

Metronidazole associated-aseptic neuritis induced irreversible optic neuritis : A Case Report Of Unfavorable Outcomes And Literature Review

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Introduction:

Metronidazole is a bactericidal, amoebicidal, and trichomonacidal agent targeting anaerobic bacteria, certain amoebic and protozoal species. It is a nitroimidazole that inhibits nucleic acid synthesis by disrupting DNA resulting in strand breakage. Its bioavailability is more than 80% when taken orally. It is a usually well-tolerated antimicrobial but can cause gastrointestinal side effects like a gastric upset in the form of nausea, vomiting, abdominal cramps, diarrhea, or constipation [1]. It has also been associated with other adverse effects like dizziness, darkening of the urine, and joint pain. Disulfiram reaction has been reported, especially in those drinking ethanol. Neuro-ophthalmologic side effects such as peripheral neuropathy, ataxia, encephalopathy, and even seizures have been reported with metronidazole use[2]. Optic neuritis, an inflammation of the optic nerve, is an unrecognized side effect of Metronidazole and has been reported in association with metronidazole administration in a few case reports. The nerve damage induced by Metronidazole can be either temporary or permanent.

Here, we are reporting a 30-year-old lady who had a bout of gastroenteritis and was given a dose of IV Metronidazole and one day after which she started noticing decreased right eye vision, which progressed to complete vision loss in her right eye. She was managed with IV Pulse steroids. She showed a slight improvement in her right eyesight.

Case Presentation:

A 30-year-old Kenyan lady who is medically free presented to our hospital with right eye blurry vision that started one week before admission and gradually progressed over one day to complete right eye vision loss. Her condition was associated with mild right eye pain, which was exacerbated by eye movement. Her left eye was normal. She denied any previous similar episodes; she gave no history of any focal weakness or sensory abnormalities. She had no headache, no dizziness, and no abnormal body movements. She reported no fever. She did not have any history of head trauma, and she denied any urinary or defecation difficulties. On further questioning, the patient elaborated that she had an episode of gastroenteritis a week before admission. She has been given IV Metronidazole 500 mg (one dose) and discharged on Pantoprazole PO 40 mg daily and Metoclopramide tablets 10 mg as needed for nausea and vomiting. The day after her discharge, she started complaining of decreased eye vision which progressively worsened to complete vision loss in one day; she did not seek medical advice due to financial issues. Upon admission, her vital signs were normal (Body Temperature: 36.7 Celsius degrees, Heart Rate: 78 beats per minute, Blood Pressure: 117/70 mmHg, SPO2: 98% on room air). She had unremarkable chest and abdominal examinations. A central nervous system examination showed normal higher mental status. Normal power, tone, reflexes, coordination, and normal sensory function. Her gait was normal. Her cranial nerves examination showed complete loss of vision in

her right eye, otherwise unremarkable. Her right eye ophthalmologic examination was significant for right afferent pupillary defect and optic disc edema with the normal macula with normal left eye examination. Her Complete blood count, serum electrolytes, renal function, liver function tests, thyroid function test, and B12 level were all normal. Her Head Computed Tomography was unremarkable.

Lumbar Puncture was done and Cerebrospinal fluid (CSF) analysis showed WBC of 44/ul (Normal range 1-5/ul), 97% lymphocytic, RBC 2/ul (Normal range 0-2/ul), Glucose 2.90 mmol/l (Normal range 2.22-3.89 mmol/l) and protein of 0.65 gm/l (Normal range of 0.15-0.45 gm/l). CSF was negative for culture and viral panel as well as oligoclonal bands. Her MRI brain and orbit MRI confirmed right optic neuritis. (**figure 1** The patient was started on IV Methylprednisolone 1000 mg daily for five doses. She showed a slight improvement in her eyesight from nil to hand movement at a 50 cm distance on discharge. Follow up visits at one week and two months after discharge for the patient showed that her vision stabilized at “close counting fingers” level with no further improvement.

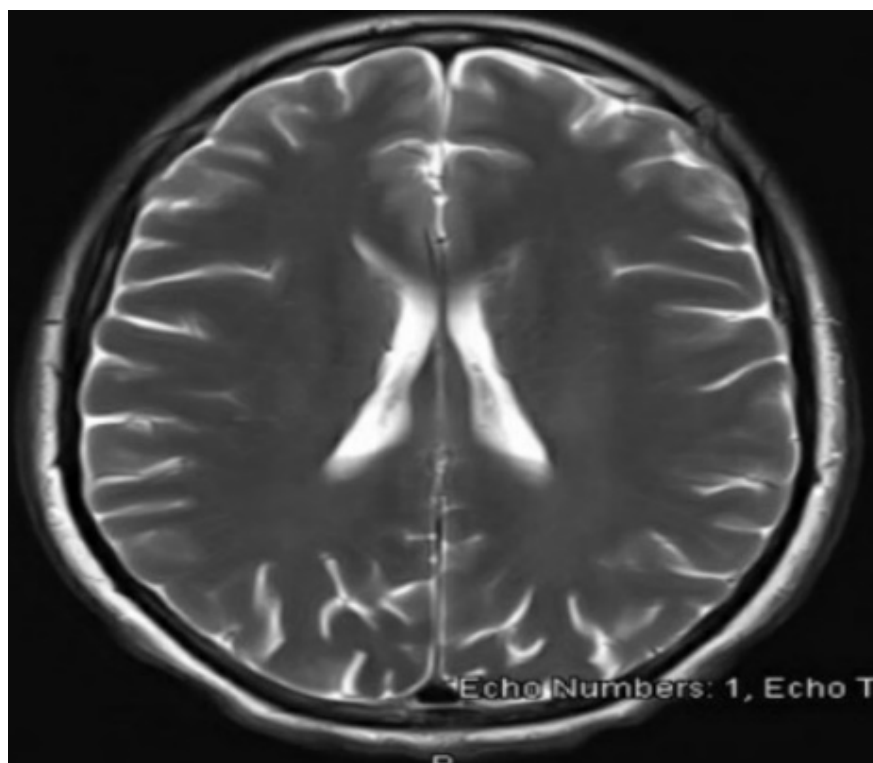




Figure-1 MRI Sections of the brain and orbit with cont

The right optic nerve appears swollen with evidence of abnormal T2WI hyperintensity involving the chiasmatic, canalicular, and proximal to mid-orbital segments with mild blurring of the retro-orbital fat.(Arrowed)

