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Repeated neurovascular imaging in subarachnoid hemorrhage when initial studies are negative

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Abstract

Approximately 15% of patients with non-traumatic subarachnoid hemorrhage have no causative lesion identified on their initial angiogram. We present two patients with non-traumatic subarachnoid hemorrhage with negative initial angiograms that were subsequently found to have small basilar perforator aneurysms on delayed neurovascular imaging. We discuss the possible mechanisms for false negative diagnostic cerebral angiograms. These patients support the current standard of care with repeat angiography in cases of subarachnoid hemorrhage when no causative lesion can be identified on initial neurovascular imaging.

Keywords

Angiography; Cerebral angiography; Intracranial aneurysm; Subarachnoid hemorrhage

1. Introduction

Ruptured intracranial aneurysms are the most common cause of spontaneous subarachnoid hemorrhage (SAH). However, in approximately 15% of cases, no causative lesion can be identified on initial neurovascular imaging.¹ Patients with angiogram-negative SAH typically tend to have a better prognosis than aneurysmal SAH, particularly with certain hemorrhage distribution patterns. For example, angiogram-negative SAH can be categorized into perimesencephalic and non-perimesencephalic hemorrhage based upon the distribution of blood on non-contrast head CT imaging.² The former is defined as blood anterior to the midbrain with or without extension to the anterior ambient cistern or basal Sylvian fissure and no complete filling of the interhemispheric fissure or extension to the lateral Sylvian

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Conflicts of Interest/Disclosures

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fissure.¹ Among patients with negative angiograms, those with perimesencephalic SAH tend to have better outcomes and lower rates of complications such as re-bleeding, hydrocephalus, and vasospasm compared to those with non-perimesencephalic SAH.³ However, recent evidence suggests the clinical course of perimesencephalic SAH may not be as benign as once thought.⁴

While the perimesencephalic SAH pattern generally provides a reassuring prognosis in most cases, angiogram-negative non-perimesencephalic SAH remains a heterogeneous category of SAH with uncertain outcomes and varying management algorithms. Here we report two patients with diffuse SAH with initial negative angiograms who were subsequently found to have small basilar artery perforator aneurysms on follow-up neurovascular imaging. These patients were then successfully treated with surgical intervention. We review the possible causes for the initial negative angiogram such as technical failure, vasospasm, thrombosis, external compression from local hematoma, and auto-obliteration of microaneurysms. While evidence suggests the basilar perforator artery aneurysm rupture may be a cause of angiogram-negative perimesencephalic SAH^{5,6}, these patients demonstrate that basilar artery perforator aneurysms may also be a cause of more diffuse hemorrhage patterns.

2. Case presentations

2.1. Patient 1

A 65-year-old woman presented to the hospital after acutely developing the worst headache of her life. Her medical history was notable for hypertension, osteoporosis, and follicular type I non-Hodgkin lymphoma that had been successfully treated with radiation therapy 8 years prior. Her only medication was risedronate and she denied any history of smoking, alcohol use, or illicit drug use. On examination she was alert and oriented without any focal neurological abnormalities. Her International Normalised Ratio was 1.0 (normal range <1.3) and her platelet count was 152,000/mm³ (normal range 150,000–400,000/mm³). A non-contrast head CT scan revealed diffuse SAH extending bilaterally into the Sylvian fissures, prepontine and ambient cisterns, and intraventricular hemorrhage in the third and bilateral lateral ventricles. The patient was transferred to our institution for further management. CT angiogram revealed a possible right posterior communicating artery aneurysm. Thirty-six hours after symptom onset the patient deteriorated clinically and became increasingly somnolent (Glasgow Coma Scale score of 8), and required intubation and external ventricular drain placement. The only area of suspicion on her CT angiogram and initial angiogram was an infundibulum of the posterior communicating artery origin. This was explored surgically 50 hours after symptom onset and proved indeed to be an infundibulum and not a true aneurysm. This had no evidence of previous hemorrhage. The infundibulum was wrapped with muslin. Catheter based cerebral angiogram performed approximately 70 hours after onset of symptoms did not reveal any aneurysm or other possible source of hemorrhage (Fig. 1).

The patient improved clinically over the following day and was extubated. During her course in the intensive care unit, she developed severe vasospasm. Despite maximal medical therapy, she developed a left insular infarct that was confirmed on MRI. Repeat catheter angiogram 11 days later demonstrated vasospasm at the M1 segment of the left middle

cerebral artery along with a small aneurysm posterior to the upper third of the basilar trunk, which was not detected on the initial cerebral angiography (Fig. 1). A craniotomy was performed and the basilar perforator aneurysm was successfully obliterated by clipping using a subtemporal approach. The patient's recovery was complicated by persistent vasospasm requiring multiple intra-arterial treatments with milrinone and nicardipine to maintain vessel patency. The patient's recovery was further complicated by deep vein thrombosis, pulmonary embolism, and cardiogenic shock. She gradually improved and was discharged to a rehabilitation facility on hospital day 47. At her 3 year follow-up, the patient had persistent weakness of her left upper and lower extremities (Glasgow Outcome Scale score of 4).

2.2. Patient 2

A 60-year-old man presented to the hospital because of acute onset of the worst headache of his life. His past medical history was notable for asthma and low back pain. He denied any history of smoking. Non-contrast CT imaging of the brain demonstrated diffuse SAH with mild enlargement of the ventricles (Fig. 2). He underwent two catheter based cerebral angiograms that did not reveal any vascular abnormality. After 10 days of observation, the patient was discharged to home.

