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CASE REPORT
Other

To treat or not to treat: left ventricular thrombus in a patient with cerebral amyloid angiopathy: a case report

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Background Cerebral amyloid angiopathy (CAA) is an important cause of cognitive impairment and spontaneous lobar intracerebral haemorrhage in older individuals. When necessary, anticoagulant treatment in these patients comes with two dilemmas; significant intracerebral bleeding risk with treatment vs. high risk of embolic stroke with no treatment.

Case summary A 66-year-old female patient presented to the emergency clinic with a ST-elevation myocardial infarction. Her past medical history revealed cognitive problems associated with lobar cerebral microbleeds on magnetic resonance imaging suspect for probable CAA. A primary percutaneous coronary intervention of the left anterior descending artery with implantation of drug eluting stent was performed. Dual antiplatelet treatment was started initially. During hospitalization, an impaired left ventricular (LV) function was observed with an apical aneurysm. Six months after the initial event, LV function remained stable however a LV thrombus was observed. Apixaban 5 mg twice daily was started based on multidisciplinary consensus and on its efficacy and safety profile in patients with atrial fibrillation. Despite treatment, patient suffered a new ischaemic stroke probably from the LV thrombus, for which vitamin K antagonist treatment was initiated and Apixaban discontinued.

Discussion Evidence for LV thrombus treatment with direct oral anticoagulants in CAA patients is scarce, however feasible based on its efficacy and safety profile. For CAA patients, the cardinal role of both clinical and radiological characteristics in determining the risk-benefit ratio for anticoagulant initiation in this specific subset of patients, is crucial. The clinical course described highlights the therapeutical dilemma of coexisting CAA and the clinical challenge it creates.

Keywords Apixaban • Case report • Cerebral amyloid angiopathy • LV thrombus

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Learning points

- Cerebral amyloid angiopathy (CAA) is an important cause of cognitive impairment and spontaneous lobar intracerebral haemorrhage in older individuals.
- Treatment of a left ventricular thrombus in CAA patients comes with two dilemmas; significant intracerebral bleeding risk with treatment vs. high risk of embolic stroke with no treatment.
- Evidence regarding safe therapeutic options, such as the administration of direct oral anticoagulants, is scarce in this patient population.
- A multidisciplinary approach (cardiologist and neurologist) as much as shared decision-making (with patient and family) are essential in determining a deliberate treatment strategy.

Introduction

Thrombus formation of the left ventricle is a common complication in patients with anterior myocardial infarction, with or without apical aneurysms.[1] Mortality is increased in these patients because of high risk of cardioembolic stroke.[2]

Although the prevalence has decreased in the era of primary percutaneous interventions, large anterior wall infarction is still an important determinant for developing a left ventricular (LV) thrombus.[1]

Guidelines indicate that treatment of LV thrombi with anticoagulants should be initiated during the initial admission and continued up to at least 6 months, guided by cardiac imaging.[3] Evidence-based research on the efficacy of this treatment, however, is scarce. Treatment can be hazardous in patients with increased risk of haemorrhagic complications.

We describe a case of a patient presenting with a large LV thrombus after anterior myocardial infarction, in whom the decision to treat with anticoagulant medication was difficult due to an earlier diagnosis of probable cerebral amyloid angiopathy (CAA). The therapeutic challenge comes with the fact that both treatment and non-treatment of the LV thrombus comes with increased morbidity and mortality risk; CAA is common in the elderly with a significant increased risk of spontaneous intracerebral haemorrhage (ICH).[4] Current literature was reviewed to provide evidence for decision-making in these challenging cases.

Case presentation

A 66-year-old woman with no prior cardiac history was admitted for primary percutaneous intervention with intermittent atypical chest pain radiating to the jaw for 1 day, and ST elevation on the electrocardiogram (ECG). Her past medical history included surgical removal of superficial melanoma of the thorax and left shoulder in 2008 and 2016, without evidence of metastasis. She suffered from impaired memory since 5 years, and probable CAA was diagnosed 2 months prior to the myocardial infarction. There were no other cardiac risk factors present at admission. Physical examination was without abnormalities.

Sinus rhythm was observed on the admission ECG, with normal heart axis, narrow QRS (120 ms) with ST elevation in leads V2 through V6. No conduction disturbances were present (*Figure 1*).

A significant rise-and-fall of serum troponin was measured with a peak of 131 ng/L (cTnI (Cardiac-specific Troponin I) $n < 14$ ng/L). Other laboratory results were unremarkable with normal liver and renal function.

