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# Acute enlargement, morphological changes, and rupture of intracranial infectious aneurysm in infective endocarditis. Serial imaging

Monique Boukobza, Olivier Naggara, Xavier Duval, Jean-Pierre Laissy

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## **Title: Acute enlargement, morphological changes, and rupture of intracranial infectious aneurysm in infective endocarditis. Serial Imaging**

**Key words:** Intracranial infectious aneurysm; Infective endocarditis; aneurysm rupture; aneurysm enlargement; aneurysm morphological change; contrast enhanced MRA.

### **Abstract**

A 72-year-old man received a transcatheter aortic valve implantation (TAVI) 2 years ago for leakage of the degenerative bioprosthesis with Corevalve n°31 implantation, presented infective endocarditis (IE) (streptococcus sanguinis) of the bioprosthetic aortic valve. One month after antibiotic treatment was initiated, he presented a left-sided hemiplegia, a right frontal hematoma. MRI/contrast-enhanced magnetic resonance angiography (CE MRA) revealed 2 infectious intracranial aneurysms (IIAs) of the right (10mm) and left middle cerebral artery (MCA) (M2 segment, 5mm). The right MCA IIA was treated within 1 day by glue-embolization. Seven days later, the patient acutely developed motor aphasia. CE MRA showed significant enlargement (15mm) and morphologic change of the ruptured left MCA IIA. This IIA was treated with Onyx-embolization.

This case adds additional evidence that IIAs, during IE, can show rapid growth and morphological change over a 7day course and emphasizes the imperative need of close imaging follow-up when IIAs are managed by antibiotic therapy.

### **Introduction**

The natural history, including growth and rupture, of unruptured intracranial infectious aneurysms (IIAs) remains unknown, even if it is considered that they have a high risk of rupture. They may develop rapidly compared to noninfectious aneurysm. Scarce radiological studies have reported their evolution over time.

We report a 72-year-old man, with infective endocarditis (IE) who presented with a ruptured IIA of the left middle cerebral artery (MCA) that increased in size from 5 mm to 15 mm in 7 days before rupture with resultant hematoma

### **Case**

A 72-year-old man was admitted 1 month ago for fevers, anemia. Two hemocultures were positive for *Streptococcus sanguinis*, originating from torpid dental infection. An antibiotic treatment was initiated with [gentamycin and amoxicillin]. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE)-did not show any valvular dysfunction

His history consisted in an aortic valve replacement by stentless bioprosthesis O'Brien n°29 associated with single internal mammary- left anterior descending (LAD) artery coronary artery bypass graft (CABP) at 60 years of age for tight aortic stenosis; he then underwent 7 years later a right coronary revascularization with a bare and a coated stent angioplasty on the right coronary trifurcation 1 year later. He further received a transcatheter aortic valve implantation (TAVI) for leakage of the degenerative bioprosthesis with Corevalve n°31 implantation.

He presented abruptly a left-sided hemiplegia and dysarthria. Brain-CT and MRI in emergency showed a right frontal intraparenchymal hemorrhage (25x15 cm) and a subarachnoid hemorrhage (SAH) at the left fronto-temporal convexity. MRI showed 3 microinfarcts, a territorial ischemia and 3 cerebellar microbleeds. Contrast-enhanced magnetic resonance angiography (CE MRA) revealed 2 IIAs of the right (10mm) and left MCA (Fig 1 – a) also identified on cone-beam CT and catheter angiography (M2 segment, 5mm) during the endovascular procedure (Fig 1-b -c-d). The right MCA IIA was treated within 1 day by glue-embolization.

Seven days later, under antibiotic therapy (gentamycin and amoxicillin) he abruptly presented a motor aphasia. Brain-CT showed left temporal intraparenchymal hemorrhage (47x22cm) with mass effect. Fluid-attenuated inversion recovery (FLAIR) sequence showed a hyperintense arterial rosary-like appearance assumed to slow flow in the left sylvian cistern (Fig 1 -e). CE MRA demonstrated the previously documented left MCA IIA to have clearly enlarged and ruptured (Fig 1 – f-g-h-i). On digital subtraction angiography (DSA), the ruptured aneurysm measured 15mm in diameter and was treated with Onyx embolization (Fig 1-j-k-l). Follow-up MRI/CE MRA (10 days and 3 months respectively) (Fig- 1 –m) and DSA (1month) showed disappearance of both IIAs, without development of new aneurysms

## Discussion

The incidence of IIAs is likely underestimated as IIAs can go undiagnosed given their resolution after antibiotic therapy. Given the rarity of IIA, the paucity of population-based studies, considering that DSA is not routinely performed during IEs, and the risks inherent in DSA - especially in fragile IE patients who are sometimes on anticoagulants- no prospective

natural history study has examined the rupture rates of IIA. Only one recent study has tried to determine the clinical course of IIAs. The main factor involving favorable clinical outcome was linked to antibiotic therapy duration [1]. Indeed, only few cases of rapid onset and rupture and of rapid growth of IIA during IE have been reported. Formed by inflammation and destruction of arterial walls - the muscular layer being usually involved- IIAs are pseudoaneurysms and carry a high risk of rupture.

Seven cases of rapid appearance and rupture [2-7] have been reported since the seminal review of 5 cases by Saito et al [8], including his own one. These 10 cases of IIAs appeared in a time-interval of 1 to 5 days, except a delay of 20 days for 1 case and 30 days for 2 other cases. In 5 of these 12 cases, a new IIA appeared at the site of the previous focal occlusion site due to septic emboli [3].

Very rapid enlargement and subsequent rupture of an IIA on a previously demonstrated IIA have been documented, to the best of our knowledge, in only 3 cases. Tashima [9] reported 1 case of enlarged IIA of an MCA branch, observed on a second angiography 2 weeks after the first DSA examination. In Koffie et al' s case [10] an IIA of an MCA branch, revealed by SAH, enlarged from 1.5 to 5mm in a time interval of 21h with catastrophic intracranial hemorrhage secondary to rupture. In John et al' s case 2 [3], at 2-week repeat angiography the IIA previously documented was stable, and follow-up angiography 4 weeks later showed an enlargement of the IIA (Table 1).

