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CASE REPORT

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Case series demonstrating the value of computed tomography perfusion in differentiating ischemic strokes from seizures in patients with isolated aphasia

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Abstract

The value of computed tomography perfusion (CTP) imaging in suspected stroke patients who are not candidates for mechanical thrombectomy is promising. This case series demonstrates how CTP imaging aided in distinguishing seizure from stroke in 5 patients who presented to the emergency department with acute onset of isolated aphasia.

1 | INTRODUCTION

Computed tomography perfusion (CTP) imaging uses an intravascular contrast agent and serial imaging to quantify blood flow through the brain parenchyma.[1] The 2019 update to the American Heart Association/American Stroke Association Guidelines for the Early Management of Patients With AIS recommend performing CTP imaging of the brain for "certain patients" as part of their initial imaging.[2] Although most data supporting the use of early CTP imaging involves identifying a perfusion mismatch to select patients for mechanical thrombectomy, data suggest careful inspection of the CTP parameters produced (ie, cerebral blood flow, cerebral blood volume, and time-to-maximum intensity of contrast from the start of the scan) can help distinguish stroke mimics from arterial ischemic stroke (AIS).[3,4,5] For patients with acute onset of isolated aphasia without other associated neurological deficits, distinguishing an ictal or postictal seizure patient from one with an AIS is beneficial, so that thrombolytic or anticonvulsive therapy can be appropriately and promptly administered. Over 18 months, we identified 5 patients with acute onset of isolated aphasia who underwent an unenhanced CT, CT angiography (CTA), and CTP of the brain as part of their diagnostic evaluation.

2 | CASE NARRATIVES

Patient 1 is a 61-year-old male with no known past medical history who presented via ambulance with a suspected stroke with isolated expressive and receptive aphasia. The unenhanced CT showed only extremely subtle decreased attenuation in the posterior portion of the left temporal lobe. The corresponding CTP images demonstrated hyperperfusion with increased cerebral blood volume, increased cerebral blood flow, and accelerated time-to-maximum intensity of contrast from the start of the scan (Figure 1, Row A), which was not

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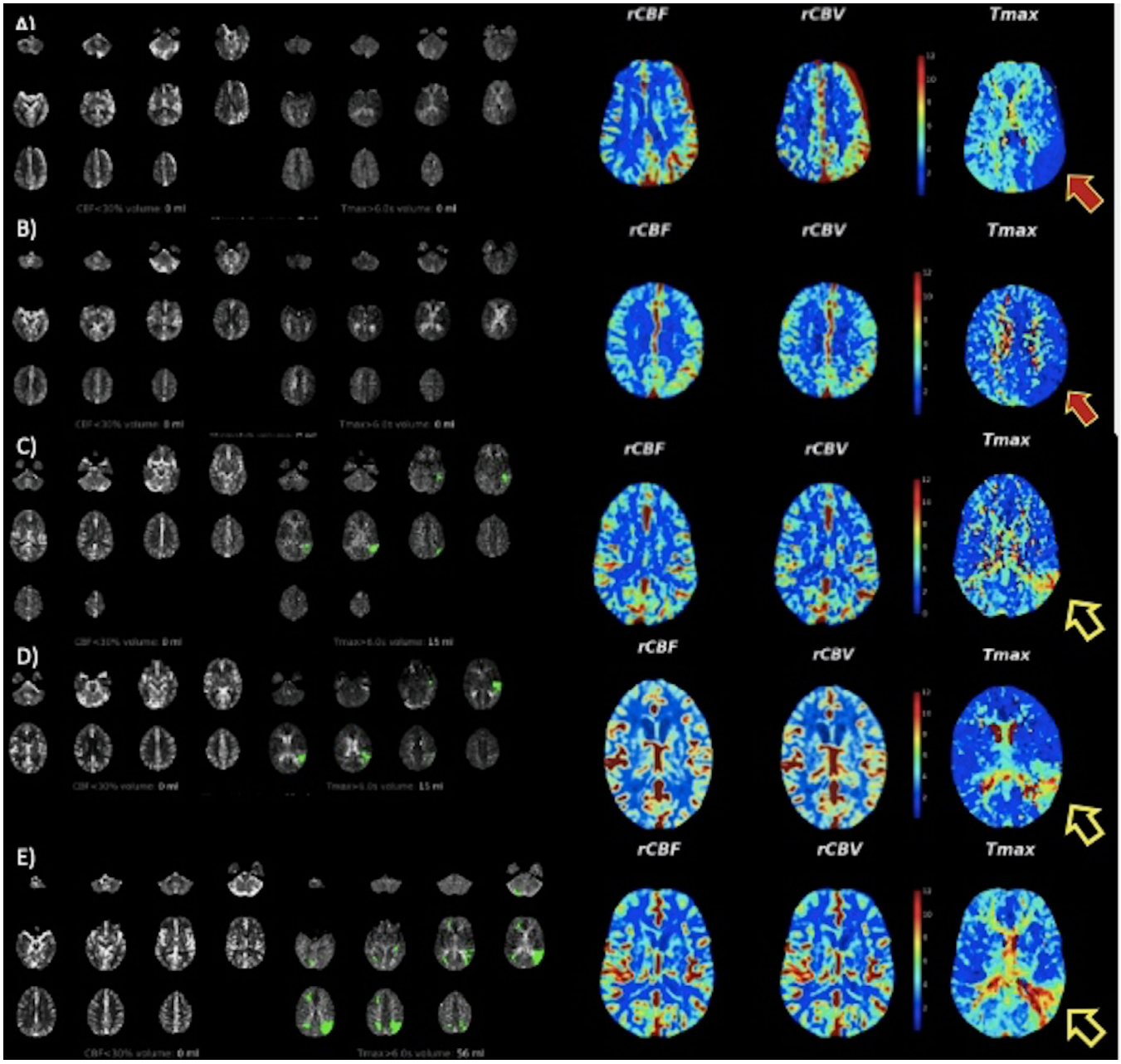

