Case series of 64 slice computed tomographycomputed tomographic angiography with 3D reconstruction to diagnose symptomatic cerebral aneurysms: new standard of care?

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#### Abstract

CT angiography (CTA) has improved significantly over the past few years such that the reconstructed images of the cerebral arteries may now be equivalent to conventional digital angiography. The new technology of 64 slice multi-detector CTA can reconstruct detailed images that can reliably identify small cerebral aneurysms, even those <3mm. In addition, it is estimated that CT followed by lumbar puncture (LP) misses up to 4% of symptomatic aneurysms. We present a series of cases that illustrates how CT followed by CTA may be replacing CT-LP as the standard of care in working up patients for symptomatic cerebral aneurysms and the importance of performing three dimensional (3D) reconstructions. A series of seven cases of symptomatic cerebral aneurysms were identified that illustrate the sensitivity of CT-CTA versus CT-LP and the importance of 3D reconstruction in identifying these aneurysms. Surgical treatment was recommended for 6 of the 7 patients with aneurysms and strict hypertension control was recommended for the seventh patient. Some of these patients demonstrated subarachnoid hemorrhage on presentation while others had negative LPs. A number of these patients with negative LPs were clearly symptomatic from their aneurysms. At least one of these cerebral aneurysms was not apparent on CTA without 3D reconstruction. 3D reconstruction of CTA is crucial to adequately identify cerebral aneurysms. This case series helps reinforce the importance of 3D reconstruction. There is some data to suggest that 64 slice CT-CTA may be equivalent or superior to CT-LP in the detection of symptomatic cerebral aneurysms.

#### Introduction

Headache accounts for approximately 5 million visits annually to emergency departments (ED) across the United States and 1% are diagnosed with a subarachnoid hemorrhage (SAH).1 Although most are due to trauma, 80% of non-traumatic SAHs are caused by rupture of an aneurysm.<sup>2</sup> Among the general population, about 1-5% of people have cerebral aneurysms, most commonly located in the Circle of Willis.<sup>3</sup> Failure to detect a ruptured aneurysm results in a high morbidity and mortality, and usually occurs in people who are otherwise healthy. Patients with an SAH typically have sudden onset of severe headache or the worst headache of my life with transient loss of consciousness or buckling of legs and later vomiting. On examination, there may be retinal hemorrhages, photophobia, nuchal rigidity, restlessness, a diminished level of consciousness, or focal neurological signs. With a dramatic presentation, the diagnosis is fairly straightforward. It is in patients who have milder or atypical signs and symptoms that may be misdiagnosed. It is estimated that about 12-25% of patients with sentinel headaches from symptomatic cerebral aneurysms are misdiagnosed.<sup>4,5</sup> This is due to three preventable reasons: failure to consider the diagnosis, failure to perform and correctly interpret the CT, or failure to perform and correctly interpret results of the lumbar puncture (LP).6

Approximately 40% of patients with a nontraumatic SAH complain of an unusually severe headache days or weeks before rupture, called a sentinel or thunderclap headache. Sentinel headaches are minor bleeds from aneurysms that can be a warning for more significant subsequent aneurismal rupture. In general, an SAH has a high mortality rate of 51%.<sup>6</sup> Of patients with aneurismal SAH, 10% die prior to arrival at the hospital, 25% in the next 24 h, and 45% in the following 30 days.<sup>7</sup>

The current standard for diagnosis of a ruptured aneurysm has been CT with LP. However, CT-LP misses up to 4% of symptomatic aneurysms. The newer technology of the 64slice multi-detector CT can provide very detailed images of the cerebral arteries. Recent literature suggests that bleeding aneurysms in headache patients may be ruled out with a much higher post test probability using CT followed by CT angiography (CTA) with three-dimensional (3D) reconstruction of the brain.<sup>8</sup>

We present a case series illustrating how 64slice CT-CTA with 3D reconstruction can be used to diagnose symptomatic cerebral aneurysms. This study was approved by our Institutional Review Board. Correspondence: Dietrich Jehle, State University of New York at Buffalo, Department of Emergency Medicine, 462 Grider Street, Buffalo, NY 14215, USA. Tel. +1.716.898.4431.

