ECRONICON OPEN ACCESS

EC PHARMACOLOGY AND TOXICOLOGY
Case Report

Acute Myelopathy Differential Diagnosis: A Case Report

Tahir Chaudhry[1]*, Alice Jiang[1], Janki Shah[1], Andrew Rudin[2], Kaiyu Ma[3], Malloy Nair[4] and Zoltan Fekete[3]

[1]*Orange Regional Medical Center, Middletown, NY, USA*

[2]*Emergency Medicine, Orange Regional Medical Center, Middletown, NY, USA*

[3]*Neurology, Crystal Run Healthcare, Middletown, NY, USA*

[4]*Infectious Diseases, Crystal Run Healthcare, Middletown, NY, USA*

***Corresponding Author**: Tahir Chaudhry, Orange Regional Medical Center, Middletown, NY, USA.

Received: October 18, 2017; **Published:** November 08, 2017

Abstract

A 57 year-old male patient presented to the ED with a chief complaint of paralysis and sensory deficits in his lower extremities. Preliminary diagnosis of transverse myelitis was soon ruled out. Differential diagnoses of Guillain-Barré syndrome, Lyme disease and West Nile virus were additionally ruled out. Upon closer analysis of the patient's medication history and bloodwork analysis, vitamin B12 deficiency-induced myelitis and metronidazole-induced neuropathy were suspected. Upon drug cessation and cobalamin supplementation, the patient rapidly regained his ability to walk within two weeks. Due to this patient's co-presentation of B12 deficiency with chronic metronidazole use and due to his rapid recovery time, this is a non-classical case that warrants further analysis.

Keywords: *Metronidazole; B12; Cobalamin; Acute Myelitis; Transverse Myelitis; Paraplegia*

Abbreviations

HPI: History of Present Illness; ED: Emergency Department; MRI: Magnetic Resonance Imaging; PCR: Polymerase Chain Reaction; CSF: Cerebrospinal Fluid; CBC: Complete Blood Count; MCV: Mean Corpuscular Volume; P.O.: Per Os: By Mouth; MMA: Methylmalonic Acid; CT: Computed Tomography; Pg: Picograms; mL: Milliliter; RPR: Rapid Plasma Reagin; ELISA: Enzyme-Linked Immunosorbent Assay

Introduction

This is a non-classical case study of co-presentation of metronidazole induced neuropathy and Vitamin B12 induced neuropathy.

HPI

A 57 year-old male with a past medical history of seborrheic rosacea presents to the ED with a chief complaint of inability to walk. He describes a sudden onset of bilateral leg weakness with loss of sensation from his genitals to his toes.

The rapid onset of his symptoms and the severity of his symptoms were concerning for acute myelitis. The preliminary diagnosis was transverse myelitis.

Materials and Methods

Detailed history taking, physical exam findings as well as laboratory exam findings were utilized to rule out certain preliminary diagnosis as well as certain other differential diagnosis. Upon completion of these methods and analysis, treatments were provided.

Results and Discussion

Initial workup involved CT scan without contrast, lumbar spinal tap and MRI of the cervical, thoracic and lumbar spine. Acute hemorrhage was ruled out by negative findings on head CT. Preliminary diagnosis of transverse myelitis was reduced due to negative findings on

lumbar spinal tap and negative findings on MRI of the spine. Physical exam findings were also negative for speech difficulty, tremors, or dysmetria. Clinical suspicion for Guillain-Barré syndrome was reduced due to absence of areflexia. Lyme disease was also unlikely due to negative ELISA analysis. Negative RPR in the blood reduced the likelihood of syphilis induced neuropathy. History was negative for injury or trauma to the spinal cord. The patient did not complain of urinary or fecal incontinence and MRI was negative for compression of the cauda equina or conus medullaris. The patient was a reliable historian with no indication of alcohol abuse or illicit substance use.

Physical exam findings were positive for ataxia with weakness in both legs-the patient could not ambulate without walker assistance. In addition, he had sensory loss from his genitals to his toes. Reflexes were symmetrical and normal bilaterally. Romberg's sign was positive for loss of proprioception. Babinski's sign was unilaterally positive for upper motor neuron pathology. Further workup including blood analysis revealed moderately low serum Vitamin B12 levels, at 227 pg/mL. As this level is considered borderline, deficiency is possible [1]. Additionally, the patient tested positive for anti-intrinsic factor antibodies. Vitamin B12 deficiency-induced myelitis was suspected to contribute to symptoms. Lichtheim's disease was not ruled out. Lichtheim's disease, as first described by Professor von Lichtheim in 1889, is a subacute combined degeneration of the posterior and lateral columns of the spinal cord [2]. It is most commonly caused by Vitamin B12 deficiency. However, Lichtheim's disease can also be caused by copper deficiency and Vitamin E deficiency [3-4]. Notably, serum ceruloplasmin, zinc and vitamin E levels were normal in this patient.