In the absence of knowledge of unfavorable morphological change, the initial morphological pattern, i.e. the saccular IIAs, should be predictive of worse outcome - rupture and/or growth - as reported by Rice et al [1] who consider that these IIAs should be treated interventionaly in addition to antibiotic therapy.

Our case adds evidence that IIAs can show rapid increase in size and morphological change over a course of 7 days. Such a rapid transformation over time, with the risk of rupture, is unpredictable and specific to IIAs related to their pathology, unlike non-infectious cerebral aneurysms. One can ask whether at this time the left MCA aneurysm was not treated initially like the right one. Given the experience of this case, such a case would be now treated as soon as possible after the diagnosis. The usefulness of repeated CE- MRA or CTA within 7 days in all IE patients is questionable. Moreover, a consensus exists about the fact that non-invasive imaging cannot often detect IIAs of 3 mm or less. The use of plain MRA does not allow detection of these MA; on the contrary, CE-MRA has shown better sensitivity than non-contrast MRA in non-infectious IA [11]. DSA should be indicated in cases of non-conclusive MRA.



The growth of these aneurysms, evaluated by serial MRA/CE MRA in large series [12] led to similar results (10% over 47 months and 3.9% per year, respectively), those of >8mm in diameter being the most concerned. In addition, aneurysm growth was associated with a high risk of rupture. One exceptional case has been reported of early and gradual enlargement, at 20, 30 and 60 days after rupture and beyond the shrinkage of a distal MCA aneurysm, proved of congenital origin on pathologic study [13]. The current case, as those previously reported, highlights 2 important clinical issues: (i) IIAs showing rapid growth, which have a high risk of rupture within a short period, need close brain imaging and often emergent intervention. Imaging monitoring should be even more stringent in IE patients under antibiotic therapy, without forgetting the risks of repeat DSA and the utility of non-invasive imaging, i.e. ACT and CE MRA; (ii) if IIA shows rapid growth with serial imaging, it should be treated without further delay.

## Conclusion

Progression and subsequent rupture of an IIA previously demonstrated by neuroimaging has rarely been documented.

Our case adds additional evidence that IIAs are dynamic lesions that can show a rapid enlargement and transformation over a short time period. The risk of rupture clearly reinforces first the necessity of repeated imaging follow-up in IE patients under antibiotic therapy. DSA should be reserved to patients in whom non-invasive vessel imaging – CE MRA/CTA- is inconclusive, and those showing IIA enlargement where active management should not be delayed.

## Figures Legends

### Figure 1

**a** – Contrast-enhanced magnetic resonance angiography (CE MRA): Maximum intensity projection (MIP) shows 2 intracranial infectious aneurysms (IIAs) in a branch of the right (10mm, short arrow) and left middle cerebral artery (MCA) (M2 segment, 5mm, long arrow).

**b**- Digital subtraction angiography (DSA), lateral view, obtained the same day, shows the saccular IIA located on a M4 branch of the right MCA (arrow).

**c**- Intraoperative DSA image shows the catheter advancing to the orifice of the right MCA IIA before the injection of glue.

**d**- Cone-beam angio-CT (CB-ACT) obtained during the endovascular procedure, shows an IIA at the M2 segment of the left MCA (5mm, arrow);

**e-** Fluid-attenuated inversion recovery (FLAIR) MRI sequence, obtained after motor aphasia onset occurred at day 7 of embolization of the right MCA IIA, shows a hyperintense arterial rosary-like appearance assumed to slow flow in the left sylvian cistern, as shown in the serial images of DSA (see below, j-k.) surrounded by an area of parenchymal hyperintensity. Contrast-enhanced magnetic resonance angiography (CE MRA): maximum intensity projection (MIP) (**f, g**) and axial (**h**) and sagittal (**i**) multiplanar reformat (MPR) shows enlargement of the left MCA IIA from 5mm to 15 mm in diameter (arrow) along with morphological changes. The ruptured IIA appears multilobulated with irregular walls. Note the presence of a localized subarachnoid hemorrhage at the left temporal convexity

**j-k -l-** DSA shows a slow fill-in within the IIA and delayed clearance (**j-k**) and the disappearance of the IIA after glue embolization (**l**)