FIGURE 1 Sequentially in each row are computed tomography perfusion (CTP) studies from the same patient. Shown first are grayscale axial slices, with color thresholding (green) to detect hypoperfusion (iSchemaView RAPID, Menlo Park, California, USA) followed by representative axial slices of the source data showing cerebral blood flow (rCBF), cerebral blood volume (rCBV), and time-to-maximum (Tmax) intensity of contrast from the start of the scan. (A and B) Patients 1 and 2 demonstrate no detectable hypoperfusion, but with CBF and CBV increased and Tmax studies showing hyperperfusion in the posterior aspect of the left temporal lobe (solid arrows). (C, D, and E) Patients 3, 4, and 5 with evidence of hypoperfusion in the posterosuperior aspect of the left temporal lobe, which is the expected location of Wernicke's area in the majority of the population. This area also contains a functional connection to the Broca's fluent speech area in the frontal lobe. The Tmax in each of those cases is consistent with hypoperfusion (hollow arrows)

consistent with acute ischemia. Therefore, the patient was not treated with IV alteplase. Shortly after returning to the emergency department (ED) from CT, the patient suffered a generalized tonic-clonic seizure, which most likely represented generalization of a focal seizure. The patient had no previous seizure history. Magnetic resonance imaging (MRI) ultimately confirmed a mass consistent with a primary diffuse glioma. The patient was treated with lorazepam and levetiracetam in the ED before hospital admission. After hospital discharge, he returned to his home state for neurosurgical evaluation and definitive treatment.

Patient 2 is an 84-year-old male with past medical history of coronary artery disease, hypertension, and diabetes who presented with

sudden onset expressive aphasia. The unenhanced CT of the brain showed no evidence of acute intracranial abnormality. The CTP study was initially interpreted as showing no perfusion abnormality. The presumptive diagnosis was an acute ischemic stroke, so the patient was treated with IV alteplase. Soon after alteplase administration, the patient experienced a generalized tonic-clonic seizure. A subsequent MRI study of the brain was negative for acute ischemia, which suggested a stroke mimic diagnosis. Reinterpretation of the CTP study concluded there was hyperperfusion to the left hemisphere (Figure 1, Row B), suggesting non-convulsive seizure activity on initial presentation manifesting as aphasia. The patient was ultimately discharged home without any functional deficits.

Patient 3 is a 66-year-old male with past medical history of hypertension and a thoracoabdominal aortic aneurysm status post repair who presented with isolated expressive aphasia. An unenhanced CT of the brain was unremarkable. The CTP study was consistent with hypoperfusion in the brain region supplied by a branch of the left middle cerebral artery (MCA), indicative of acute ischemia without completed infarction (Figure 1, Row C). CTA of the brain confirmed the branch vessel occlusion. He was treated with alteplase, but because of the distal location of the clot the patient was not considered a candidate for mechanical thrombectomy. The patient's speech was noted to improve throughout the next day and was documented to be back to baseline by hospital discharge.

Patient 4 is a 75-year-old female with diabetes who presented with expressive aphasia and a last-known-well time of ≈ 10 hours before presentation. The unenhanced brain CT was negative; however, the CTP study was remarkable for a 15 mL area of hypoperfusion concerning for ischemia without completed infarction in a left MCA branch distribution (Figure 1, Row D). Because the patient was outside the treatment window for IV alteplase and the presenting hospital could not perform mechanical thrombectomy, she was emergently transferred to a comprehensive stroke center for further management. On arrival to that facility, she was reported to have improved significantly. After discussion with a neurointerventionalist, the family ultimately decided to forgo invasive treatment. The patient was eventually discharged home without any neurologic deficits.