Past medical history was positive for 6 months of metronidazole use. Metronidazole has been shown to cause a variety of rapid onset, neurotoxic side effects including encephalitis and peripheral neuropathy [5-7]. As such, metronidazole induced neuropathy was suspected to contribute to symptoms. The patient was started on B12 injections, thiamine injections and folic acid P.O. The patient was also instructed to cease metronidazole treatment.

The patient showed rapid improvements of neurological deficits in response to B12 injections and metronidazole cessation. The patient regained muscle strength and ability to walk without assistance within two weeks of original presentation. At two weeks, the patient tested negative for Romberg's sign and Babinski's reflex. The patient's sensory level gradually began to improve, but some sensory loss remained.

On one month follow up, the patient retained his ability to ambulate and sensation was returned to normal in all areas of his body except his genitalia. Additionally, the patient's B12 levels improved and were measured well within the normal range.

Differential diagnosis of West Nile Virus was ruled out by improvement of neurological deficits, but viral infection of unknown etiology was not ruled out. Subacute combined degeneration of the spinal cord was not ruled out and metronidazole-induced neuropathy was also not ruled out.

Analysis of CBC demonstrated that the MCV was within reference range. Anemia was absent, and homocysteine and MMA were within reference range. However, it should be noted that this patient's presentation mimics the classic symmetrical neuropathy, weakness and myelitis seen in late B12 deficiency [1,8-10]. Indications supporting the diagnosis of B12 deficiency include moderately low B12 levels in the blood, presence of intrinsic factor antibodies, bilateral sensory loss, bilateral motor weakness, ataxia, positive Babinski's sign and positive Romberg's sign.

Spinal cord involvement is the most common symptom of B12 deficiency [11]. Neuropsychiatric symptoms of B12 deficiency can precede anemia and microcytosis [11]. Pernicious anemia is the most common cause of B12 deficiency [8]. Although there was no macrocytosis or elevation of MMA and homocysteine in this patient's serum, there have been cases of neuropsychiatric manifestations of B12 deficiency in the absence of macrocytosis and the absence of elevated MMA and elevated homocysteine [12].

It should be noted that nitrous oxide can induce a rapid onset B12 deficiency with rapid onset gait ataxia and loss of proprioception [13]. However, the patient denied exposure to nitrous oxide and had no recent anesthesia. Therefore, the etiology of this patient's rapid onset myelitis remains unclear.

Classically, full correction of B12-induced neurological deficits takes about 6 to 12 months to correct [14]. While metronidazole induced cerebellar toxicity has been shown to improve in less than 10 days [15]. The proposed mechanism of action of metronidazole-induced neuropathic symptoms remains unclear, however, one proposed mechanism is the binding of metronidazole to RNA, inhibiting neuronal protein synthesis [16].

This patient's clinical symptoms and lab values may have been indicative of B12 deficiency-induced myelitis while the rapid onset of his severe symptoms was due to an unclear etiology. Additionally, the patient's rapid, two-week improvement of motor deficits after metronidazole cessation mimicked the time course of metronidazole-induced cerebellar toxicity with neuropathy in which ataxia improved within 10 days, but sensory loss improved at a slower pace [15].

It is unclear whether this patient's rapid onset myelitis and neuropathy were due to B12 deficiency-induced myelitis, chronic metronidazole use, or a combination of the two. It is also unclear if this patient's symptoms were due to unknown viral etiology.

This patient's rapid onset of neuropathy, his co-presentation of chronic metronidazole use with borderline low vitamin B12 levels, as well as his rapid recovery time illustrate why this is a non-classical case that warrants further research to understand the true etiology of this patient's illness.

