Contemporary Neurology 2025
Mystery Case 1

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DISCLOSURES

- **Name:** Dane M. Chetkovich, MD, PhD
- **Relevant Financial Relationships:** None
- **Consultant for:** None
- **Speaker's Bureau for:** None
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- **Stockholder in:** None
- **Employee of:** Vanderbilt University Medical Center
- **Off-Label Use:** I will/will not discuss off-label use of medications/devices.

Learning Objectives

At the conclusion of this activity/session, participants will be able to:

1. Determine localization of neurological disease in a patient presenting with unique symptoms
2. Create a differential diagnosis for patients presenting with unique symptoms
3. Describe the diagnostic criteria for specific neurological diseases
4. Demonstrate the proper use of diagnostic testing to determine the neurological cause of specific unique symptoms

HPI

- 56 year old female with a past medical history significant for obesity who underwent gastric sleeve bypass 1 year ago.
- On the day prior to admission she developed **RUE clumsiness and unsteady gait that started the previous day while shopping**
- She also complained of right face numbness
- She also reports a 6 month Hx of worsening numbness and tingling in the lower extremities

Additional Hx

- **Medical Hx:**
  - No diabetes or hypertension
  - Bariatric Surgery 4 years ago => Lost significant weight from BMI 37 to 24
- **Medications:**
  - None
- **Social Hx:** Never smoker; Occasional alcohol 1-2 glass of wine per week
- **Family Hx:** Heart disease and obesity; Father died at age 67 from MI

Initial localization and differential diagnosis?

Neuro Exam

- Alert and oriented fully, normal speech language and cognition; odd affect; “La belle indifference”
- Cranial nerves normal except subtle decreased sensation R face to PP and Temp
- Motor exam normal
- Sensory exam: decreased PP and T right hemibody. Absent proprioception and vibration in BLE, reduced in fingers;
- Coordination: moderate to severe dysmetria RUE and RLE
- Gait- wide based; unsteady; and Romberg test positive

Refined localization thoughts?

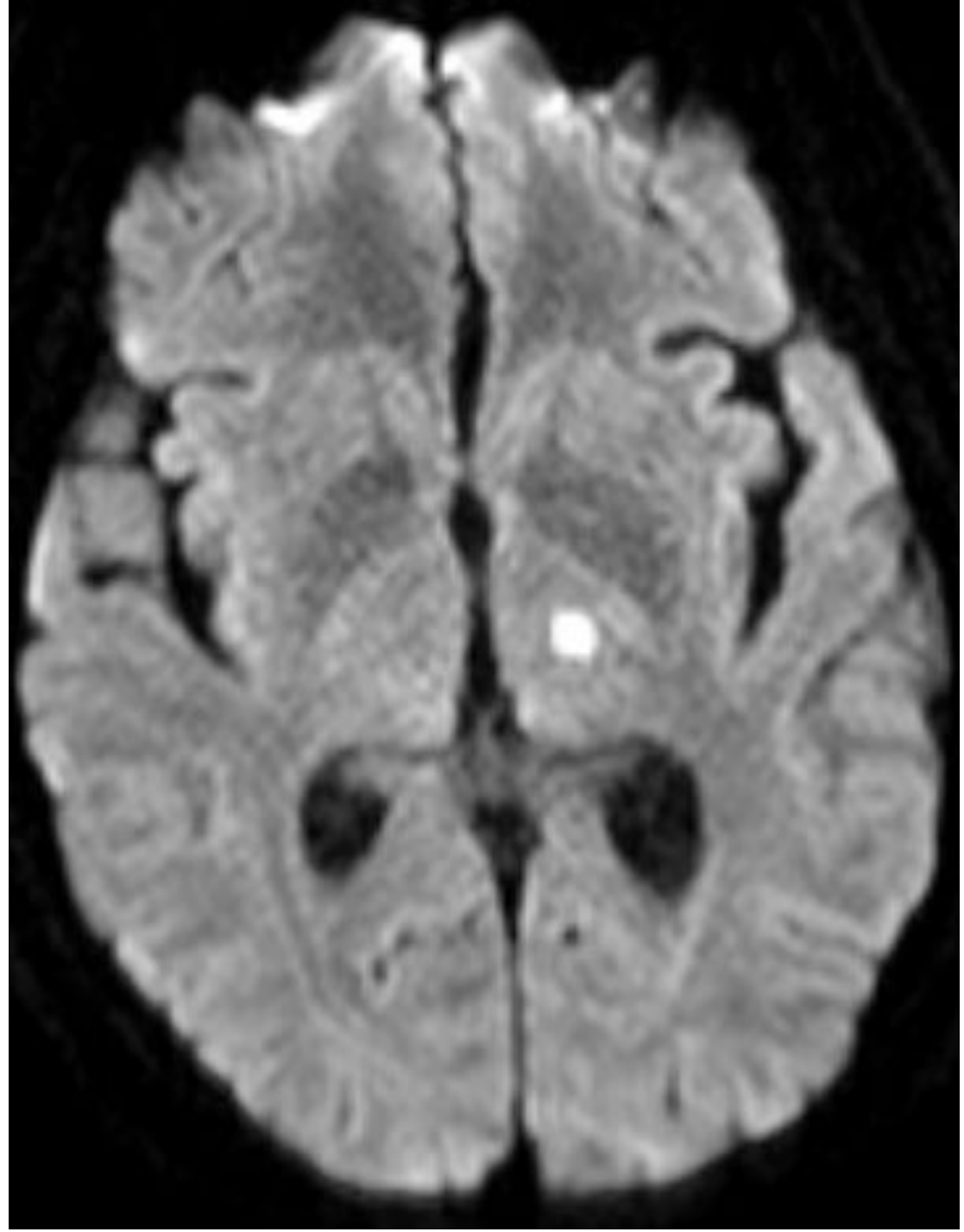
Refined differential diagnosis?