**m:** Ten-day follow-up CE MRA show the disappearance of the IIA.

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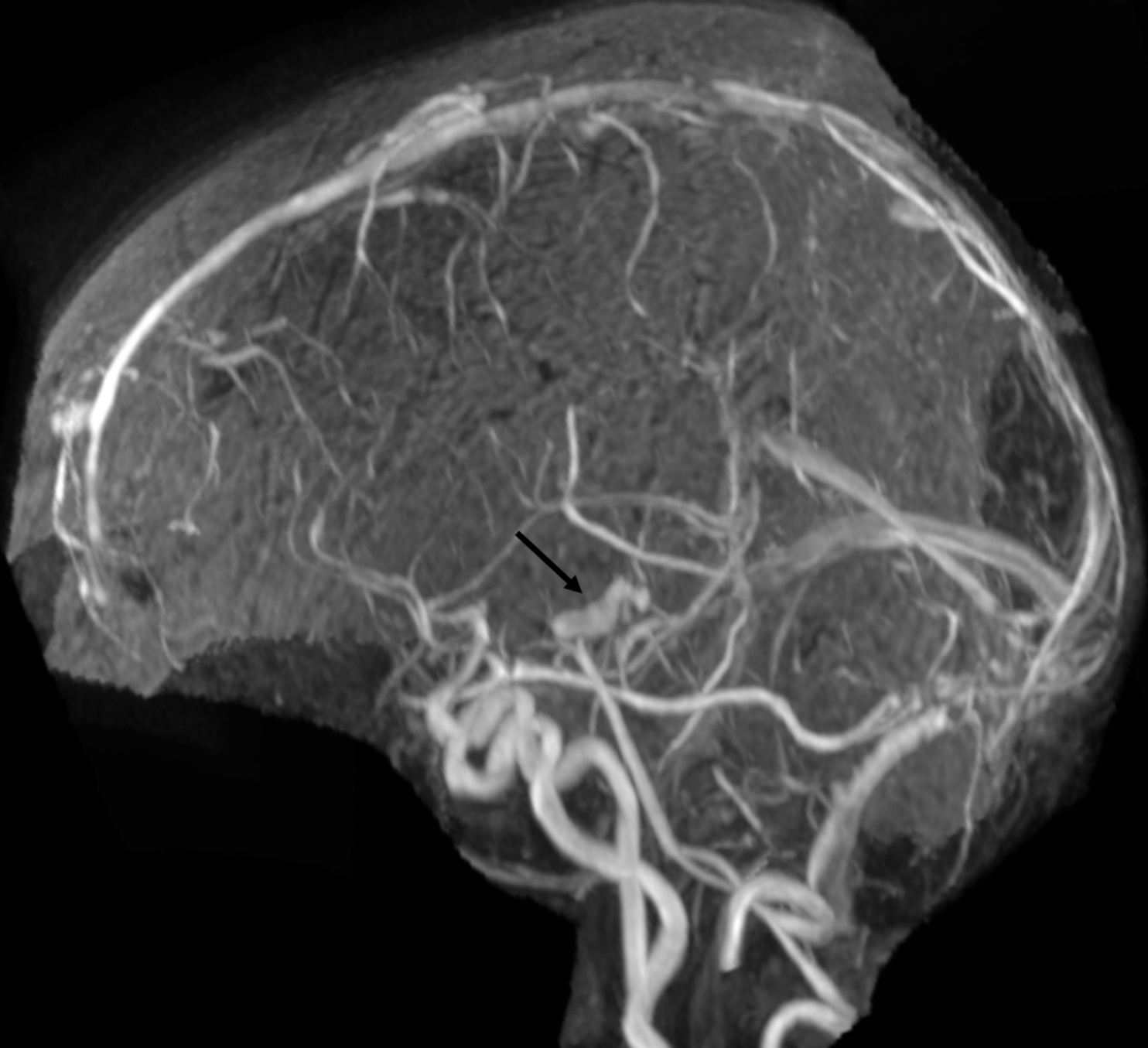
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(Filt. 3)

FINAL

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CAU: 0.2 deg  
L: 0.1 deg  
Tilt: 0 deg  
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LAT  
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FRAME = 6 / 21  
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XA 1000x1000