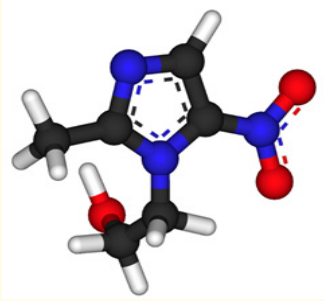

Figure 1: *Metronidazole Chemical Structure [17].*

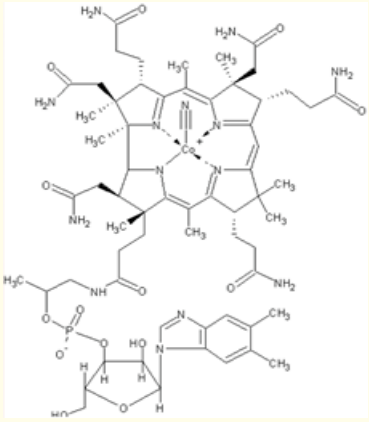

Figure 2: *Vitamin B12 Chemical Structure [18].*

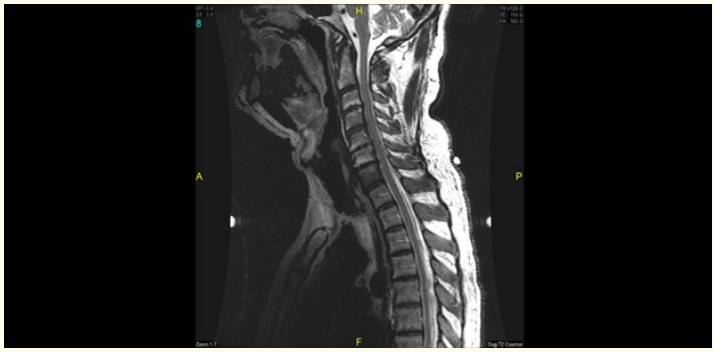

Figure 3: *MRI of Cervical and Thoracic Spine.*

Conclusion

Classical causes of acute myelitis include transverse myelitis, Guillain-Barré syndrome, Lyme disease, and West Nile virus. Non-classical presentations of acute myelitis warrant further work-up and more detailed history taking. Non-classical presentation of acute myelopathy includes co-presentation of B12 deficiency with drug-induced neuropathy that is rapidly correcting.

All the aforementioned pathologic entities have different treatment modalities and each require prompt diagnosis for fast healing and improved patient outcomes.

Conflict of Interest

No conflict of interest is present.

Bibliography

1. Schrier Stanley L. "Clinical Manifestations and Diagnosis of Vitamin B12 and Folate Deficiency". *Up to Date*.
2. Lichtheim. "Zur Kenntis der perniciosen Anemie". Verhandlungen des Deutschen Kongress fur innere Medizin 6 (1889): 84-96.
3. Kumar N., *et al*. "Copper Deficiency Myelopathy Produces a Clinical Picture Like Subacute Combined Degeneration". *Neurology* 63.1 (2004): 33-39.
4. Agamanolis Dimitri P. Nutritional CNS Disorders. Deficiency of the lipid-soluble vitamin E occurs in cases of intestinal malabsorption such as cystic fibrosis, congenital biliary atresia, intestinal resection, and abetalipoproteinemia (Bassen-Kornzweig syndrome) (2014).
5. Hitender Kumar., *et al*. "Rapid onset peripheral neuropathy: A rare complication of metronidazole". *Journal of Indian Academy of Clinical Medicine* 13.4 (2012): 346-348.
6. Johnson Melissa. "Metronidazole: an Overview". Up to Date, Wolters Kluwer.
7. Carroll MW., *et al*. "Efficacy and safety of metronidazole for pulmonary multidrug-resistant tuberculosis". *Antimicrobial Agents and Chemotherapy* 57.8 (2013): 3903-3909.
8. Stabler SP. "Vitamin B12 deficiency". *The New England Journal of Medicine* 368.2 (2013): 149-160.
9. Lindenbaum J., *et al*. "Neuropsychiatric disorders caused by cobalamin deficiency in the absence of anemia or microcytosis". *The New England Journal of Medicine* 318.26 (1988): 1720-1728.
10. Healton EB., *et al*. "Neurologic aspects of cobalamin deficiency". *Medicine* 70.4 (1991): 229-245.

11. Briani Chiara., *et al*. "Cobalamin Deficiency: Clinical Picture and Radiological Findings". *Nutrients* 5.11 (2013): 4521-4539.

12. Durand C., *et al*. "[Psychiatric Manifestations of Vitamin B12 Deficiency: a Case Report]". *L'Encephale* 29.6 (2003): 560-565.

13. "Patterns of Abnormal Hyperintense Signal of the Spinal | Open-i". U.S. National Library of Medicine, National Institutes of Health.

14. Schrier Stanley L. "Diagnosis and Treatment of Vitamin B12 and Folate Deficiency". *Up To Date* (2016).

15. Kato H., *et al*. "[Clinical Characteristics of Metronidazole-Induced Encephalopathy: A Report of Two Cases and a Review of 32 Japanese Cases in the Literature]". *Journal of the Japanese Association for Infectious Diseases* 89.5 (2015): 559-566.

16. Bradley WG., *et al*. "Metronidazole neuropathy". *British Medical Journal* 2.6087 (1977): 610-611.

17. "Metronidazole 3D 1 w3r.Png". Wikimedia, Fvasconcellos, (2010).

18. "Cobalamin". Wikimedia, NEUROtiker (2007).

Volume 5 Issue 1 November 2017