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# Case #1

A 54-year old woman with a history of hypertension, hepatitis C, and asthma presented to the ED with complaints of a constant headache for one and a half weeks with blurred vision, nausea, and two episodes of emesis. In the past, she had had similar but less severe headaches when her blood pressure was elevated. She had increasing right foot pain that had started three days before without injury. Physical examination was unremarkable except for the right foot pain.

Head CTA showed a 4 mm aneurysm involving the M1 segment of the left middle cerebral artery (MCA) and no acute hemorrhage (Figure 1). LP results were clear, colorless, 1 RBC, 1 WBC, glucose 58, protein 33, and no culture growth after two days.

She was admitted to neurosurgery for observation and continued workup. On admission, her blood pressure was 195/113 and pulse was 80. MRI/MRA also showed a 4 mm aneurysm arising from the left MCA. Six days later, she was discharged in stable condition. Two months later, she had an uncomplicated craniotomy and clipping for an unruptured cerebral aneurysm of the left internal carotid artery bifurcation and insertion of a lumbar drain. She had an uneventful post-operative recovery.

#### Case #2

A 34-year old woman with a history of migraines and sinusitis presented to the ED





with bifrontal headaches. She also had photophobia, nausea, and vomiting. Head CT at that time showed some sinusitis. CTA at that time was read as showing no aneurysm. A 3D reconstruction was not performed; however, if it had been done the aneurysm would have been grossly apparent (Figure 2). She went home from the ED with a presumed negative imaging result.

Eight days later, her family found her unresponsive in her home. She had been last seen in a normal condition the day before. On arrival, emergency medical services (EMS) found her on the floor drooling. She had a generalized tonic-clonic seizure and received lorazepam. In the ED she continued to have seizures. Blood pressure was 120/86 and pulse 90. On physical examination, pupils were 3 mm and sluggish, and her gaze was to the left. She was intubated, and then sent down for a CTA. CTA revealed intraventicular hemorrhage with hydrocephalus, a 5 mm aneurysm arising from the anterior communicating artery, and a congenital hypoplastic A1 segment of the right anterior cerebral artery. She was taken to surgerv for repair of the intracerebral hemorrhage with a ruptured cerebral aneurysm. A left craniectomy for the aneurysm was performed together with placement of a lumbar drain, subcutaneous placement of skull into the right abdomen, and bedside ventriculostomy. She was placed on a phenobarbital drip and treated in the Intensive Care Unit (ICU).

During her stay in the ICU, she was maintained on pressors and a broad spectrum antibiotic for sepsis. The EEGs showed no cerebral activity despite discontinuation of phenobarbital. On post-operative Day 5, she was acidotic, hypotensive, and had fixed and dilated pupils. She continued to deteriorate further, and became bradycardic and asystolic without response to ACLS. pressure on admission was 164/85. The following day, LP results were as follows: clear, colorless, 0 RBC, 0 WBC, glucose 63, protein 60, and negative gram stain. The next day, he was discharged home with neurosurgery follow up. For the moment, he has declined surgical intervention.

### Case #4

A 46-year old woman with a history of migraines and back/neck disk injury had been complaining of increasing headache, up to 10/10 in intensity, for one week. She described it as hurting *all over her head*, with varying intensity for four days, and currently resolved. Motrin had not offered any relief. She did not have any visual changes, seizure activity, weakness, paresthesias, or trauma. She did report nausea and frequent vomiting. Her blood pressure was 118/72 and pulse was 75. Physical examination was unremarkable. Her Glasgow Coma Scale was 15, 3+ deep tendon reflexes bilaterally, and her cranial nerves were grossly intact.

