Nitrous Oxide Induced Subacute Combined Degeneration

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INTRODUCTION

Subacute combined degeneration (SCD) is a rare neurological outcome of vitamin B12 deficiency that leads to demyelination of the dorsal columns in the spinal cord.

Symptoms of SCD:
- Paresthesia
- Progressive weakness
- Sensory ataxia

Causes of B12 deficiency:
- Restricted diet
- Gastritis
- Surgical manipulation of the GI tract
- Inflammatory bowel disease
- Pernicious anemia

Rare cause of SCD: Nitrous oxide (N_2O). These patients have normal levels of B12, but they present with SCD because N_2O can lead to B12 inactivation.

CASE SUMMARY

Case: 35 year-old woman with two presentations for difficulty with ambulation and lower extremity numbness.

2017
- Symptoms:
  - Numbness and tingling in bilateral lower extremities
  - Difficulty with ambulation
- MRI (Figure 2)
- Conclusion: Suspected folate deficiency
- Treatment:
  - 3 days of steroids
  - B12 and folate replacement
  - Gabapentin
- Prognosis: Patient's symptoms reportedly improved 2 weeks after discharge. Lost to follow-up thereafter.

2018
- Symptoms:
  - Ascending parasthesias in bilateral lower extremities
  - Weakness in bilateral lower extremities
  - Difficulty with ambulation
- Physical Exam:
  - Diminished proprioception on toe and ankle manipulation
  - Diminished temperature and vibratory (at the bilateral malleoli) sensation.
- Conclusion: B12 inactivation
- Etiology: Intermittent "Whippet" use
- Treatment:
  - 3 days of steroids
  - B12 and folate replacement

SUMMARY OF LAB DATA

	2017	2018
MMA	Normal	Elevated
B12	Elevated	Normal
Folate	N/A	Normal
Homocysteine	Elevated	Elevated
Suspicion	Folate Deficiency	B12 Inactivation

FIGURES AND IMAGING

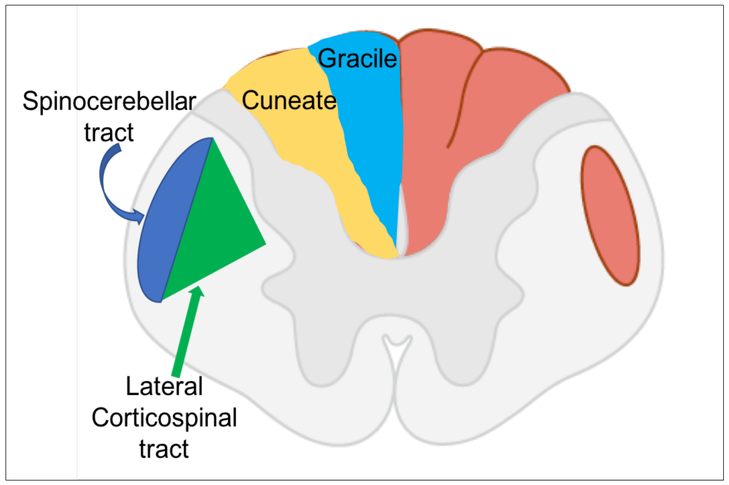

Figure 1- Cervical spine cross section
Green: Motor neuron fibers from the cortex to the limbs.
Dark Blue: Proprioceptive information from the skeletal muscles and joints to the cerebellum.
Light Blue: Fine touch and proprioception from the lower body to the thalamus.
Yellow: Fine touch and proprioception from the upper body to the thalamus.
Red: Areas typically affected in SCD.

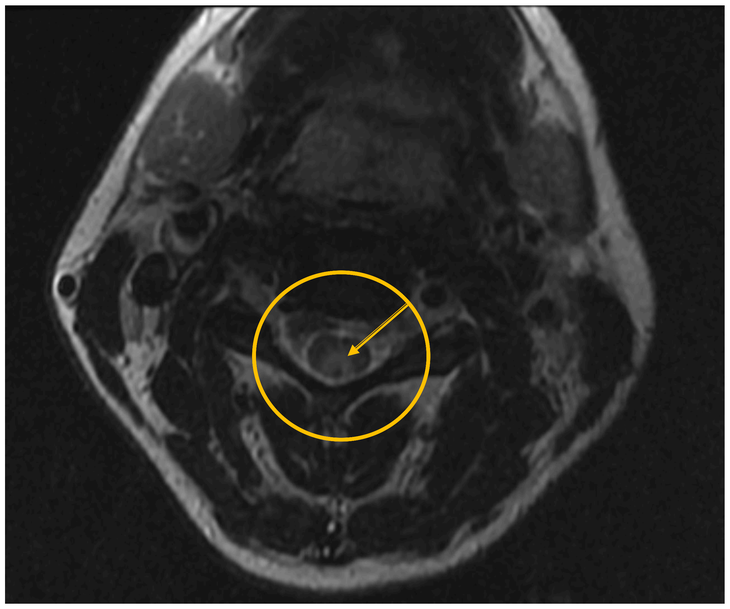

Figure 2- Cervical spine MRI
Sequence: FSE T2
Yellow arrow: Demonstrating the "inverted V-sign" classically associated with SCD
Take away: The inverted V shape is created by inflammation of the dorsal columns which present as a hyperintense lesion in the T2 sequence of MRI.

