Concurrent encephalopathy and peripheral neuropathy: A rare case of metronidazole toxicity

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Received 27 Oct 2021
Accepted 20 Dec 2021

ABSTRACT

Metronidazole is a nitroimidazole antibiotic widely used in clinical practice for anaerobic bacteria and protozoa. Though well tolerated, it rarely has severe neurological toxicity. We are reporting a case of a 59-year old female with liver abscess who developed concurrent encephalopathy and peripheral neuropathy after a few days of high-dose metronidazole therapy. MRI brain of patient showed characteristic hyperintense lesion in bilateral dentate nuclei of cerebellum. Nerve conduction study showed demyelinating pattern and sensory neuropathy predominantly affecting lower limbs. The patient recovered well after the withdrawal of the offending agent.

Keywords: **Encephalopathy, Metronidazole, Peripheral neuropathy**

Introduction

Metronidazole is a nitroimidazole antibiotic that is widely used in clinical practice for over 50 years against most gram-negative bacteria, anaerobic gram-positive bacteria, and protozoa[1]. It is a well-tolerated drug with minimal side effects like nausea, abdominal pain, and diarrhea[2]. Cerebellar dysfunction, altered mental status, and seizures are rare neurological side effects of metronidazole reported in the literature[3]. We report a case of a 59-year old female who had concurrent metronidazole encephalopathy and peripheral neuropathy within few days of initiation of parenteral metronidazole for liver abscess.

Case discussion

A 59-year old female was referred to our center for further management of liver abscess. Abdominal pain and decreased appetite were the initial symptoms of the patient. At the time of admission, her sensorium was intact, Blood pressure was 110/80 mmHg, pulse rate was 82 beats per minute, respiratory rate was 18 cycles per minute, and temperature was 98 degrees Fahrenheit. Systemic examination revealed mild abdominal tenderness in right hypochondrium, and other systemic examinations including the nervous system were normal at the time of admission. We started her on intravenous ceftriaxone and metronidazole.

After nine days of hospital stay, she developed tingling sensation and weakness over bilateral lower limbs. On examination, she was confused and had medical research council grade 3/5 power in ankle flexion and extension. She had ataxia and slurred speech. Other motor examinations, sensory examination, and cranial nerves examinations finding were normal. Blood sugar levels, thyroid function tests, and vitamin B12 levels were within the normal limit.

A nerve conduction study was done which showed demyelinating motor and sensory neuropathy predominantly over lower limbs as illustrated in figure 1.

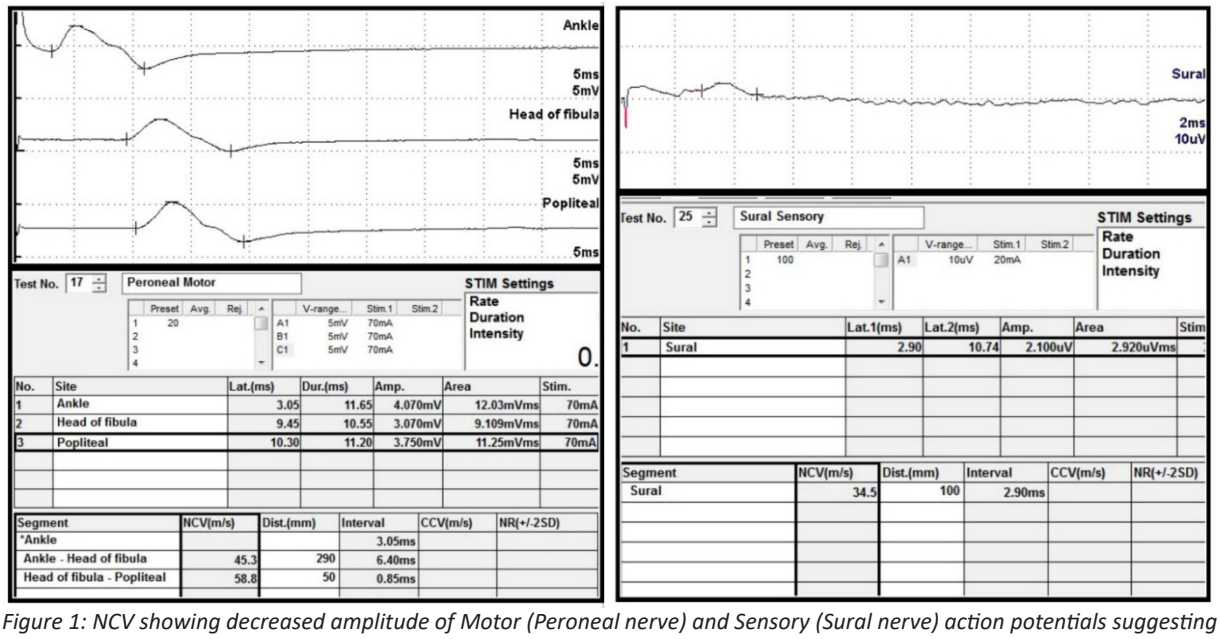

Figure 1: NCV showing decreased amplitude of Motor (Peroneal nerve) and Sensory (Sural nerve) action potentials suggesting early axonal neuropathies.

