronidazole 400 mg thrice a day. He was prescribed tablet ciprofloxacin 500 mg twice a day to cover secondary bacterial infection. He was a smoker and alcohol consumer until about last 10 years back. There was no history of diabetes mellitus, renal failure, occupational toxins exposure, chronic diarrhea or consumption of any other medications.

On examination, his BMI was 22.5/kgm$^2$. There was no hyperpigmenation or hyopigmented patches, no pallor, or evidence of nutritional deficiencies. He had a regular pulse of 80 /min and blood pressure of 120/ 80 mmHg without a postural drop. His abdomen was soft, non-tender with no palpable organs. He had intact memory and speech with normal tone and bulk of muscle. The power was 5/5 in all proximal and distal musculatures of hands and feet. The gait was slow, unsteady with frequent tendency to fall. Rombergs sign was positive. Plantar was mute over both feet with absent ankle jerks bilaterally. His joint and position sense was impaired over both legs.

Ultrasonography of abdomen showed a heterogenous hypoechoic area of 4.6*4.5*4.1 cm with a volume of 46.5 cc in segment VI of right lobe of liver. His blood sugar was 99mg/dl, serum $Na^+$ 142meq/L and serum $K^+$ 3.8meq/L. Nerve conduction test showed motor

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sensory polyneuropathy of both axonal and demyelinating type (Fig.1). Antinuclear antibodies (ANA), thyroid-stimulating hormone, vitamin B12, lipid profile, erythrocyte sedimentation rate, HIV serology all were normal. The symptoms disappeared in five days after cessation of metronidazole during hospital stay. On 20 days after stopping metroniazole during follow up in OPD the symptoms disappeared and nerve conduction study was normal.

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**Nerve Conduction Study Report**

Lab No. 1223 /2010 Date: 3/12/2010
Patients Name: Ram Subedi Age: 42 years Sex: M
Address: Jhapa
Bill / Hospital No.: 1214275/99857
Referred by: Medicine
**Clinical details and provisional diagnosis:** unsteady gait; slurring of speech; liver abscess; numbness and tingling sensation over the bilateral feet region for 11 days→ peripheral neuropathy probably due to metronidazole therapy?
**Clinical question:** nerve conduction study of relevant nerves.

**Observation**

Compound mixed (motor) and sensory nerve studies of the following nerves and their respective F-waves were done.

| Nerves tested | Motor | | | F-wave latency | Sensory | | |
|---|---|---|---|---|---|---|---|
| | Dist. Lat. | Amplitude | CV | Minimum | Latency | Amplitude | CV |
| Rt. median | Normal | | | Normal | Normal | | |
| Lt. median | Not done | | | Not done | | | |
| Rt. ulnar | Normal | | | Normal | Normal | **Borderline** | Normal |
| Lt. ulnar | Not done | | | Not done | | | |
| Rt. radial | Normal | | | Not done | Normal | **Decreased** | Normal |
| Lt. radial | Not done | | | | | | |
| Rt. & Lt. tibial | Normal | **Decreased** | Normal | Normal | Please see sural response | | |
| Rt. com. peroneal | Normal on distal stimulation; **decreased amplitude** on proximal stimulation | | | Normal | | | |
| Lt. com. peroneal | Normal | | | Normal | | | |
| Rt. & Lt. sural | Please see motor responses of tibial / common peroneal | | | Not applicable | Normal | **Decreased** | Normal |

**IMPRESSION**

The study is suggestive of motor-sensory polyneuropathy of mixed (both axonal and demyelinating) type involving the peripheral nerves of the upper and lower limbs. The tested motor nerves of the upper limbs are spared.

**Dr. Dilip Thakur**
Assistant Professor

Signature of any of the two faculties is sufficient.

**Dr. BH Paudel**
Professor

**Clinical Neurophysiology Lab**

Please see the actual record attached for details of tested variables.
☎ Department of Physiology: 00977 25 525555 Ext.: 2470 or 2476 or 2324.

*Fig.1 Nerve conduction test showing motor sensory polyneuropathy of both axonal and demyelinating type.*

## Discussion

Metronidazole has been widely used to treat trichomonas vaginitis for many years without producing major side effects. Peripheral neuropathy is one of the complications, albeit rare, of metronidazole use. Many other medications like chloramphenicol, fluoroquinolones,chloroquine,dapsone,ethambutol, griseofulvin,isoniazid, are associated with peripheral neuropathy. The neurotoxic side effects of these medications are rare compared to the relatively high incidence of neuropathy associated with antiretroviral drugs and antineoplastic agents.[3]

The usual presentation of metronidazole induced neuropathy is predominantly sensory than motor, and are similar to other toxic or neuropathies of various etiologies. This distal symmetric polyneuropathy present as distal paresthesias, often with burning, dysesthetic, and glove stocking sensory loss. Both small and large fiber modalities may be involved, the latter reflected in distally in the form of diminished or absent tendon reflexes. Onset may be insidious, subacute, or acute, and symptoms typically progress if the offending agent/s is continued. In most cases, symptoms improve after the drug is discontinued but with isoniazid, recovery can be slow and incomplete, especially after prolonged use.[4]

The exact incidence of metronidazole (MTZ) related sensory disturbances and neuropathy is unknown.[5] Several mechanisms may contribute to the neurotoxicity of metronidazole like inhibition of neuronal protein synthesis by metronidazole-mediated RNA binding, which causes axonal degeneration. Nitro radical anions and semiquinone generated during reactions between catecholamines and metronidazole contribute to metronidazole neurotoxicity.[6-7] The enzymatic conversion of metronidazole to an analogue of thiamine may mimic nutrition-deficiency neuropathy.[7] Reports of individual cases and small case series found that up to 50% of patients treated with MTZ

develop sensory disturbances.[8] In our patients, the time course and onset of symptoms following MTZ treatment is consistent with their dysesthesias being the result of MTZ-related toxic sensory neuropathy. After discontinuing MTZ, the symptoms and sign disappeared.

The cumulative neurotoxic dose of metronidazole in the literature varied from 13.2 grams[9] to 228 grams[10] with duration of therapy after which neuropathic symptoms ranging from 11 days to 6months.[10] Our patients developed neuropathy after taking 46 grams of metronidazole for hepatic amebeiasis for 30 days and is similar to Gupta et al 11report. Conventional nerve conduction studies in some patients with suspected MTZ-related neuropathy showed features of an axonal sensory neuropathy.[12] Of the tests for diagnosis neuopathy, Quantitative sudomotor axon reflex testing (QSART) may be the best electrodiagnostic test. Unfortunately there is no gold standard for comparison[13], of these findings.

**Conclusion**

We report a case of unusual development of peripheral neuropathy after starting metronidazole (MTZ). So, early recognition of symptoms, rationale use and rapid withdrawal of MTZ are important for recovery of neuropathy.

**Acknowledgement**

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