Brain CTA revealed bilateral cerebral aneurysms at the bifurcation of the internal carotid artery. The right aneurysm measured  $18 \times 10$  mm and the left aneurysm measured  $9 \times 9$  mm (Figure 4). On hospital Day 4, she underwent a craniotomy for clipping of the right internal carotid artery aneurysm since it was larger than the left and thus more at risk of hemorrhage. There was no sign of recent hemorrhage with surgery and she had a gradual but uncomplicated recovery. On post-operative Day 6, she was discharged and sent home.

On post-operative Day 16, she was sent from the neurosurgery clinic to the ED for a 2-day right facial droop. There was no extremity weakness or change in speech. Physical exam-



Figure 2. Computed tomography angiography showing a 5 mm aneurysm arising from the anterior communicating artery. The aneurysm had not been detected until 3D reconstruction was performed.



Figure 3. Computed tomography angiography showing a 4.5 mm aneurysm of the left side of the basilar artery.

# Case #3

A 48-year old man with a history of hypertension and on no medications presented to the ED after an 8-h history of chest pain. The pain was constant and radiated to his back. In addition, he complained of a throbbing headache. In the ED he was afebrile with blood pressure 200/109, pulse 74, and oxygen saturation 96%. Physical examination was unremarkable.

Initial cardiac workup and routine laboratory tests in the ED were negative. EKG showed T-wave depression in inferior leads. CTA of brain showed a 4.5 mm left basilar artery aneurysm with no evidence of hemorrhage, masses, shift, or edema (Figure 3).

He was admitted to neurosurgery service for evaluation and was placed on telemetry. Blood



Figure 1. Computed tomography angiography showing a 4 mm aneurysm in the M1 segment of the left middle cerebral artery.



Figure 4. Computed tomography angiography showing an  $18 \times 10$  mm and a  $9 \times 9$ mm aneurysm at the right and left bifurcations of the internal carotid arteries, respectively.

ination only showed scarring from craniotomy and right facial droop. CTA showed perfusion of both carotids, a small sub-acute left frontal sub-dural hemorrhage, a small right frontal lobe infarct with some right basal ganglia involvement, and mild enhancement of the left frontal lobe, most likely due to reperfusion. She was referred to neurosurgery for further follow up of her left cerebral aneurysm and underwent clipping of her left cerebral aneurysm two months later with an uneventful post-operative course.

### Case #5

An 81-year old woman with hypertension, osteoporosis, anxiety, depression, and hypothyroidism presented to the ED with five days of headache rated 7-8/10 on presentation. She described the headache as being at the base of her head with nausea and dizziness. Her blood pressure was 144/55 and pulse 68. Physical examination was unremarkable.

Head CTA showed a  $5\times3$  mm midline aneurysm arising from the anterior communicating artery (Figure 5). Head CT without contrast showed a mild amount of acute SAH present along the sulci, both parietal lobes, left parasellar cistern, and in the interhemispheric fissure. She was transferred to another hospital for endovascular treatment of her aneurysm and was lost to follow up.

#### Case #6

A 52-year old woman in mild distress and with a history of cocaine abuse and hypertension presented to the ED with chronic headache, nausea and blurred vision of approximately one year, chest pain on right side of approximately one month, and intermittent left lower quadrant abdominal pain that was worse on presentation. She did not have a headache or chest pain while in the ED. For the previous three years she had used hydrocodone, drank alcohol daily, and controlled her hypertension with clonidine. Her blood pressure was 163/100 and pulse was 82. Physical examination was normal except for left lower quadrant tenderness and bilateral adnexal tenderness. She received treatment for pelvic inflammatory disease based on the clinical examination.

Brain CTA revealed two aneurysms in the right internal carotid artery: one at the right posterior communicating artery measuring  $6\times4$  mm and a second at the distal cavernous portion measuring  $8\times8$  mm (Figure 6). A later LP revealed no sign of recent hemorrhage, clear fluid, 22 RBC, and 2 WBC.

She was admitted to neurosurgery. The risk of hemorrhage from the aneurysms was repeatedly explained to her and the option of endovascular treatment was recommended. However, she declined neurosurgical treatment. Follow up was scheduled with the neurosurgery clinic. She subsequently agreed to surgery and underwent coiling of her cerebral aneurysms with an unremarkable post-operative course.