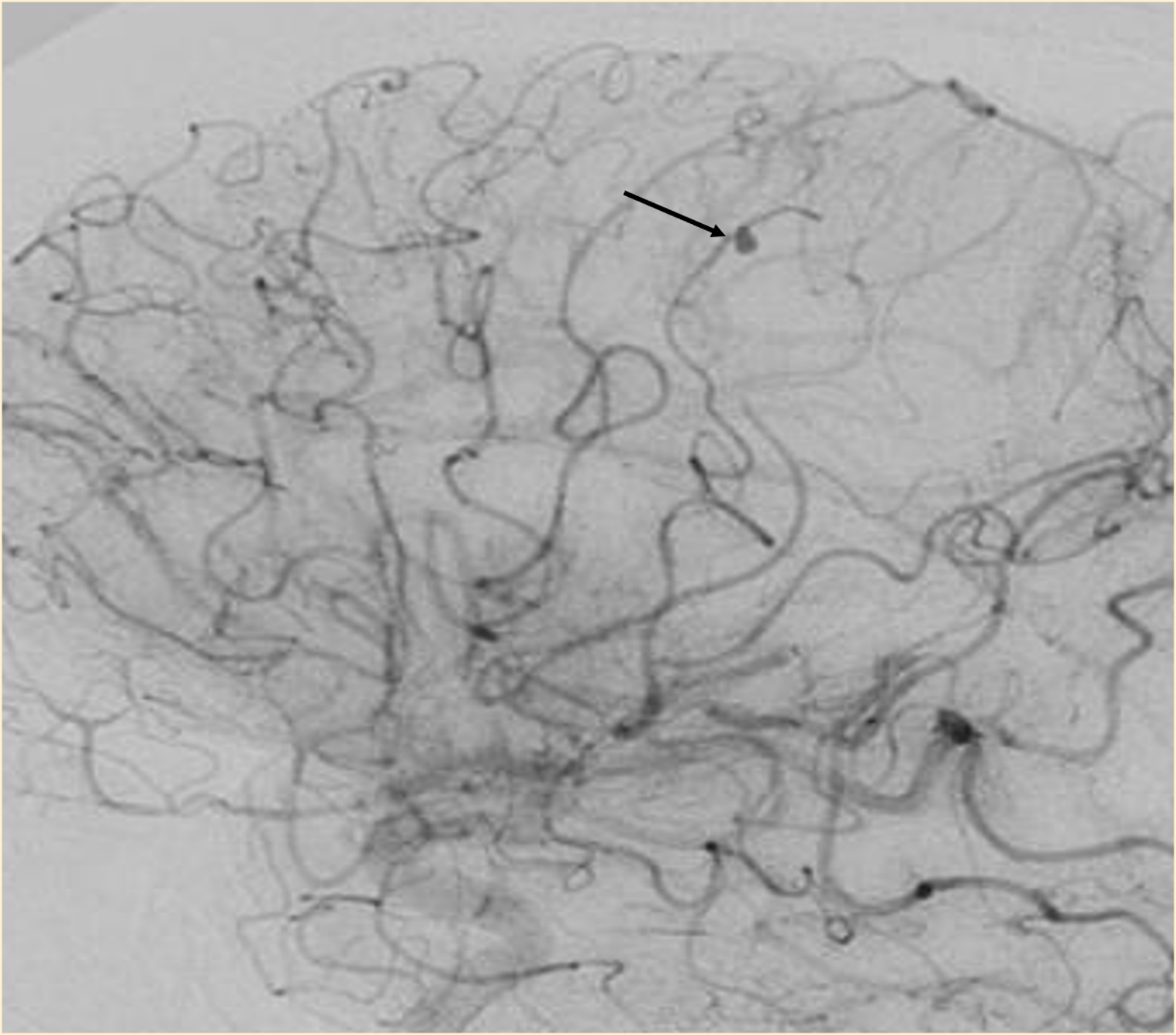


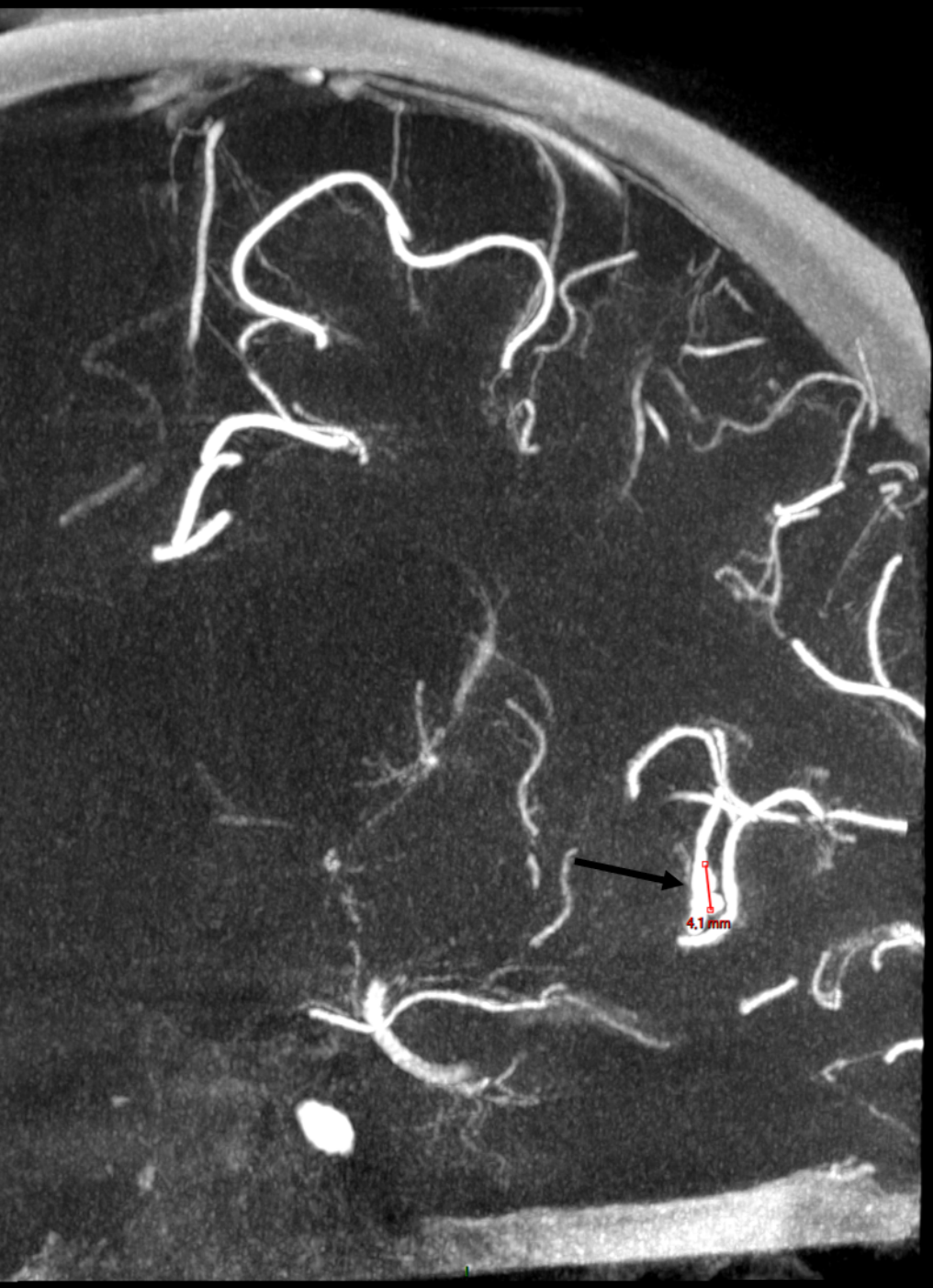


R

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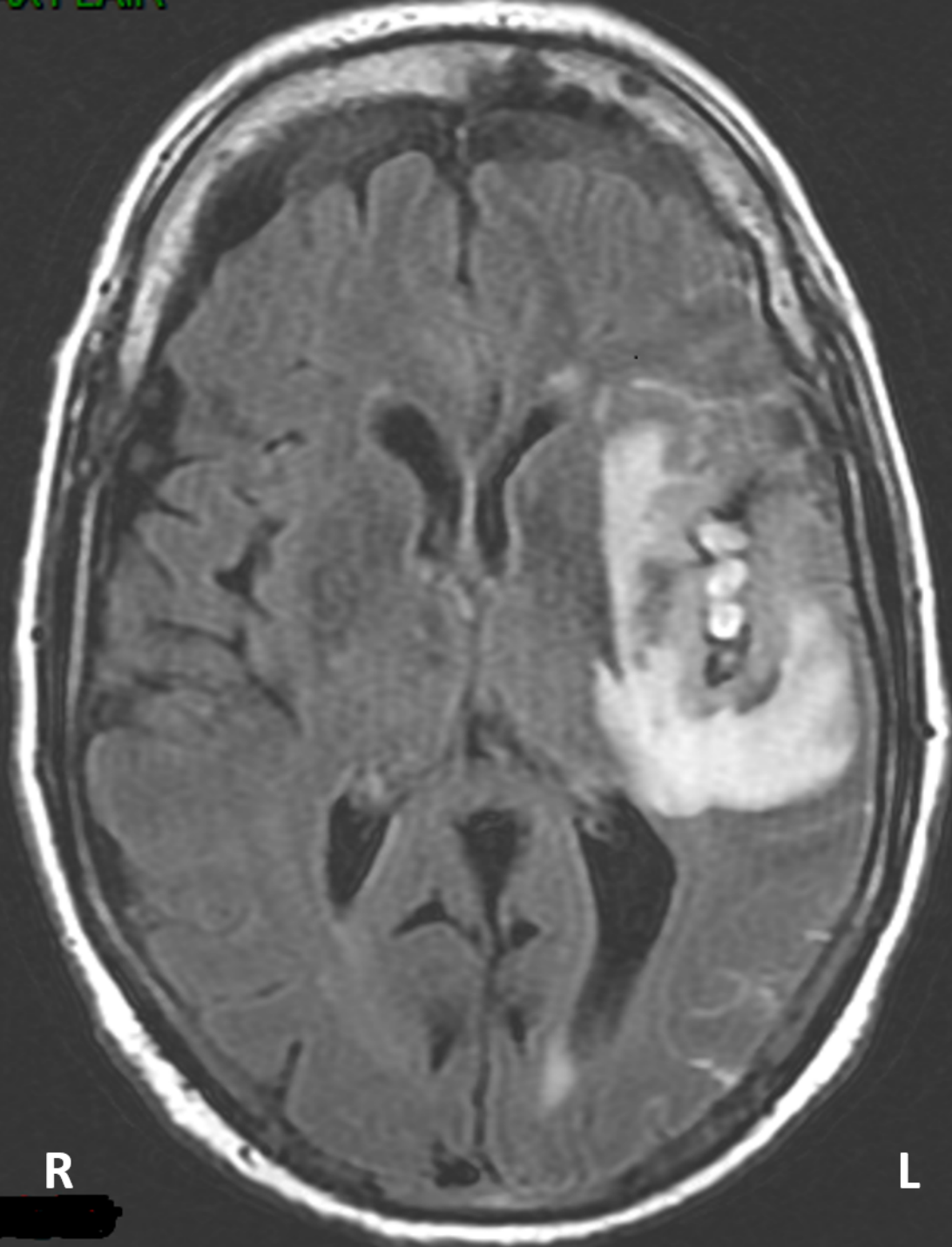