Radial approach coronary angiography was performed and the culprit vessel was shown to be the left anterior descending artery of the left coronary artery with a 100% obstruction in the distal segment. Two 2.5–16 mm drug eluting stents were placed with restoration of thrombolysis in myocardial infarction 2 flow (*Figure 2*). Other coronary vessels were non-obstructed. Echocardiography with microbubbles (Optison™) injection revealed an LV function of 35% with

Timeline

Months prior to day of admission	
Thirty-six months	Cognitive complaints
Two months	Probable cerebral amyloid angiopatdy was diagnosed; no intracerebral haemorrhage present, no signs of siderosis on brain magnetic resonance imaging.
Day of admission	ST-segment elevation anterior myocardial infarction was diagnosed (estimated delay 4–10 h)
	Radial approach percutaneous coronary intervention was performed for the left anterior descending artery of the left coronary artery. Two 2.5–16 mm drug eluting stents were positioned in the 100% stenosis of the distal segment.
	Left ventricular function (LVF) was estimated 35% with akinesia of apical segments and an apical aneurysm without thrombus formation.
Three months after admission	Out-patient follow-up; LVF was estimated 35%. Apical segment akinesia, apical aneurysm present, no clear signs of a left ventricular (LV) thrombus present.
Six months after admission	Out-patient follow-up: LVF was estimated 35% with apical aneurysm, an LV thrombus was detected during echocardiography. Apixaban was started, aspirin and clopidogrel discontinued.
Twelve months after admission	Out-patient follow-up: LVF was estimated 35% with apical aneurysm, signs of LV thrombi present.
Thirteen months after admission	An ischaemic stroke in the anterior cerebral artery territory was diagnosed, with a thrombus in the A2-segment on computed tomography angiography; apixaban was discontinued, phenprocoumon started.

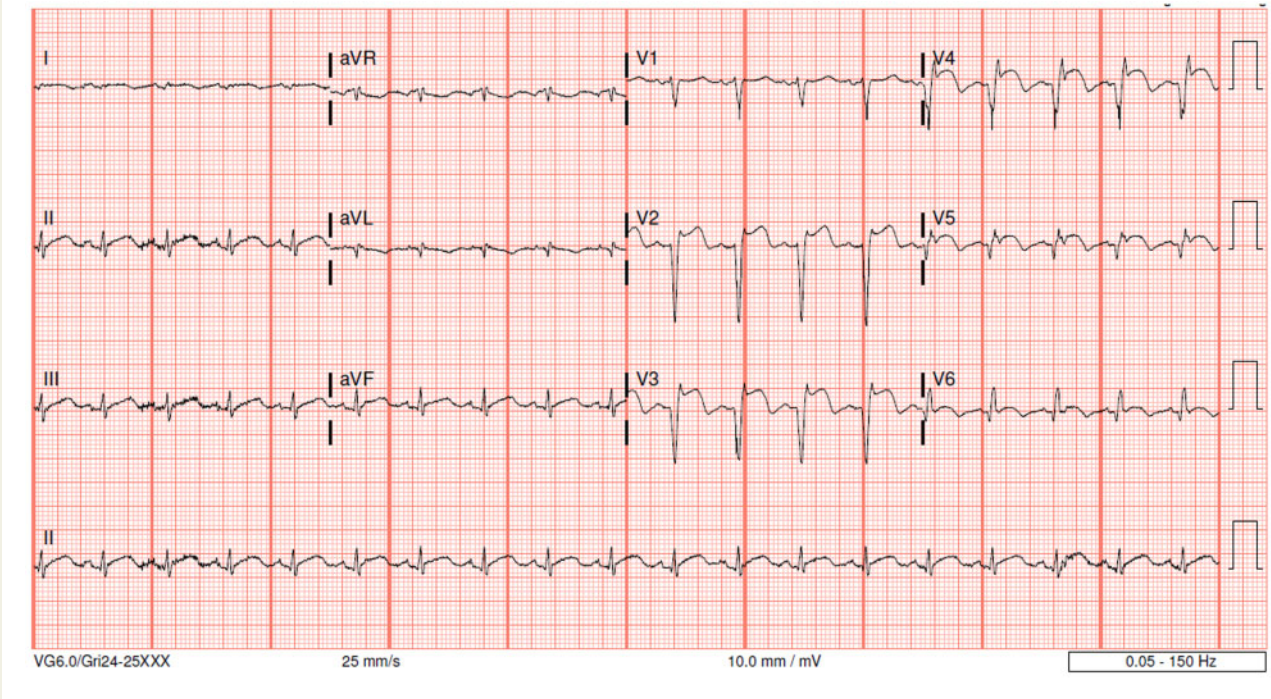

Figure 1 Baseline electrocardiogram.

hypokinesia of the anterior wall with akinesia of apical segments and aneurysm formation, without LV thrombi present (Supplementary material online, *Video Appendix*).

