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CASE REPORT

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Stroke prevention in an octogenarian with atrial fibrillation, cerebral amyloid angiopathy and intracerebral hemorrhage

Claudia Stöllberger[1] | **Josef Finsterer**[1] | **Birke Schneider**[2]

[1]Klinik Landstraße, Wien, Austria

[2]Sana Kliniken Lübeck, Lübeck, Germany

Correspondence
Claudia Stöllberger, Anton Sattlergasse 4/22, Wien A-1220, Austria.
Email: claudia.stoellberger@chello.at

Key Clinical Message

Left-atrial-appendage-closure (LAAC) is suggested as alternative to antiplatelet/anticoagulant therapy (AP/AC) for stroke-prevention in patients with cerebral-amyloid-angiopathy (CAA), intracerebral hemorrhage (ICH) and atrial fibrillation (AF). Disadvantages of LAAC are the need for postinterventional AP and impairment of left atrial function, thus promoting heart-failure. Therefore, in an 83-year-old edoxaban-treated AF-patient with ICH and CAA, only antihypertensive therapy with neither AP/AC nor LAAC was recommended. Twenty-seven months without stroke/ICH support this strategy, which needs confirmation by a randomized-trial.

KEYWORDS

anticoagulant therapy, atrial fibrillation, cerebral amyloid angiopathy, cerebral bleeding, left atrial appendage closure

1 | INTRODUCTION

Cerebral amyloid angiopathy (CAA) is characterized by amyloid fibrils in the wall of small cerebral blood vessels. Vessels affected by CAA are predisposed to rupture, which is a major cause of spontaneous and frequently recurrent lobar cerebral hemorrhage.[1] Prevention of stroke or arterial embolism in patients with cerebral amyloid CAA, intracerebral hemorrhage (ICH) and atrial fibrillation (AF) is a therapeutic dilemma.[2] Both antiplatelet drugs (AP) and anticoagulants (AC) increase the risk of recurrent ICH, why left atrial appendage closure (LAAC) is suggested (Table 1).[3–5] By presenting the following case, we critically discuss the different therapeutic options.

2 | CASE DESCRIPTION

An 83-year old male patient with arterial hypertension, dyslipidemia, monoclonal gammopathy, and chronic obstructive pulmonary disease was admitted with an ICH. Four months previously, edoxaban 60 mg/day had been prescribed because of AF. The patient showed a homonymous hemianopsia to the right side. The National Institutes of Health Stroke Scale score was 2 and the Glasgow coma scale 15. On admission, blood-pressure was 170/80 mm Hg, and the NT-pro-BNP level 1819 ng/L (reference: <486). The electrocardiogram showed AF with a ventricular rate of 75/min, and transthoracic echocardiography disclosed an enlarged left atrium, left-ventricular wall thickening, and diastolic dysfunction. Computed

TABLE 1 Studies about left atrial appendage closure in patients with cerebral amyloid angiopathy.

Author	Renou et al.[4]	Schrag et al.[3]	Blanc et al.[5]
Data collection	Prospective	Retrospective	Retrospective
Period of patient recruitment	2011–2015	2016–2020	NR
Patients, *n*	25	26	39
Mean age, years	73.7	73	79.3
Type of CAA according to modified Boston criteria[6]	Probable 68%, Possible 32%	Probable 100%	Probable 82%, Possible 18%
History of ICH, %	100	50	NR
Method of LAAC	Interventional: Amplatzer cardiac plug or Watchman	Interventional: Watchman, Amulet or Lariat; Surgical: Atriclip or surgical ligation	NR
Follow-up			
Follow-up duration, months	Mean 12.6	Mean 25	Median 12
Device-related problems	Device embolization $n=1$, Sudden cardiac death $n=1$, Device-related thrombus $n=1$, Peri-device leak $n=9$	Device-related thrombus $n=1$	NR
AP after LAAC: duration, %	≥6 months in 94%	Long-term in 73%, none in 27%	≥1 month, number NR
Incidence of ICH/year	4.35%	NR	4.4%
Incidence of ischemic stroke/year	4.35%	1.8%	7.7%
Mortality/year	6.5%	NR	NR

Abbreviations: AP, antiplatelet therapy; CAA, cerebral amyloid angiopathy; ICH, intracerebral hemorrhage; LAAC, left atrial appendage closure; NR, not reported.