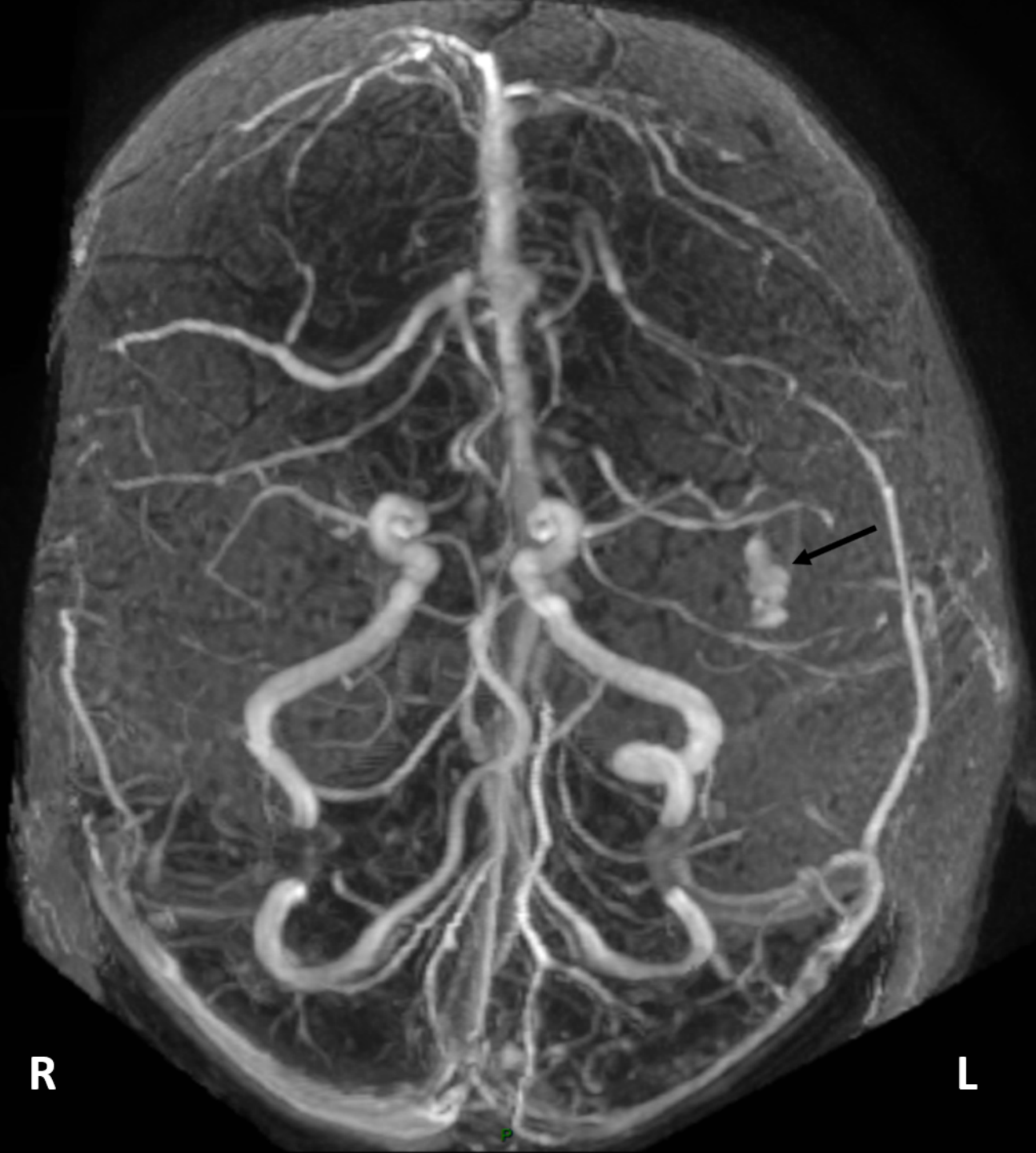
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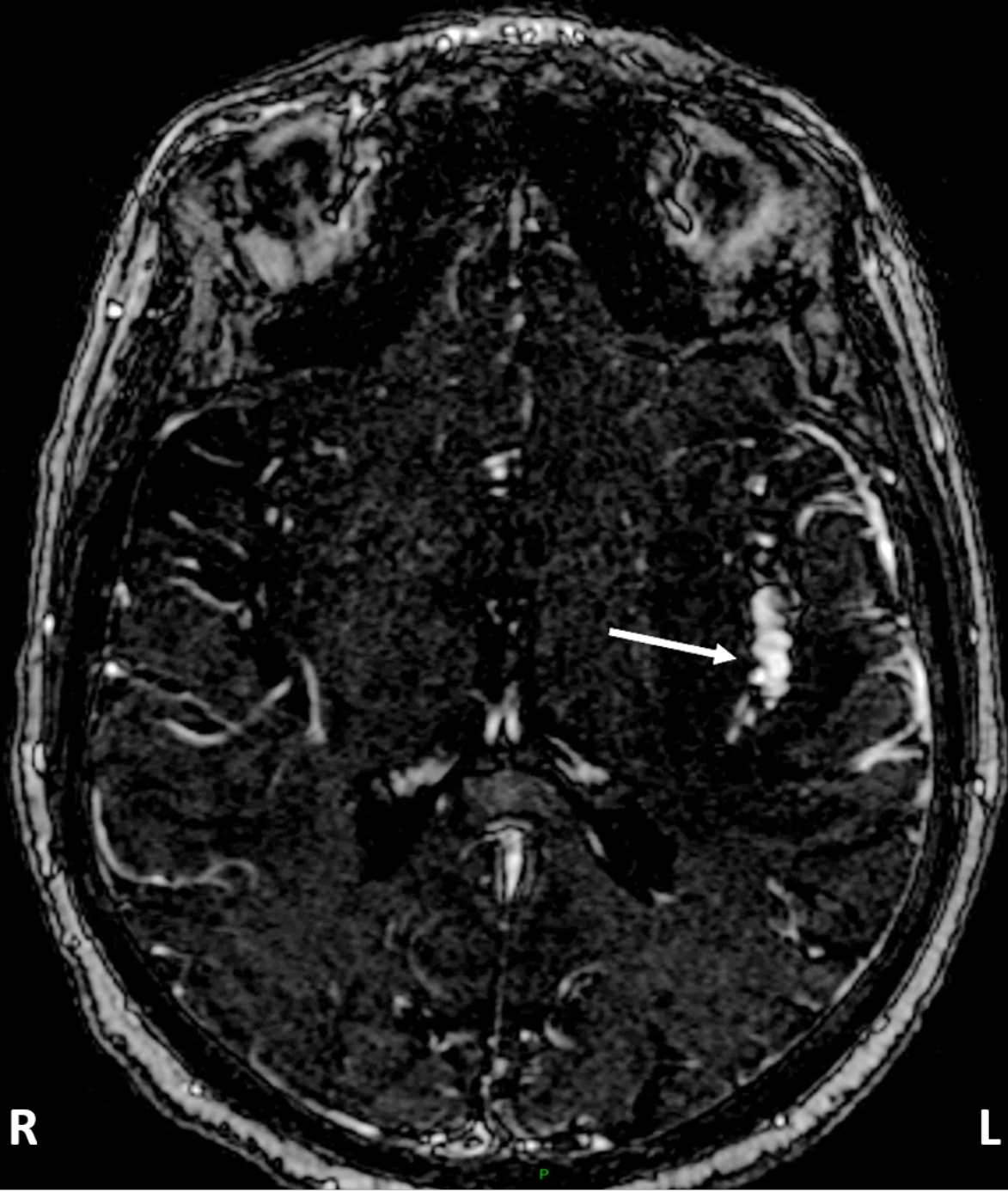