Initial Labs

- Comprehensive Chemistry- normal
- CBC- Normal
- PT/PTT/INR- Normal
- A1C- 5.2

CTH and CTA

- **CTH:** Negative for acute disease
- **CTA:** No stenosis or occlusion; no ICAD

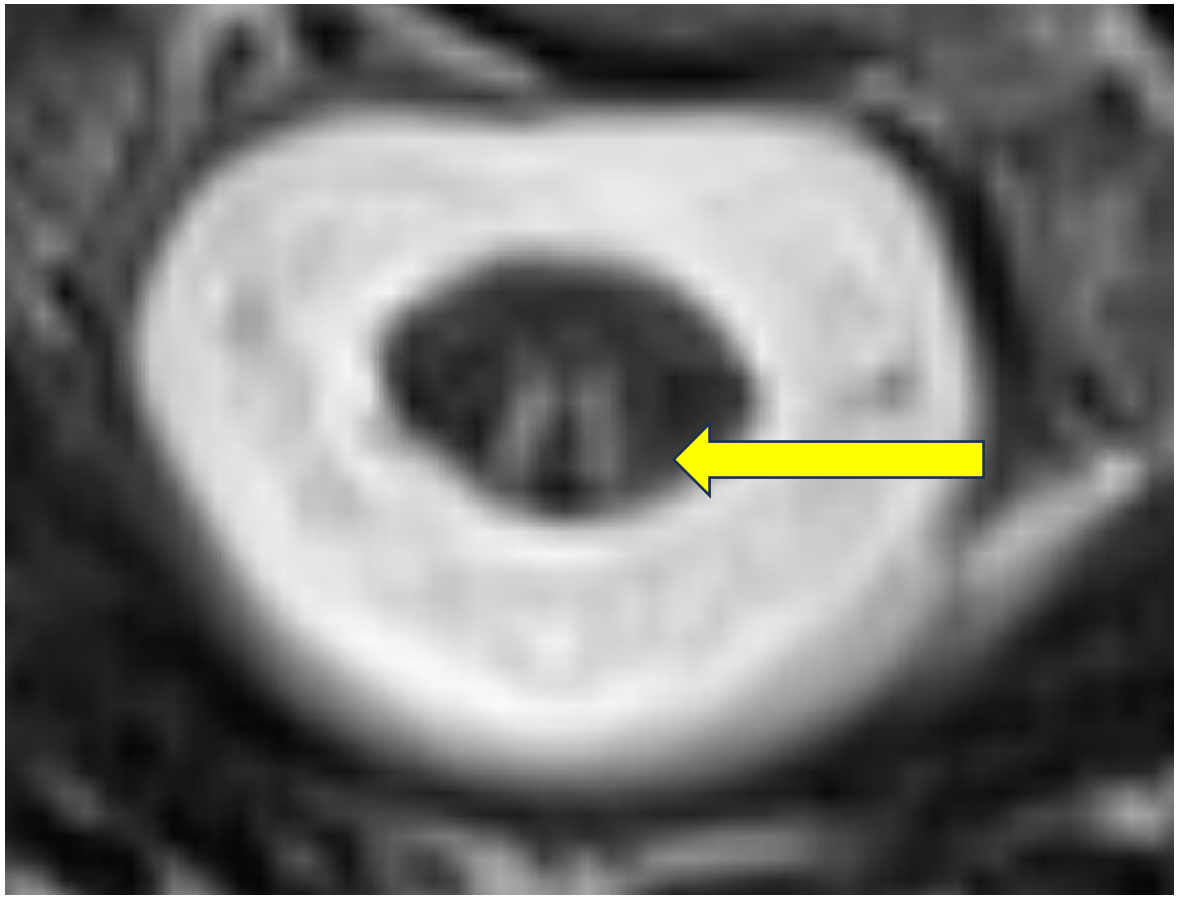


Stroke Workup

- **Cholesterol panel normal**
- **TEE negative**
- **Cardiac event monitor negative**

MRI C-Spine

C-spine dorsal column hyperintensity



Labs

- B1 (whole blood)- 97 normal
- TSH, ANA, RF-normal
- SPEP- neg
- RPR- NR
- Lyme- neg
- Copper- normal
- Folate: 6.2 (>4.0 umol/L)
- **Vitamin B12: 137 (180-914 umol/L)**
- **Homocysteine: 155 (7-16 umol/L)**
- **Methylmalonic acid: 2.3 (< or =0.40 nmol/mL)**