REFERENCES

1. Hemmer B, Glocker FX, Schumacher M, et al. Subacute combined degeneration: clinical, electrophysiological, and magnetic resonance imaging findings. J Neurol Neurosurg Psychiatry 1998; 65:822.
2. Vasconcelos OM, Poehm EH, McCarter RJ, et al. Potential outcome factors in subacute combined degeneration: review of observational studies. J Gen Intern Med 2006; 21:1063.
3. Diamond AL, Diamond R, Freedman SM, Thomas FP. "Whippets"-induced cobalamin deficiency manifesting as cervical myelopathy. J Neuroimaging 2004; 14:277.
4. Doran M, Rassam SS, Jones LM, Underhill S. Toxicity after intermittent inhalation of nitrous oxide for analgesia. BMJ 2004; 328:1364.
5. Sotirchos ES, Saidha S, Becker D. Neurological picture. Nitrous oxide-induced myelopathy with inverted V-sign on spinal MRI. J Neurol Neurosurg Psychiatry 2012; 83:915.

VITAMIN B12 REACTIONS

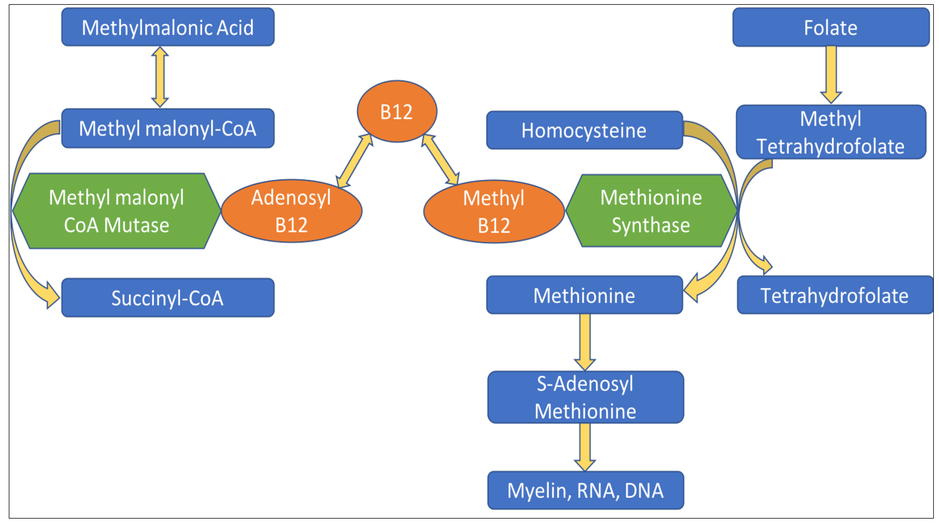

Figure 3- This figure shows the involvement of Vitamin B12 as a coenzyme for methionine synthase to convert homocysteine to methionine. Methionine is later converted to S-Adenosyl Methionine (SAM), the methyl group donor for the synthesis of DNA, RNA, and myelin. N_2O irreversibly oxidizes B12 and prevents its participation in this reaction.

DISCUSSION

N_2O utility:
- Anesthesia
- Euphoria (Recreational use)

Patients at risk for N_2O use:
- Younger population => "Whippets"
- Health care workers => Direct access to medical N_2O

Our patient's presentation summary:
- "Inverted-V sign" on MRI (Figure 2)
- Normal folate levels, elevated MMA, normal B12
- Recreational "whippet" use

Conclusion: SCD secondary to B12 inactivation in the setting of N_2O use. Demyelination of the dorsal columns caused paresthesias, weakness, and proprioceptive loss on physical exam.

Treatment: B12 supplementation

Prognosis: Partial neurological recovery in most patients, although full recovery is possible. Our patient demonstrated near full recovery during the 2017 episode but only partial recovery at the 1 month follow-up after the 2018 hospitalization.

Positive prognostic factors:
- Early treatment
- Negative Romberg and Babinski's sign
- Age <50
- MRI spine lesions involving <7 vertebral segments

Take home point: The neurological manifestations of vitamin B12 deficiency are well known. This case highlights the need to consider N_2O recreational use, especially in younger patients presenting with symptoms concerning for deficiency yet with normal B12 levels.