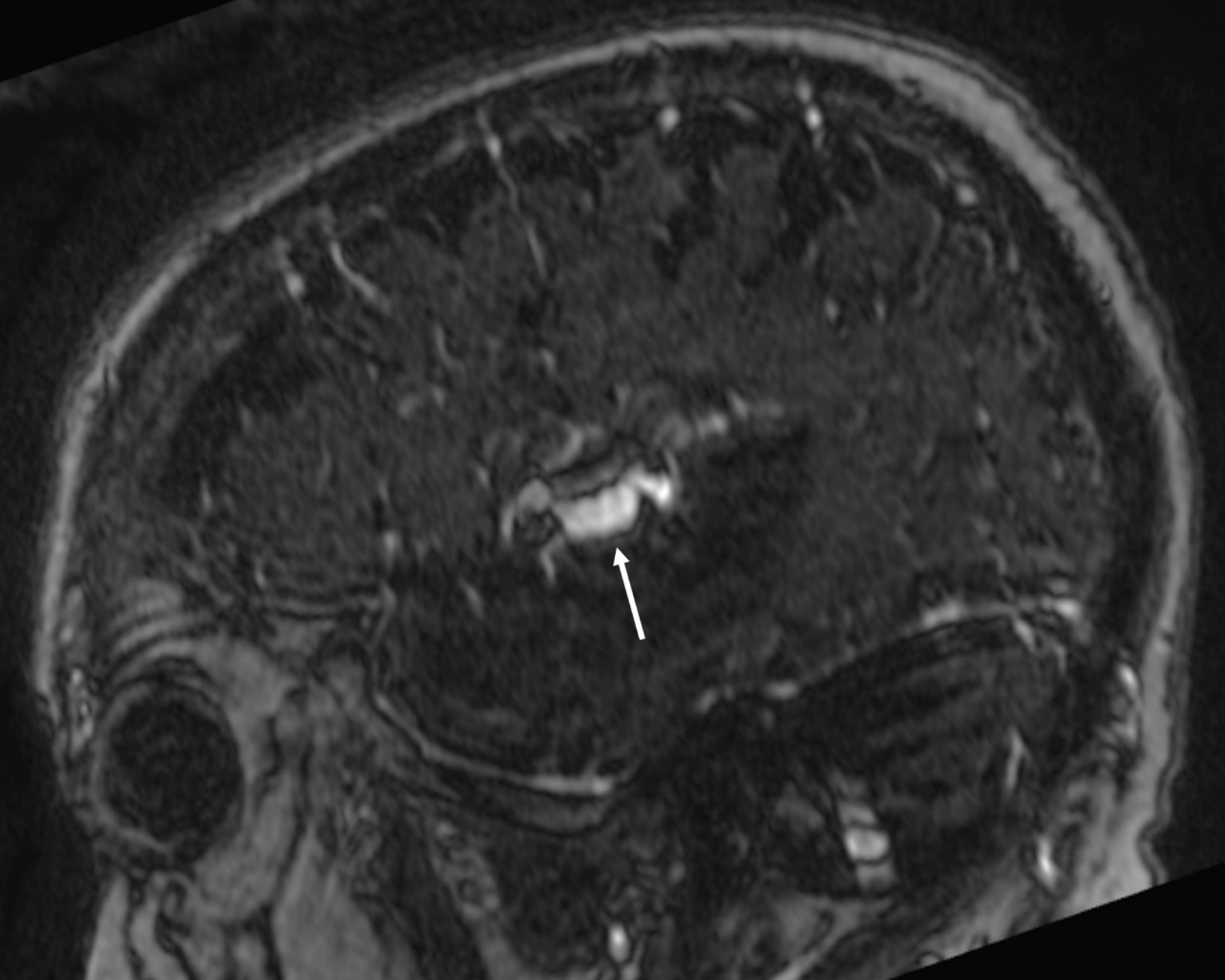
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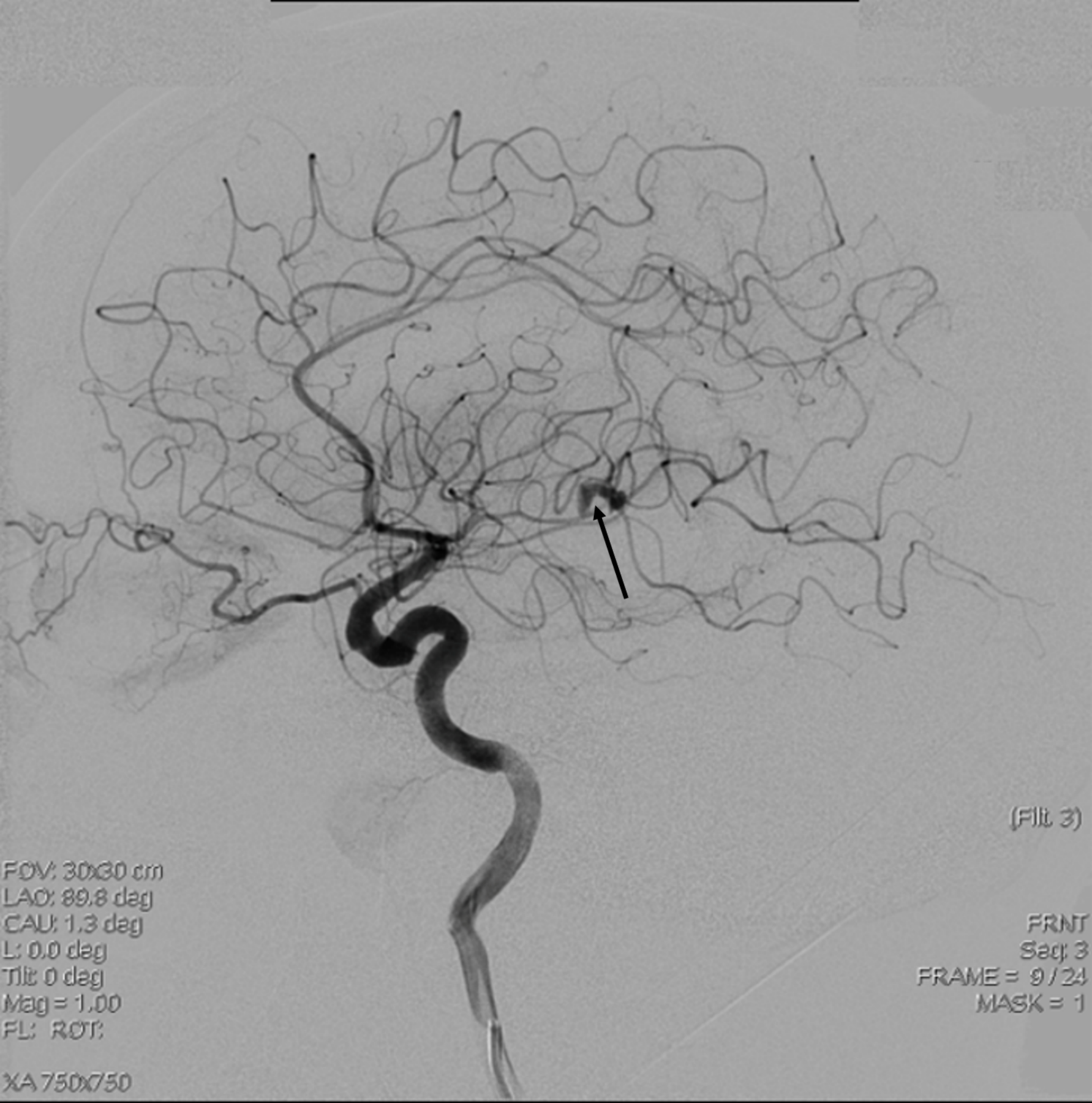