# Case #7

A 56-year old man with hypertension and hypercholesterolemia presented with syncope and new onset seizures. At an outlying hospital, he had had a negative head CT and was treated with multiple anticonvulsants. He had a second seizure and was then transferred to the tertiary care hospital. The patient was delirious with metabolic acidosis and was unable to provide a history. His blood pressure was 177/115, pulse 94, and body temperature was 103.4°F. Physical examination revealed a confused and restless man, with dried blood in the oral cavity and on the tongue, and moving of all four extremities. CBC showed an increased WBC of 29.7, CMP showed bicarbonate level of less than 5, AG of 36, and glucose of 341. CSF revealed an initial RBC of 40,000 decreasing to 4,705, glucose 143, protein 88, and negative cultures. Brain CTA revealed an intracranial aneurysm involving the junction of the M1 and M2 segments of the right MCA measuring 8×5 mm and no intra- or extracranial hemorrhage (Figure 7).

The patient was admitted to the ICU. Given the new onset of seizures and the possibility of rupture with bloody CSF, he underwent surgery on hospital Day 3 for right frontal temporal craniotomy with clipping of aneurysm and insertion of lumbar drain. Surgery was uncomplicated and no bleeding point from the aneurysm was noted. On post-operative Day 2, brain CTA revealed postsurgical changes with a small subdural hematoma, hygroma, and pneumocephalus along with slight diffuse edema of the right cerebral hemisphere and a mass effect on the right cerebral hemisphere with minimal midline shift. CT also demonstrated sinusitis, which may have been responsible for the fever. He had an uneventful recovery and was transferred to the ward on postoperative Day 5. He continued to recover and on post-operative Day 7 was eventually discharged and sent home with follow up at the neurosurgery clinic.





Figure 5. Computed tomography angiography showing a 5 x 3 mm midline aneurysm arising from the anterior communicating artery.



Figure 6. Computed tomography angiography showing a  $6 \times 4$  mm aneurysm at the right posterior communicating artery and an  $8 \times 8$  mm aneurysm arising from the distal cavernous portion of the right internal carotid artery.



Figure 7. Computed tomography angiography showing an 8 x 5 mm aneurysm involving the junction of the M1 and M2 segments of the right middle cerebral artery.

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#### Discussion

In this series of cerebral aneurysms, CTA initially identified aneurysms in 6 patients; CTA without 3D reconstruction was falsely read as negative for aneurysms in one patient. CT without contrast was initially negative for SAH or aneurysms in all patients except one. LP was interpreted as negative in 4 patients. Six patients underwent surgery for repair of aneurysm and one patient declined surgery and is being followed. One patient died due to misdiagnosis when 3D reconstruction was not initially performed, and one patient underwent surgery at another hospital and was lost to follow up.

The current approach for an SAH diagnosis is to perform a non-contrast brain CT which has 91% sensitivity for detecting an SAH less than 12 h after rupture in alert patients. Sensitivity decreases to 50% seven days after rupture.9 Thus, CT will miss an SAH that a) has a delayed presentation to the ED and b) has a small volume of bleeding and is self-limited. Also, interpretation of CT and quality of image are other factors that contribute to misdiagnosis.<sup>10</sup> If the CT is negative, then an LP is performed. Blood vessels are located in the subarachnoid space, which communicates with the CSF. Thus, when an aneurysm ruptures, blood is released into the subarachnoid space and can be detected by an LP. However, a negative LP does not rule out an unruptured aneurysm. Day et al. describe a case in which a patient had severe headaches due to an unruptured cerebral aneurysm with diffuse cerebral vasospasm.11 Raps et al. found that while unruptured aneurysms are often incidental, and asymptomatic; symptoms can manifest as a result of thrombosis, intramural hemorrhage, embolism, and mass effect.12 It is important to keep in mind that patients with an incidental unruptured aneurysm may present symptoms that are completely unrelated, such as those secondary to benign primary headaches.