After discharge the patient experienced persistent lethargy. Approximately 8 weeks later he developed a recurrent, sudden onset headache and presented to the emergency department. Imaging revealed a right frontal convexity subacute subdural hematoma with 1.1 cm midline shift to the left without evidence of SAH. He was then transferred to our institution. His neurological examination demonstrated no focal deficits. Compared to his previous imaging obtained during his first admission 8 weeks prior, CT angiogram revealed a 2 mm aneurysm of the distal basilar artery trunk (Fig. 2). On hospital day 4 he underwent burr-hole drainage of the subdural hematoma and a right temporal craniotomy and clip obliteration of the basilar artery aneurysm. The patient improved clinically over the following days and he was discharged to a rehabilitation facility on post-operative day 13. At his 5 month follow-up the patient had resumed an independent life.

3. Discussion

3.1 False-negative angiography

The two patients that we report are examples of diffuse SAH with negative initial cerebral angiography. It is estimated that 15% of patients presenting with SAH have initial angiograms which are negative. Catheter based angiography remains the gold standard for diagnosis following SAH. Although its sensitivity in detecting hemorrhage etiology is excellent, it is certainly not 100%. Particularly in the case of non-perimesencephalic hemorrhage, follow-up catheter angiography at intervals of 1 and 6 weeks from the time of hemorrhage have been shown to improve the sensitivity of detecting a vascular lesion when the initial angiogram is negative.⁷

3.2. Possible causes of negative angiography

Many different hypotheses have been proposed for the phenomenon of negative angiography in the setting of an occult ruptured aneurysm. These include vasospasm⁸, thrombosis of aneurysm sac⁹, microaneurysm obliteration at time of hemorrhage¹⁰, small aneurysm at a vascular bifurcation which is difficult to visualize despite multiple views, and technical error.¹¹ The two patients presented here both had predominantly diffuse SAH. The aneurysms were discovered at different times in the two patients: the first 11 days after symptom onset in the setting of repeat angiogram for middle cerebral artery vasospasm and the second by CT angiogram in the setting of non-traumatic subdural hematoma approximately 8 weeks after the initial SAH. Retrospective analysis of initial imaging by multiple experts versed in neuroradiology (a team consisting of neurosurgeons, interventional neuroradiologists, and diagnostic neuroradiologists) revealed no evidence of these aneurysms by initial angiogram. These angiograms were considered to be of excellent technical quality, meaning no patient movement, good contrast opacification of all four vessels, and adequate number of views (including numerous oblique angles). It is possible that both patients had *forme fruste* microaneurysms which were either too small to be visualized upon initial angiography or were obliterated as a result of the initial hemorrhage.

Aneurysms of basilar perforator arteries are not common. Recently, Gross et al. performed a review of the literature which demonstrated a total of 12 cases.⁵ Only one of these 12 was not initially visualized on the first angiogram. Notably, half of these patients presented with a perimesencephalic hemorrhage pattern¹², and may suggest that basilar artery perforator aneurysms as a more likely cause of angiogram-negative SAH than previously thought.¹ Careful evaluation must always be taken to identify even the smallest of aneurysms. Park et al. report a series of 13 patients with perimesencephalic hemorrhage pattern resulting from 1 mm aneurysms that were only visualized by three dimensional rotational angiography. In 12 of these patients, the aneurysm was not initially visualized by conventional digital subtraction angiography.⁶ The two patients presented here suggest that basilar perforator artery aneurysms may also be the source of more diffuse SAH in addition to the perimesencephalic hemorrhage pattern.

3.3. Implications for management of angiogram-negative SAH

Repeat angiography in the setting of initial angiogram-negative SAH has been recommended within 1 to 2 weeks after initial angiogram.⁷ In the setting of diffuse SAH a third angiogram has been recommended at a period of 6 weeks.⁷ While randomized trials do not exist to support any imaging protocol in this scenario, data from large retrospective series such the recent report from Dalyai et al. provide useful data from the experience of a high-volume neurovascular center.⁷ Although surgical exploration may be indicated at any point by a suspicious local hemorrhage, the information gained from repeat angiography may outweigh the benefit of early exploration.¹⁰ Our published experience suggests that CT angiography may be an appropriate modality for initial imaging in the setting of acute SAH, but if findings are initially negative, further work-up with catheter based angiography is warranted.^{13,14}

4. Conclusion

These patients demonstrate that ruptured basilar artery perforator aneurysms can result in diffuse SAH, in addition to perimesencephalic hemorrhage. Negative angiography warrants diligent follow-up neurovascular imaging to identify lesions initially occult to both CT angiography and digital subtraction angiography.

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Fig. 1.

Digital subtraction angiography, anterior-posterior view (A, B) and axial CT angiogram (C, D) of Patient 1. There is no aneurysm seen on the initial imaging (A, C), while follow-up imaging performed 11 days later (B, D) demonstrates a small, basilar artery perforator aneurysm (arrow).

Fig. 2.

Axial CT angiography of Patient 2. Initial imaging (A) was negative for aneurysm. However, CT angiography performed 8 weeks later (B) demonstrates a small, basilar artery perforator aneurysm (arrow).