Computed tomography of the head was normal. MRI brain revealed symmetrical high signal intensity in bilateral cerebellar dentate nuclei as illustrated in figure 2. We made the final diagnosis of metronidazole induced encephalopathy and mixed type peripheral neuropathy. Metronidazole was stopped. There was gradual improvement in speech and ataxia of the patient after the stoppage of the metronidazole.

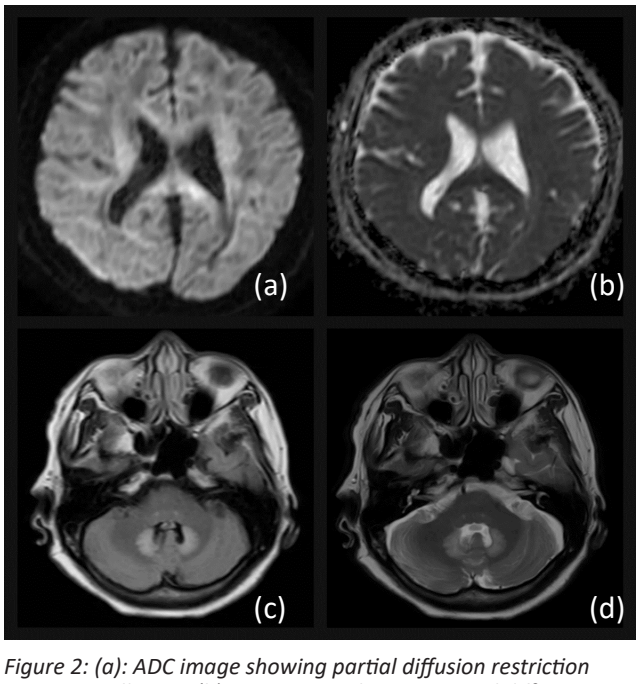

Figure 2: (a): ADC image showing partial diffusion restriction in corpus callosum. (b): DWI image showing partial diffusion restriction in corpus callosum. (c): FLAIR image showing high signal intensity in bilateral dentate nuclei. (d): T2 weighted image showing high intensity in bilateral dentate nuclei

Discussion

We reported a case of a 59-year-old patient with metronidazole-induced encephalopathy and peripheral neuropathy based on clinical symptoms of slurring of speech, confusion, tingling sensation and reduction in power of lower limbs, and nerve conduction finding of demyelinating motor neuropathy and sensory neuropathy, and MRI brain findings of high signal intensity lesion at bilateral cerebellar dentate nuclei. Her neurological recovery was complete after the stoppage of metronidazole.

Metronidazole has the potential to cross the blood-brain barrier and cause central nervous system side effects. Ning et al. reported a case of a 22-year-old patient who developed encephalopathy in the form of confusion, seizure, and gait imbalance after two months of metronidazole therapy[4]. The patient also had peripheral neuropathy similar to our patient. Sapkota et al. reported about a patient with liver abscess who developed metronidazole-induced slurring of speech after two months of metronidazole therapy[5]. Neurological adverse effects of metronidazole are dose and duration dependent[3]. The proposed hypothesis of metronidazole toxicity is inhibition of thiamine pyrophosphorylation as a thiamine analog but intricacies of mechanism is yet not fully understood[6]. Any patient on high dose metronidazole therapy who develops confusion and cerebellar symptoms, metronidazole encephalopathy is one of the possibilities as in our patient.

Our patient had MRI brain finding of high signal intensity at bilateral cerebellar dentate nuclei similar to the patient with metronidazole induced encephalopathy as reported by Sapkota et al.[5] and Rana et al.[7]. Metronidazole encephalopathy typically involves dentate nuclei of cerebellum in symmetrical manner. She had peripheral neuropathy involving predominantly lower limbs. Similar case report of metronidazole induced peripheral neuropathy presented with involved tingling sensation and weakness of lower limbs was reported by Guptaet al. and Maskeyet al.[8]. Metronidazole induced peripheral neuropathy usually shows glove and stocking pattern of neuropathy, predominantly involving sensory nerve and that often recovers after withdrawal of the drug[9].

We managed our patient of metronidazole encephalopathy by withdrawing the offending agent. She recovered within weeks of withdrawal of metronidazole. Similar improvement in symptoms after withdrawal of metronidazole was reported by Sapkota et al.[5], Rana et al.[7], and Ning et al.[4]. Li et al. reported a patient with metronidazole encephalopathy who deteriorated even after withdrawal of the culprit drug and recovered after intravenous high dose methylprednisolone therapy. Mostly metronidazole encephalopathy improved after withdrawal of the culprit drug, however, steroids and thiamine can be rarely used.

Conclusions

Metronidazole encephalopathy is possible in patients who were treated with high-dose metronidazole for long duration. Confusion, slurring of speech and imbalance are the common clinical manifestation of metronidazole encephalopathy. Cerebellar dentate nuclei hyper intense lesion in T2 weighted/ Flair is the characteristic lesion of this condition. This condition mostly recovers after the withdrawal of the culprit drug.

Acknowledgement

We would like to acknowledge Mr. Laxman Timilsina for technical support in writing this case report.

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