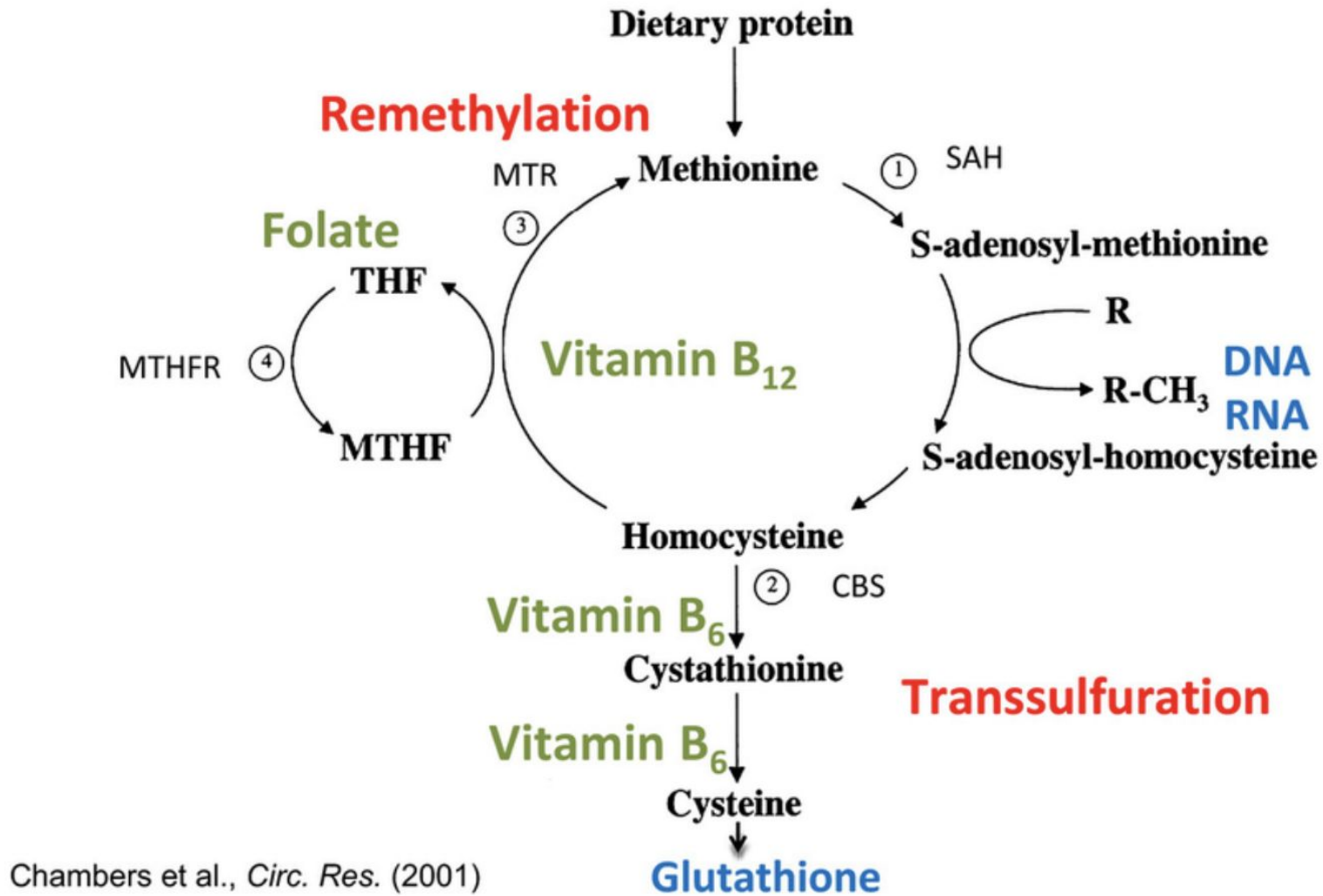
Explanation of symptoms

- Dorsal column dysfunction likely due to **Vitamin B12 deficiency**. Bariatric surgery associated with decreased uptake of B vitamins
- Acute right ataxia and hemisensory loss likely due to small vessel stroke- **Thalamic ataxia syndrome** i.e. contralateral ataxia from infarct affecting ventral part of ventrolateral thalami with involvement of spinothalamic pathways projecting to VPM and VPL

Treatment

- DAPT for minor ischemic stroke (NIHSS ≤5) x 21 days
- Ongoing ASA
- B12 1mg IM and po qd with follow-up testing in 1 month

Methionine - Homocysteine Cycle



Chambers et al., *Circ. Res.* (2001)

The methionine – homocysteine cycle contains re-methylation and transsulfuration components. The enzyme S-adenosyl homocysteine hydrolase (SAH) contributes to methylation of DNA and RNA. Other abbreviations: CBS = cystathionine–b–synthase; MTR = 5-methylterathydrofolate-homocyteine methyltransferase; MTHFR = methyltetrahydrofolate reductase; THF-tetrahydrofolate; MTHF = methyltetrathydrofolate.

Homocysteine and Vascular disease

- Moderately elevated homocysteine levels have been associated with an increased risk of cardiovascular and cerebrovascular disease, venous thromboembolic disease, and obstetric complications.
  - US Preventive Services Task Force (USPSTF) found that, independent of Framingham risk factors, each 5 micromol/L higher homocysteine level was associated with a 20 percent greater risk of CAD. Hyperhomocysteinemia has also been associated with lower-extremity peripheral arterial disease and heart failure
- In experimental studies, homocysteine has primary atherogenic and prothrombotic properties, suggesting a possible mechanism for these associations.
- Clinical trials have found that reducing levels of homocysteine with B vitamin supplementation **does not prevent cardiovascular disease** or reduce the incidence of recurrent venous thromboembolism (VTE) or arterial thrombosis.