To Anticoagulate or Not: Weighing Microbleeds Against Embolic Risk

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OBJECTIVES

1. Recognize that cerebral amyloid angiopathy is a common cause of intracerebral hemorrhage in the elderly
2. Identify cerebral amyloid angiopathy on imaging
3. Recognize risks and benefits in anticoagulation in patients with amyloid angiopathy

ABSTRACT

Background: Cerebral amyloid angiopathy (CAA) is a common but underrecognized cause of lobar hemorrhage in the elderly. CAA is the deposition of amyloid in cerebral vessels, causing microbleeds and increasing risk of spontaneous lobar hemorrhage. CAA is prevalent, found in 20% of 60 to 70-year-olds and 42% of those 70 to 80-year-olds. Anticoagulating patients with CAA increases the risk of intracerebral hemorrhage, posing a challenge in deciding whether to anticoagulate for thrombolysis or prevention.

Case: We present a 65-year-old man with a history of previous hemorrhagic stroke, hypertension, type 2 diabetes, ESRD on dialysis, peripheral vascular disease, and neoplasms/hypertension present for three months.

Patient was fast admitted for diplopia to the Neurology service. Brain MRI showed pure cerebral hemorrhage consistent with CAA, and he was instructed not to take anticoagulation in the future.

One month later, he was admitted to the Internal Medicine service with atrial flutter and intermittent heart failure. He started on warfarin with plan for outpatient cardioversion.

Two months later, he was re-admitted to Medicine with sudden paresthesia after Thanksgiving dinner. Exam was notable for irregular rhythm, elevated JVP, but no neurological deficits. ECG showed atrial with rates of 100% and sub- therapeutic INR. Prior T2-weighted brain MRI was reviewed, which showed hypointense lesions in the basal ganglia and thalamus, consistent with microbleeds from significant amyloid angiopathy.

Assessment: Given the CAA and atrial fibrillation, the risks and benefits of anticoagulation were reviewed with Stroke and Electrophysiology Services. Review of literature showed that in patients with prior intracerebral hemorrhage, warfarin increased recurrence risk by five to tenfold. Use of aspirin, independent of dose, increased the risk of intracranial bleeding by four-fold in patients with prior amyloid angiopathy-associated bleeds. This patient was estimated to have an annual ischemic stroke risk of 4.5% based on CHADS-VASC 2010 of 4 for diabetes, hypertension, heart failure, and peripheral vascular disease.

Plan: Given the CAA and many microbleeds, the risk of re-bled on warfarin was felt to be greater than the benefit of ischemic stroke prevention and anticoagulation prior to cardioversion. Warfarin was discontinued. Aspirin 30mg was added for 7 days, followed by ODT and a repeat MRI at three months to assess imaging and hemorrhage. The patient was discharged with a follow-up MRI, which showed no intracranial hemorrhage but deferred given ESRD. The increased risk of hemorrhage on warfarin was discussed to the patient, and an incident report was filed.

Significance: This case highlights that cerebral amyloid angiopathy is common, increases the risk of intracerebral hemorrhage, and should be weighed carefully in a risk-benefit analysis of anticoagulation. Current anticoagulation models do not include CAA or microbleeds in bleed prediction, raising role of further studies to re-evaluate bleed prediction scores.

This patient’s T2 Brain MRI shows multiple microbleeds from cerebral amyloid angiopathy, which are the punctate hypointensities in periphery (yellow). These are complicated by prior parietal hemorrhages (orange). Hypertension also causes microbleeds, but typically in basal ganglia.

CEREBRAL AMYLOID ANGIOPATHY CAUSES MICROBLEEDS

RISK OF BLEED vs. RISK OF EMBOLIC EVENT

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Prevalence of CAA by Age</th>
<th>Prevalence of CAA by Age</th>
</tr>
</thead>
<tbody>
<tr>
<td>61-70</td>
<td>20%</td>
<td>20%</td>
</tr>
<tr>
<td>71-80</td>
<td>40%</td>
<td>40%</td>
</tr>
<tr>
<td>81-90</td>
<td>60%</td>
<td>60%</td>
</tr>
<tr>
<td>91-100</td>
<td>80%</td>
<td>80%</td>
</tr>
</tbody>
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Data adapted from Atome, 2004

<table>
<thead>
<tr>
<th>Table 2: Multivariate analysis of predictors of recurrent lobar ICH in patients with CAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable</td>
</tr>
<tr>
<td>Predicted lobar hemorrhage (other than intracerebral)</td>
</tr>
<tr>
<td>Microbleeds</td>
</tr>
<tr>
<td>2-4</td>
</tr>
<tr>
<td>&gt;4</td>
</tr>
<tr>
<td>CT/MRI present (prior event)</td>
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<tr>
<td>Anticoagulant exposure after index event</td>
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</tbody>
</table>

Abnormalities: CAA = cerebral amyloid angiopathy; CI = confidence interval; CT/MRI = Cercbral Magnetic Resonance Imaging; ICH = intracerebral hemorrhage.

REFERENCES


Birn et al. Aspirin and recurrent intracerebral hemorrhage in cerebral amyloid angiopathy Neurology 2010; 75:800-805


DISCUSSION

This is a case of cerebral amyloid angiopathy

- Characteristic: Presence in elderly
- Deposition of A-beta amyloid protein in intracranial vessels

- CAA: Brain MRI T2 hypointensities, Peripheral vascular disease

- Complications: Intracranial hemorrhage, Dementia

- Significant: Increased bleed in anticoagulation

- Intervene should balance increased bleed risk with ischemic stroke risk when deciding anticoagulation

Additional Considerations:

1. Should cerebral amyloid angiopathy/microbleeds be incorporated into bleed prediction scores?

2. Should we change the brain imaging to assess microbleeds before starting anticoagulation for risk assessment?