Patient received medical treatment with aspirin, clopidogrel, a statin, a betablocker, and an angiotensin-converting enzyme inhibitor initially. During outpatient follow-up, LV function remained stable at 35%. An LV mass was detected after 6 months (*Figure 3*).

The neurologist was consulted regarding this complication and its therapeutic consequences. A conjoined decision was made by the cardiologist and neurologist to discontinue aspirin and clopidogrel and start apixaban twice daily 5 mg, based on its efficacy- and safety profile in CAA patients with atrial fibrillation (AF)[5] as well as multidisciplinary consensus. Despite stable cardiac function, she suffered from an ischaemic stroke 1 year later, the LV thrombus considered being the cause.

With no new ICH or hemosiderosis present on repeat brain magnetic resonance imaging (MRI), apixaban was discontinued and phenprocoumon [vitamin K antagonist (VKA)] was started. During follow-up, no complications or adverse events were reported.

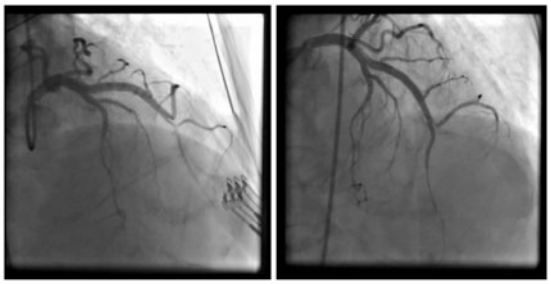

Figure 2 Distal left anterior descending artery culprit stenosis—pre-percutaneous coronary intervention (left) and post-percutaneous coronary intervention (right).

Discussion

CAA is characterized by the deposition of amyloid-β (Aβ) peptide, combined with degenerative changes in the capillaries, arterioles, and small- and medium-sized arteries of the cerebral cortex, leptomeninges, and cerebellum. Possibly due to impaired cerebral clearance of amyloid-β with increasing age.[6] CAA has a wide clinical presentation with lobar ICH and cognitive decline as its main hallmarks.[7]

The diagnosis of *probable* CAA, the highest level of diagnostic certainty currently achievable without histologic tests, is made through the modified Boston criteria. These comprise of combined clinical, imaging and pathological parameters.[8] Iron sensitive MRI sequences demonstrating microbleeds restricted to cortical and subcortical brain regions (*Figure 4*), together with an age >55 years and the absence of any other cause of haemorrhage, led to the diagnosis probable CAA in our patient.

Before initiating anticoagulant therapy, the ICH risk in individual CAA patients should be carefully evaluated, as CAA is held responsible for somewhere between 37% and 74% of all non-traumatic ICHs.[4] The frequently used HAS-BLED score is not suitable for

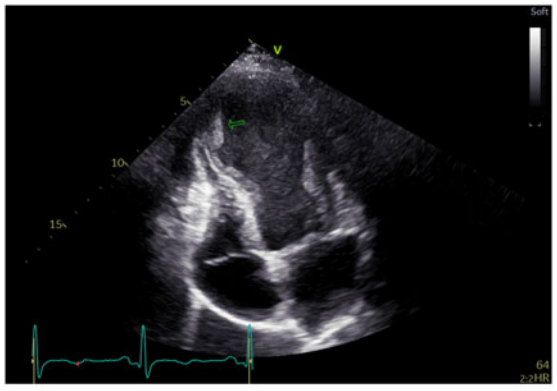

Figure 3 Left ventricular thrombus mass (arrow).

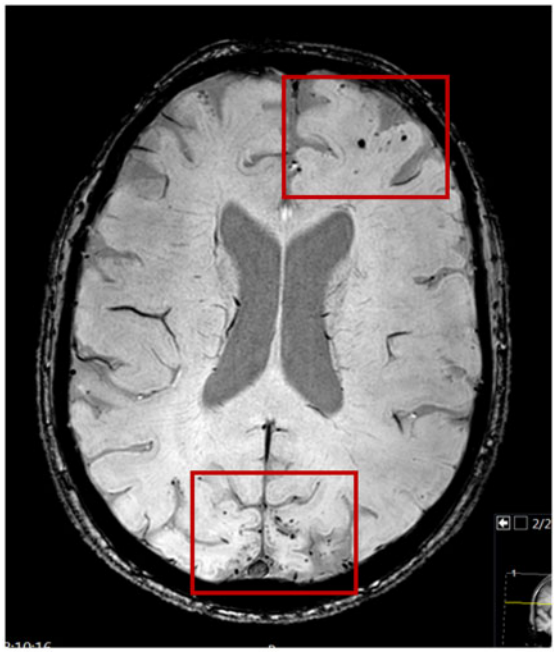

Figure 4 Magnetic resonance imaging with lobar microbleeds—3T magnetic resonance imaging, susceptibility weighted imaging.