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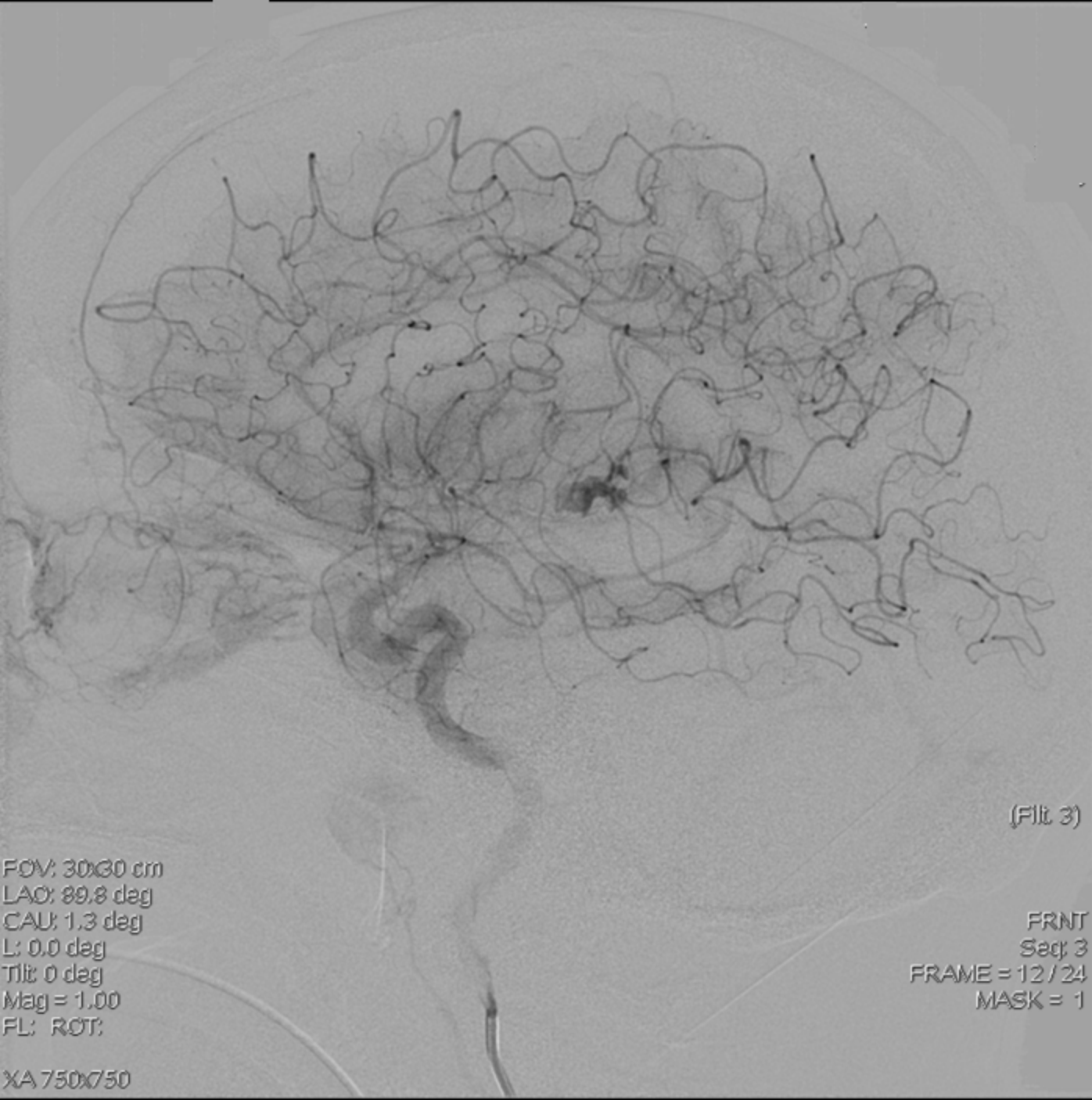


