Homocysteinemia: A Tale of Two Strokes

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Introduction

Stroke is a leading cause of disability and death in the United States. While most of primary care's focus is on reducing modifiable risks, such as hypertension, tobacco use, and diabetes, there are several other risk factors that are important to consider.

Elevated homocysteine is found in approximately 5-7% of the population and is an independent risk factor for stroke and other cardiovascular events. Homocysteine is both pro-thrombotic and neurotoxic; it increases the chance of a primary stroke and can also leads to higher rates of negative sequelae.

Normal values for homocysteine range from 5-10 umol/L, but even mild elevations at 10-15 can increase stroke risk, as in the following two cases.

Patient A

A 38 year old African American female with no past medical history presented to the ED with acute R sided weakness. CT revealed a large clot in her left MCA; she was treated immediately with TPA. Her symptoms improved, but she was left with mild R sided deficits.

- Normotensive in ED; no hx of elevated BP
- Lipid panel normal
- Non-smoker, no hx of alcohol use, no hx of drug use, no family hx of vascular events
- Coagulopathy workup normal except for **elevated homocysteine of 13.7**

She was started on aspirin, statin, and Eliquis. She was diligent with her medication regime and follow up, but three months later developed acute worsening of her R sided weakness along with dysarthria.

CT revealed a hemorrhagic transformation in the same location as before. She did not require surgical intervention, but continues to have severe R sided deficits. For now, her anticoagulation medications are being held.

Patient B

A 49 year old male presented to the ED with transient loss of vision in the lateral half of his left eye, which resolved by time of examination. Like Patient A, he was also normotensive with no hx of smoking or family hx of cardiovascular events

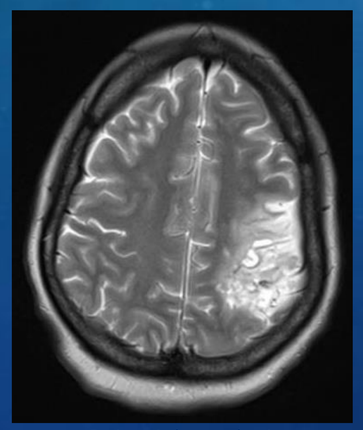
PMhx:

- 7 years prior: provoked DVT after long flight; put on anticoagulation for 3 months
- 2 years ago: unprovoked DVT and PE. Coagulopathy workup normal except for **elevated homocysteine of 16.3**. Placed on Xarelto.
- 1 year prior: started taking b12 and folate to help lower homocysteine levels
- 2 months prior: at direction of naturopath, stopped taking Xarelto, as his homocysteine levels were normal.

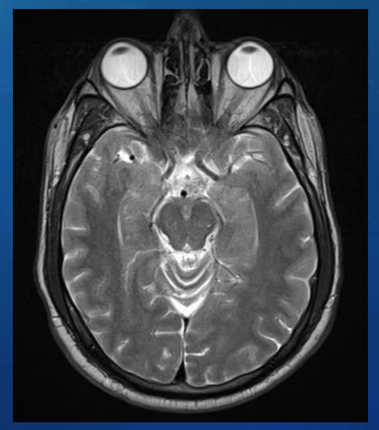
CT head and venous doppler in ED negative for acute pathology, but MRI done the next day revealed several small punctate foci of acute ischemia in the R occipital lobe. Folate and B12 were above normal limits, and repeat homocysteine was 7.7.

Hematology and neurology recommended preventative treatment with aspirin, statin, and lifetime anticoagulation with Xeralto. Patient kept on this regimen for 3 months, but then discontinued everything except b12/folate.

6 months later, he had an episode of aphasia and L sided facial drooping. CT confirmed a second stroke in the R frontal lobe. He was successfully treated with TPA, and is now on life-long anticoagulation with Eliquis.



Patient A: hemorrhagic transformation of L MCA



Patient B: punctate lesions in R occipital lobe

Discussion

Neither of these patients were typical stroke patients – in both cases, they were young, non-smokers, normotensive, and without family hx of vascular events. Patient A highlights the importance of looking for other, rarer causes of stroke such as coagulopathies. Patient B highlights the importance of doing a full stroke workup even when symptoms have resolved – initially the patient had been very reluctant to be admitted.

Patient B did not want to be on long-term anticoagulation and was hopeful that a supplements would normalize his homocysteine and reduce his risk of blood clots and stroke. While folate and B12 reduce homocysteine levels, they unfortunately do not seem to reduce the risk of cardiovascular events. More recent trials suggest there may be some small reduction of primary strokes, but that supplementation with B12/folate does nothing to prevent further strokes or reduce the severity of them, and that these patients should still remain on anticoagulation.

While the mainstay of stroke prevention for patients with pro-thrombotic causes is anticoagulation therapy, these types of medications are not without their risks, as with the case in Patient A. 10-40% of patients that have a primary ischemic stroke will later have either hemorrhagic transformation or a separate hemorrhagic stroke, and the risk increases with antithrombic use.

Approximately one in every 20 patients in the US has elevated homocysteine levels, but not all of these patients develop stroke or other cardiovascular events. Because of this, routine screening for elevated homocysteine is not recommended at this time. Further research needs to be done to determine which patients with elevated homocysteine are actually at increased risk, and what prevention options are best for them. However, patients with known Homocysteinemia may also require further screening for DVTS, vascular disease, osteoporotic fractures, and dementia, and will require close monitoring over their lifetimes.

References:

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