Discussion:

Metronidazole is an effective antimicrobial that was first used against trichomonas infections in the late 1950s and then was found to have effects on anaerobic bacteria and protozoal species. It is frequently used and usually has gastrointestinal side effects of gastric upset and metallic taste feeling. Its neurological adverse effects have been infrequent and only reported in case reports; these include dizziness, ataxia, encephalopathy, and seizure [2]. Ophthalmic side effects have been rarely reported and only seen in case reports and are not frequently recognized by healthcare providers. Here we described a case report of 30-year-old lady who was medically free until around 20 days before her admission when she had a bout of gastroenteritis and was given a dose of Metronidazole 500 mg IV the next day. She noticed progressively worsening vision in her right eye, which progressed to complete vision loss in one-day duration. She did not seek medical advice due to financial issues and stayed for around one week waiting for spontaneous recovery of her vision. Upon admission, she was vitally stable, and her physical examination was unremarkable apart from complete vision loss in her right eye and right pupillary afferent defect. Her Basic laboratory blood tests were normal, and her MRI findings were consistent with left optic neuritis. CSF analysis showed lymphocytic pleocytosis and elevated protein level but was negative for culture, viral panel, and oligoclonal bands. Her hospital course has been uneventful, and she was started on IV Methylprednisolone 1000 mg daily for five days. She showed a slight improvement in her right eye vision from complete vision loss to hand movement at 50 cm distance which then did improve to only counting fingers at 50 cm distance.

An extensive literature review was done, and we found 10 case reports and 1 case report with a literature review discussing the neuro-ophthalmic profile of Metronidazole. The age of patients ranged from 6 to 67 years, 8 were males, and 9 were females. All of the cases we could extract data for were administered

Metronidazole orally. The dose ranged between 250 mg to 1500 mg per day, and the duration of drug administration to symptom development was from one dose of 250 mg up to chronic use of 2 years. 15 patients developed optic neuritis, three patients developed aseptic meningitis, one patient developed myelitis, and two patients had cerebellar involvement. All the patients were managed with the withdrawal of Metronidazole, except one patient with aseptic meningitis who was treated with a 3rd generation intravenous cephalosporin for one week, and another patient with optic neuritis who was initiated on coenzyme Q10 for 3 months in addition to cessation of metronidazole. Most patients fully recovered their vision, but one whose damage was irreversible, and seven other patients had 71% reversibility of their sight (Please see table 1 for the summary and comparison of literature review and our case).

Conclusion:

Metronidazole is an effective and widely used antimicrobial commonly associated with gastrointestinal side effects. In addition, its neuro-ophthalmic profile, though rare, can be sight-threatening, resulting in irreversible vision loss. Therefore, clinicians should be attentive to the adverse effect of even one dose of intravenous or oral Metronidazole.

Reversibility	Treatment	Outcome	Duration	Dose	Route of administration	Gender	Age	Case
Some reversibility	IV Pulse steroid 500 mg IV Methylprednisolone for 5 days	Right optic neuritis and aseptic neuritis	One dose	500 mg	IV	Female	30 years old	Our Case
Yes	Cefotaxime 500 mg BID IV for one week	Aseptic meningitis	One week	400 mg BID	Oral	Male	49 years old	A.Vihar et al [3]
Yes	Stopping Metronidazole	Bilateral optic neuritis	8 months	400 mg BID	Oral	Female	67 years old	Nicole M McGrath et al [4]
No	Stopping Metronidazole	Bilateral optic neuritis and meylitis	1 week	1000 mg OD	Oral	Female	57 years old	Pai-Huei-Peng et al [5]
Yes	Stopping Metronidazole	Optic neuritis	Two years	NA	NA	Male	36 years old	Natalie Anwyll et al [6]
Yes	Stopping Metronidazole	Aseptic meningitis	One dose	250 mg	Oral	Female	20 years old	Audrey P et al [7]

Reversibility	Treatment	Outcome	Duration	Dose	Route of administration	Gender	Age	Case
Yes	Stopping Metronidazole	Optic neuropathy and cerebellar toxicity	For two years	500 mg TID	oral	Female	58 years old	Erin Nu et al [8]
Yes	Stopping Metronidazole	Bilateral optic neuritis	Two weeks	NA	Oral	Female	6 years and 8 years old	Bourao R et al [9]
Yes	Stopping Metronidazole	Aseptic meningitis	One dose	400 mg	Oral	Male	42 years old	Sujoy Khan e a [10]
Some reversibility	Stopping Metronidazole	Optic neuritis	7-365 days	750-1000 mg daily	Oral	4 females and 3 males	7 patients from 26-53 years old	Putnam et al [11]
Yes	Stopping Metronidazole Starting coenzyme Q10	Optic neuropathy and cerebellar toxicity	Over 6 months	500 mg TID	Oral	Male	17 years old	Kim M Cecil et [12]
Yes	Stopping Metronidazole	Optic neuropathy	2 years	1500 mg daily	Oral	Male	20 years old	De Bleecke et al [13]

Table-1 Comparison of our case and summary of literature review

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