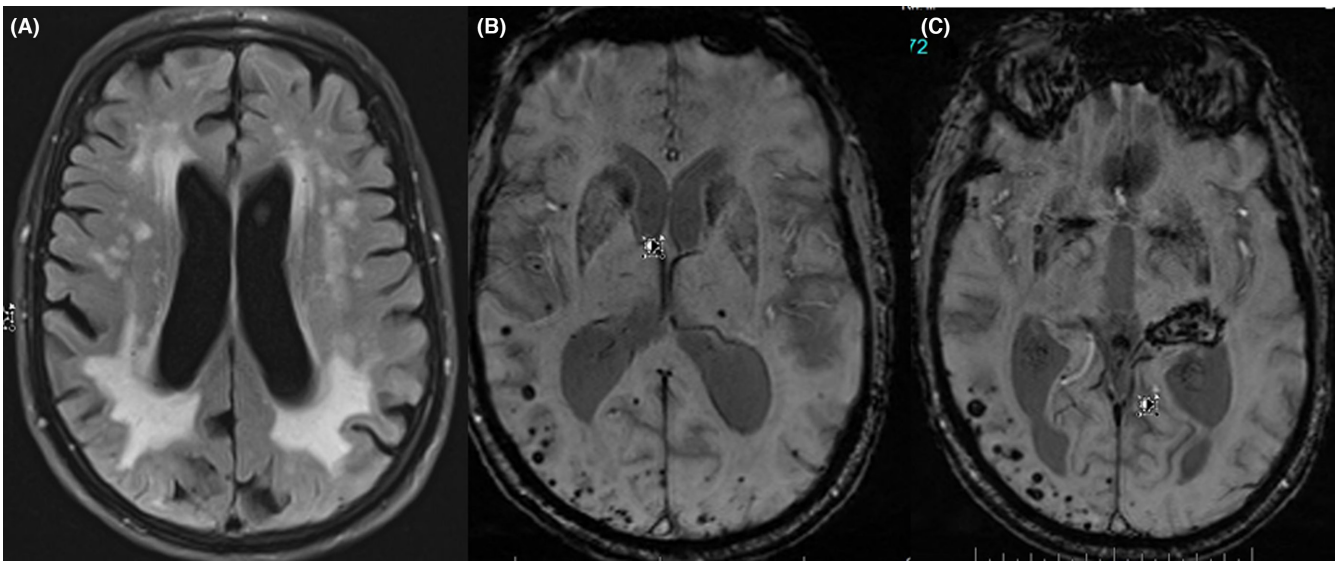

FIGURE 1 Cerebral magnetic resonance imaging showing global atrophy, leukoaraiosis, periventricular T2 hyperintense spots (A), subcortical microbleeds (B), and bleeding in the left thalamus (C). These findings were consistent with the diagnosis "probable cerebral amyloid angiopathy" according to the modified Boston criteria.[6]

tomography and magnetic resonance imaging revealed a left thalamic bleeding with ventricular rupture and cerebral microangiopathy, indicating "probable cerebral amyloid angiopathy" (Figure 1).[6] Edoxaban was stopped. Since he recovered rapidly, no reversal agents were given. The neurologic deficit and ICH resolved within 16 days.

3 | DISCUSSION

For this patient, the following therapeutic options were considered to prevent stroke or embolism:

1. Dose reduction and change of the anticoagulant therapy (AC). Recurrent ICH in CAA, however, has been reported also under the non-vitamin K antagonist oral anticoagulants (NOAC) rivaroxaban and apixaban.[7] Furthermore, no data are available concerning a change from NOAC to a vitamin K antagonist with INR self-management.
2. Change from AC to antiplatelet drugs (AP) would not eliminate the risk of recurrent ICH. An increased risk of lobar microbleeds has been observed in CAA-patients with a history of ICH treated with AP.[8]
3. A further option is LAAC.[3–5] Although apparently an elegant solution, LAAC has several disadvantages which are frequently disregarded. The left atrial appendage (LAA) plays an important hemodynamic role. Since the LAA myocardium is 2.6 times more compliant than the left atrial body, the LAA contributes to left atrial reservoir function and is essential for the adaption to pressure and volume overload. In addition, the LAA is the main site for the release of atrial natriuretic peptides. After LAAC a decrease of natriuretic peptide levels has been observed.[9] Consequently, LAAC may promote the development of heart failure (HF).[10] HF, however, increases the risk for stroke in AF and has, therefore, been included in the $CHADS_2$- and CHA_2DS_2VASc-score (C for congestive HF). Overall, in our patient with an already elevated NT-proBNP level, LAAC may be harmful since the procedure can result in congestive HF, thereby increasing his CHA_2DS_2-VASc-score and his embolic risk. In addition, the risk for recurrent ICH would also be increased since AP are usually recommended to prevent device-associated thrombus formation. As listed in the table, the evidence for LAAC in patients with CAA is limited to the small numbers of patients and incomplete data (Table 1).[3–5]
4. Tight blood-pressure control with neither AC nor AP is a further option, supported by limited data from the Rochester-Epidemiology Project-Database: Of 35 patients (mean-age 81 years) with AF, CAA and ICH, 25 received neither AP nor AC. During 2.7 years, only one of these 25 patients suffered from an ischemic stroke and 3 from recurrent ICH.[11] In addition, increased age, like in our patient, has been identified as a strong predictor for recurrent ICH in patients with CAA.[12]

In view of these data and the lack of randomized trials, we recommended our patient with CAA, ICH and AF neither LAAC nor AP nor AC, but a healthy lifestyle with a blood-pressure target of <130/80 mmHg. He was discharged with amlodipine, valsartan, rosuvastatin, montelukast, formoterol, and tiotropium.

Twenty-seven months later, his blood-pressure remains well controlled. He has an active life with daily walks. Without AP/AC and LAAC no further hemorrhagic or ischemic events occurred. This observation supports our therapeutic decision which should be confirmed by a randomized trial.

AUTHOR CONTRIBUTIONS

Claudia Stoellberger: Conceptualization; data curation; investigation; methodology; writing – original draft; writing – review and editing. **Josef Finsterer:** Data curation; investigation; visualization. **Brike Schneider:** Formal analysis; methodology; writing – original draft; writing – review and editing.

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The authors report no involvement in the research by the sponsor that could have influenced the outcome of this work.

CONFLICT OF INTEREST STATEMENT

The authors certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

DATA AVAILABILITY STATEMENT

Data are available at Klinik Landstrasse, Wien, Austria.

CONSENT

Informed consent was granted by the patient in oral and written form.

ORCID

Claudia Stöllberger https://orcid.org/0000-0001-7335-3120

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