predicting intracranial haemorrhage in this specific patient group as patients with prior ICH were originally excluded from development.[9] Evaluation of clinical symptoms, and the presence of MRI markers seem to be more reliable factors when balancing risk and benefits of treatment with oral anticoagulants in individual patients. Recurrent ICH is common in CAA patients, with an average recurrence rate of 9% per year.[10] A patient with probable CAA *with* a history of lobar ICH should be considered to have a higher risk of treatment related ICH, compared to a patient with probable CAA *without prior* lobar ICH.

An important MR marker in diagnosing CAA is cortical superficial siderosis (cSS). A recent meta-analysis reported both the presence (hazard ratio 2.26; 95% confidence interval 1.31–3.87) and the extent of cSS as the most important MRI prognostic risk factors for lobar ICH recurrence.[11] In addition, in CAA patients without a history of ICH, detection of cSS is associated with an 19% increased risk of future first-ever symptomatic lobar ICH in 5 years follow-up.[10] Both microbleeds and cSS are only visible on high-resolution MRI with iron-sensitive sequences as part of a standard imaging protocol.

It is essential, in our opinion, to obtain adequate information on the presence of these specific markers before a decision is made to initiate anticoagulant therapy.[6] Prediction-models combining both clinical and radiological features, were significantly more accurate than the HAS-BLED in predicting future symptomatic ICH.[12] Contemporary bleeding risk criteria such as the ARC-HBR are more complete than the HAS-BLED, however, the *combination* of clinical symptoms and MRI markers is essential in assessing the risk on anticoagulant-related future ICH in CAA patients. Antiplatelet therapy like aspirin increases the risk of intracranial haemorrhage to a lesser extent than anticoagulants in CAA patients.[12] In our patient it is reasonable to provide dual antiplatelet therapy as indicated.[13]

Although recurrent ICH poses a potential life-threatening risk in CAA patients, so does the risk of systemic emboli from an LV thrombus. LV thrombus systemic embolization risk ranges between 10% and 40%.[14] Guidelines indicate that patients at risk of LV thrombus formation after large anterior infarction with diminished LV function <40%, and patients with a proven LV thrombus, should be treated with VKA for at least 3–6 months or longer guided by ultrasonography.[1] Evidence on the efficacy and safety of direct oral anticoagulants (DOAC's) in treating LV thrombi is however lacking and based on smaller non-randomized observational studies or case reports.[1] Regarding efficacy, the randomized AVEROES study showed that Apixaban, compared to aspirin, was associated with a reduction of (embolic) infarctions in AF patients not suitable for VKA treatment, without an increase in the number of microbleeds.[5] CAA patients with AF showed comparable low risks when using DOACs compared to VKA treatment.[15]

Starting apixaban in our patient seemed justifiable from limited evidence. Unfortunately, recurrent ischaemic stroke occurred; possible sources for this could include the LV thrombus itself, carotid artery disease or DOAC non-compliance.

Additionally, cardiac MRI might be useful to determine DOAC effectiveness and resolution of LV thrombus. AF was not deemed a risk in our patient, as two 24 h rhythm observations at home showed only sporadic ventricular extrasystoles which the patient felt, but no other rhythm disorders were detected or experienced.

The clinical course described highlights the dilemma of an LV thrombus and coexisting CAA and the clinical challenge it creates. In recent literature, the formation of a multidisciplinary 'heart-brain team' was recommended.[15] We support this suggestion and additionally stress the cardinal role of both clinical and radiological findings in determining the risk-benefit ratio for anticoagulant treatment in this specific subset of patients.

Lead author biography

Alexander D. Hilt is a medical doctor and currently working as a PhD researcher at the Department of Cardiology of the Leiden University Medical Center. His thesis focuses on applying common and new Value-Based Healthcare methods on a macro and micro level in cardiovascular healthcare. Prior to the start of his research, he completed 3 years of clinical work in the neurological and cardiology field. In January 2021, he will start his residency training to become a cardiologist.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

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Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

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