A vicious degeneration: immune, intake, or comBined

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Case Presentation

The patient is a 72-year-old man with a history of weight loss over the past year due to malnutrition who presented with subacute progressive weakness in his bilateral lower extremities, ataxia, and sensory deficits in fine touch, vibration, and proprioception.

Workup

- Hemoglobin 9.1
- MCV 120.8
- MRI brain, cervical, thoracic, lumbar spine revealed inverted V sign in dorsal columns.
- Vitamin B12 level 138
- Methylmalonic acid 78,271
- Intrinsic factor antibodies positive
- Anti-parietal cell antibodies positive

Case Conclusion

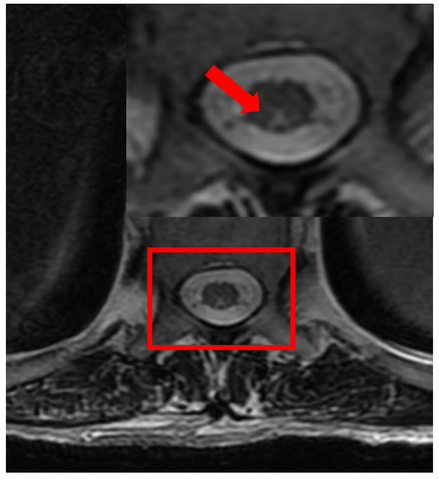
The patient was diagnosed with subacute combined degeneration secondary to B12 deficiency. His deficiency was thought secondary to pernicious anemia although he also had a malnutrition component. He was treated with intramuscular vitamin B12 and his weakness and sensory deficits improved.

Discussion

Subacute combined degeneration:

- Deficits:
    - Sensory: fine touch, vibration, proprioception
    - Motor
    - Sparing of pain and temperature sensation
- Pathophysiology: damage to white matter dorsal column/medial lemniscus and corticospinal tracts in spinal cord caused by cobalamin deficiency/methylmalonic acid accumulation
- Similar to copper deficiency myeloneuropathy

Figure 1: Inverted V Sign on thoracic spinal MRI



T2 MRI of thoracic spine in transverse plane shows the “inverted V sign,” a V shape in the dorsal columns consistent with subacute combined degeneration.

Discussion (cont.)

Inverted V sign:

- Bilateral high-intensity T2 signal in posterior funiculus in the shape of a V on an MRI of the spinal cord in cross section (2, 3)
- Pathognomic for subacute combined degeneration

Laboratory testing

- Vitamin B12 < 200 consistent with deficiency
- Vitamin B12 200-300 with elevated methylmalonic acid = functional B12 deficiency (4)
- Associated with megaloblastic anemia
- Pernicious anemia a/w intrinsic factor antibodies and parietal cell antibodies
    - Intrinsic factor antibodies interfere with the assay that tests B12 levels in serum (4)

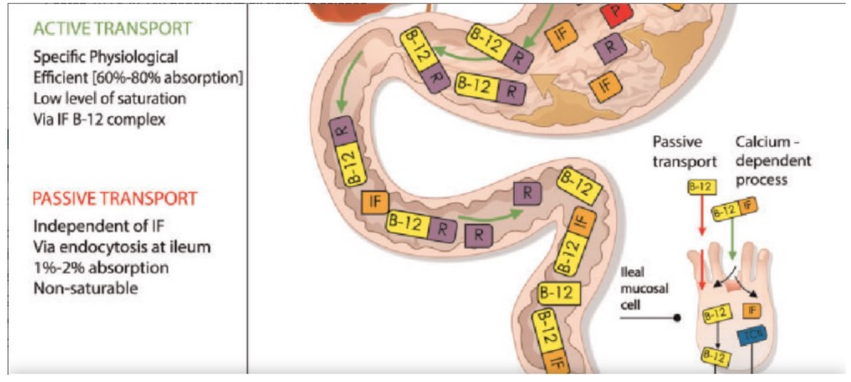
Treatment of pernicious anemia

- Historically, intramuscular given absence of intrinsic factor which is a cofactor for B12 absorption in the gut
- B12 is also absorbed by passive diffusion along the entire GI tract without IF
- Oral repletion is likely equal to IM even in the setting of pernicious anemia (1)
    - If severe neurologic manifestations, such as SCD, recommend IM repletion

Conclusions

- B12 deficiency can be caused by antibodies to intrinsic factor or parietal cells.
- B12 deficiency can lead to subacute combined degeneration, a demyelinating condition in the DCML and corticospinal tracts of the spinal cord.
- The inverted V sign on an MRI is pathognomic for subacute combined degeneration.
- A patient can have functional B12 deficiency even with vitamin B12 levels in the 200-300 range if their methylmalonic acid levels are elevated.
- Intramuscular repletion of vitamin B12 is historically recommended for pernicious anemia, but further research has shown that oral repletion is non-inferior in these patients.

Figure 2: Vitamin B12 absorption in GI tract



In addition to intrinsic factor-mediated uptake of vitamin B12 in the ileum, 1% of ingested B12 is absorbed throughout the GI tract by passive diffusion. (5)

References

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