Witham et al. reported a patient in whom a classic thunderclap headache without SAH was found to have an aneurysm at very high risk of rupture.13 Although this is a rare presentation, a thunderclap headache with no SAH may be an indicator of a cerebral aneurysm with the potential for future rupture. McCarron et al. thought that CSF spectrophotometry performed after 12 h and within two weeks of symptom onset would identity all SAH patients who had a negative CT.14 However, they reported a case in which CSF spectrophotometry was negative, but during surgery the patient was found to have evidence of an old hemorrhage. Brain CT followed by LP increases the diagnostic sensitivity from 91% for CT alone to 96%.7 This means that an LP may be negative in up

to 4% of patients presenting with symptomatic cerebral aneurysms. The drawback with LP is that, currently, there are no standards concerning what is a negative LP and it is difficult to differentiate between a traumatic tap and a positive test for blood in the CSF.15 This, along with absent xanthochromia and failure to perform an LP in patients with a negative, suboptimal, or equivocal CT result, further contributes to misdiagnosis. Furthermore, any procedure carries serious risks. Risks of an LP include spinal headache, pain, bleeding, infection, and epidural hematoma. However, by eliminating the LP, mimics of SAH such as spinal SAH and idiopathic intracranial hypertension may be missed. The occasional meningitis patient with rapid symptom onset may also mimic a patient with SAH.

In CTA, a 100 mL bolus of non-ionic contrast is used. The use of contrast has some drawbacks. Its excludes patients with significant renal insufficiency from being able to undergo this test. Diabetic patients are at an increased risk for contrast-induced nephropathy. Patients with anaphylactoid reactions to contrast will need pre-medication, which further delays tests. Moreover, patients who undergo CTA are exposed to a significant dose of radiation (7.53 mSv for a CTA<sup>16</sup> vs 0.01 mSv for a chest X-ray<sup>17</sup>). Like many other tests, CTA is not perfect; it does not have 100% sensitivity in the diagnosis of aneurysms, particularly when using earlier generations of CT equipment. In 1999, Korogi et al. reported that early generation CTA had a sensitivity of 95-100% for aneurysms larger than 5 mm.18 For aneurysms with a diameter of 3-4 mm the sensitivity was 83%, and for aneurysms with a diameter less than 3 mm the sensitivity was 64%. Benefits of CTA include availability and faster data acquisition time than MRA, higher resolution, and ability to perform 3D reconstruction. Threedimensional reconstruction is important in accurately identifying cerebral aneurysms since it shows their location and reveals those that may be missed by looking at the 2D slices. In addition, 3D reconstruction allows for easier anatomical spatial orientation and clarification of the relationship of the aneurysm to other vascular structures and the skull base, allowing a more accurate interpretation to be obtained.

Some of the above drawbacks can be mitigated. Use of intravenous fluids before and after contrast reduces the risk of contrastinduced nephropathy in the populations at risk.<sup>19</sup> Pre-medication with antihistamines and corticosteroids, and the use of low osmolality contrast can lower the risk of an anaphylactoid reaction in predisposed patients.

Use of newer 64-slice CTA technology has been shown to have a much better sensitivity of 97.9% (with a 95% CI=88.9-99.9%) for detection of aneurysms.<sup>20</sup> In another study using Future improvements in the detection of cerebral aneurysm and prediction of their risk of rupture may occur with the use of fourdimensional CTA. This technique uses 3D CTA with temporal resolution in the cardiac cycle to visualize dome pulsation of the aneurysm to help predict its future hemodynamic behavior.<sup>21</sup>

## Conclusion

This case series demonstrates some of the advantages of CT-CTA over CT-LP for detection of SAH and symptomatic aneurysms, as well as the importance of 3D reconstruction when interpreting a CTA. Improvements in multidetector CTA have greatly increased the sensitivity for detecting smaller aneurysms. One major advantage of CTA is the ability to detect unruptured symptomatic aneurysms which would be undetected by LP. The literature and our case series suggest that 64-slice CTA with 3D reconstruction may be equivalent or superior to CT-LP for the detection of symptomatic cerebral aneurysms.

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