Patient 5 is a 53-year-old male with a past medical history of hypertension and heart failure. He presented to the ED with isolated expressive aphasia that began less than an hour before arrival. Based on the perceived resolution of any significant neurologic deficits by the treating emergency physician, brain CTP imaging was not immediately performed. An unenhanced CT of the brain was negative. When the CTA and CTP study were obtained, which was ≈ 1 hour after performance of the unenhanced CT, there was evidence of a right-sided MCA branch vessel occlusion, along with ischemia, without completed infarction, in the expected anatomic location of the occlusion (Figure 1, Row E). Because symptoms had resolved, IV alteplase was not administered and the patient was admitted for observation and medical management. An MRI revealed punctate acute cortical infarcts in the left posterior parietal lobe and left posterior insular cortex. He was discharged on hospital day 3 without any functional deficits.

3 | DISCUSSION

In this case series, 5 patients presented to the ED with isolated aphasia and subsequently underwent advanced neuroimaging per our health care system's "code stroke protocol" to include an unenhanced CT, CTA, and CTP. In each case, the CTP was diagnostically useful because of perfusion patterns that helped distinguish between AIS and seizure, therefore guiding subsequent patient management. Perhaps most important, CTP can spare seizure patients from receiving IV alteplase, which carries the risk of hemorrhagic complications. Alternatively, CTP can also be informative in the setting of ischemia caused by distal MCA branch vessel occlusion, as it may promptly identify perfusion deficits referable to this vascular distribution. Although this site of vascular occlusion is not routinely accessible to mechanical thrombectomy, among arterial occlusions visible on CTA, those involving such vessels are the most amenable to recanalization with IV alteplase.[6] Confirming ischemia without completed infarction in this vascular distribution provides compelling evidence to treat with IV alteplase.

One of the patients in our series had a delay in diagnosis resulting from a failure to recognize *hyper*perfusion during the initial interpretation of the CTP study. Commercially available CT brain perfusion software (eg, iSchemaView RAPID, Menlo Park, California, USA) is optimized to highlight areas of diminished blood flow and volume in the setting of acute ischemic infarct (ie, *hypo*perfusion). Users of such software must be vigilant to the presence of abnormally elevated brain perfusion (ie, *hyper*perfusion), which can be seen with other brain pathology mimicking stroke, such as seizures and brain tumors. A careful evaluation of all CTP parameters shown in Figure 1 may help avoid this interpretative pitfall.[4,5,7,8] Nonetheless, CTP findings associated with seizure are not straightforward, as the entire spectrum of hypoperfusion, normal perfusion, and hyperperfusion can be found. Hyperperfusion is more common during the ictal phase, which can be present without overt tonic clonic activity and was suggested in patients (1 and 2) Conversely, normal perfusion appears most commonly in postictal states with associated neurologic deficits.[7] Although hypoperfusion and hyperperfusion can also be present in such Todd phenomenon patients, seizure-related hypoperfusion patterns are distinct from those of ischemic hypoperfusion.[5] For example, seizure-related hypoperfusion can cross the typical anatomical boundaries of vascular territories and will exist without a concomitant vessel occlusion or stenosis. The presence of hypoperfusion that does not conform to an anatomic vascular distribution should raise the possibility of recent seizure activity, especially if supported by clinical presentation and history of prior brain insult. Additionally, the CTP parameter values associated with seizure can differ from those described for infarcted and ischemic brain tissue.

Although unenhanced CT remains the imaging standard for treatment with IV alteplase,[2] it is possible in the future that as CTP becomes more widely available and data are generated to support a role for it in distinguishing other common stroke mimics (eg, conversion disorder) from ischemic stroke, CTP may emerge as the imaging standard when stroke or stroke mimic are suspected. Although randomized data are

lacking, when normal brain perfusion is present on CTP in a patient with neurologic deficits consistent with a cortical ischemic syndrome, a stroke mimic should be highly entertained.[9] As data suggest an increasing number of stroke mimics are being treated with IV alteplase, perhaps because of campaigns to decrease "door-to-needle" times, changing the imaging standard to CTP may assist in decreasing this concerning trend.[10] Nonetheless, although practical considerations make CTP an appealing first-line diagnostic tool when AIS is in the differential diagnosis, it must be emphasized that an electroencephalogram remains the gold standard for diagnosing seizure. Additionally, it should be noted that AIS can cause nonconvulsive status epilepticus, but this is infrequent.[11]

As our cases demonstrate, CTP can be a helpful tool for differentiating between seizure and stroke in patients presenting to the ED with isolated aphasia. Whether or not CTP can be equally beneficial in identifying other stroke mimics remains unclear. As CTP increasingly is performed to assess patients with suspected acute ischemic stroke, it is likely to replace unenhanced CT as the imaging standard for many clinical scenarios.

CONFLICTS OF INTEREST

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