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FL: ROT:

FRNT  
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FRAME = 9 / 24  
MASK = 1

XA 750x750



(Flt 3)

FOV: 30x30 cm  
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CAU: 1.3 deg  
L: 0.0 deg  
Tilt: 0 deg  
Mag = 1.00  
FL: ROT:

FRNT  
Sec: 3  
FRAME = 12 / 24  
MASK = 1

XA 750x750



			Blood culture	IIA (DSA)							
	Age (ys) Sex	Valve lesion	Species	location	Size (mm)	Associated findings	Treatment 1	Follow-up 1	Follow-up 2	Treatment 2	Outcome
<b>Tashima, 1995<sup>8</sup></b>	M/48	Native*	Enterococcus fecalis		NA	NA	Antibiotics*	D15:DSA: IIA enlarge		clip	No residual IIA, asymptomatic
<b>Koffie, 2015<sup>9</sup></b>	M/49	Aortic, mechanical	Cocci +	R MCA (M2)	1.5	scattered SAH		H21: coma. Hematoma. IIA 5mm		evacuation /clip MCA(M2)	Post-op D1: died
<b>John, 2016<sup>10</sup>, Case 2</b>	F/31	Aortic, prosthesis	Streptococcus viridans				Antibiotics*				
IIA 1				R MCA, distal	2	microhemorrhages, old SAH		D14: stable	4w: resolve		
IIA 2				L MCA (M2)	2			D14: stable	4w: enlarge	Coil + Onyx E°	1month: No residual IIA
<b>Present case, 2020</b>	M/72	Aortic, Bioprosthesis	Streptococcus sanguinis			3 microinfarcts, ischemic stroke, microbleeds	gentamycine, amoxicillin				
IIA 1				R MCA, distal	10					Glue E°	No residual IIA
IIA 2				L MCA (M2)	5			D7: hematoma. IIA: 15mm		Onyx E°	No residual IIA

**Table 1: Summary of literature cases of rapid enlargement and subsequent rupture of an intracranial infectious aneurysm**

IIA: intracranial infectious aneurysm; DSA: digital subtraction angiography; \*: unspecified; NA : not available; D: day; R: Right; MCA: middle cerebral artery; H: hour; L: left; SAH: subarachnoid hemorrhage; w: week; E°: embolization.