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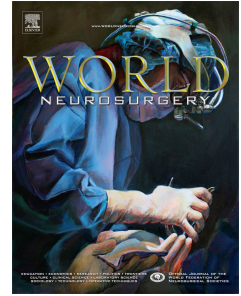
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## **Pituitary apoplexy associated with carotid compression and a large ischemic penumbra**

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**Abstract**

**Background:** Pituitary apoplexy is an acute clinical syndrome caused by pituitary gland hemorrhage or infarction. Rarely, this clinical syndrome is associated with cerebral infarction secondary to compression of an internal carotid artery. We report an unusual case of pituitary apoplexy associated with a cerebral infarct with a large ischemic penumbra.

**Case Description:** The patient presented with headaches and visual disturbance and was found to have pituitary apoplexy. His neurologic exam rapidly deteriorated to include obtundation, ophthalmoplegia, and left hemiplegia. CT perfusion images revealed a right hemispheric infarct with a large ischemic penumbra. Emergent decompressive transsphenoidal resection was performed. The patient had dramatic neurologic recovery, and post-operative imaging revealed salvage of most of the previously identified penumbra.

**Conclusion:** Cerebral perfusion imaging is a useful diagnostic tool for identifying the subset of pituitary apoplexy patients that may benefit from emergent surgical intervention.

## Background

Pituitary apoplexy is an acute clinical syndrome caused by hemorrhage or infarction in the pituitary gland, most commonly in association with a pituitary adenoma<sup>1</sup>. Although this condition was first recognized in 1898<sup>2</sup>, the term pituitary apoplexy was not applied to the clinical syndrome until 1950<sup>3</sup>.

Common signs and symptoms associated with pituitary apoplexy include headache, altered mental status, and acute visual disturbance, including new visual field loss, reduced visual acuity, and diplopia from ophthalmoplegia. These reflect rapid increase in size and pressure of sellar contents with compression of adjacent structures, particularly the optic nerves and chiasm and the internal carotid arteries and extraocular motor nerves of the cavernous sinuses<sup>4</sup>.

Here, we report an unusual case of cavernous internal carotid artery (ICA) compression and subsequent cerebral infarction associated with pituitary apoplexy. Uniquely, initial diagnostic workup included perfusion images revealing a small completed infarct surrounded by a large cerebral volume at risk of additional infarction. Emergent surgical decompression of the sella preserved much of this ischemic penumbra.

## Case Description

The patient is an otherwise healthy 46-year old male who presented to his primary care physician with acute onset of headache and was newly diagnosed with systemic hypertension. After taking anti-hypertensive medication, he developed dizziness, blurry vision, and syncope, prompting presentation to an outside hospital's emergency department. CT scan of the head revealed an expansile, contrast-enhancing sellar mass (Figure 1A), and the patient was admitted for further work-up and management of suspected pituitary apoplexy. He was treated with intravenous fluids and hydrocortisone. Approximately 20 hours later, the patient developed progressive bilateral visual field loss, right third and fourth cranial nerve palsies, and left hemiparesis. An MRI scan showed a large, hemorrhagic sellar mass (Figure 1B), compression of both cavernous ICAs, and lack of carotid flow void in the right cavernous sinus (Figure 1C). Diffusion-weighted sequences revealed scattered punctate areas of restricted diffusion in the right cerebral hemisphere (Figure 2A), consistent with both embolic and watershed infarcts.

In the context of suspected right cavernous ICA compression and clinical and radiographic evidence of left hemispheric ischemia, CT angiogram and perfusion (CTA/P) were performed. The CTA demonstrated laterally displaced but patent ICAs with significant compression-related stenosis, worse on the right than on the left (Figure 2B). CTP revealed an increased time-to-peak ( $T_{max}$ ) throughout most of the right anterior (ACA) and middle cerebral artery (MCA) distributions (Figure 2C). Cerebral blood flow (CBF) and cerebral blood volume (CBV) were decreased in the central portion of this territory, consistent with infarcted tissue, and CBV was increased throughout the remainder of the territory, consistent with ischemic penumbra (Figure 2D-E).

At the time of the CTA/P, which was completed approximately 24 hours after initial symptom onset, and 4 hours after the onset of progressive neurologic deterioration, the patient was intermittently following commands with his right side, but he was hemiparetic on the left. His right pupil became small and non-reactive, and he developed a right sixth nerve palsy. As he became progressively more obtunded, he was intubated, vasopressive medications were initiated to maintain perfusion to the penumbral tissue, and he was transferred to our facility for a higher level of care. By the time of his arrival, now approximately 11 hours after the onset of progressive neurologic deterioration, his pupils had become fixed bilaterally, corneal and

vestibulo-ocular reflexes had been lost, and left-sided hemiparesis had progressed to hemiplegia. The decision was therefore made to proceed to the operating room for emergent surgical intervention.

The sella was approached via an endoscopic, endonasal, transphenoidal route. Opening the sphenoid sinus exposed an expanded, attenuated sellar floor disrupted by tumor (Figure 3A). Bone was removed from the anterior walls of both cavernous sinuses, and Doppler ultrasound was used to confirm the lateral location of the ICAs relative to the intended dural opening. Necrotic, hemorrhagic tumor was extruded as the sellar dura was opened (Figure 3B). The tumor was internally debulked. The pituitary gland, severely compressed, displaced superiorly, and likely necrotic, was identified and preserved. Gross total resection of tumor was achieved without violation of suprasellar arachnoid. The sellar void was filled with abdominal fat and the sellar floor was repaired with a polyethylene-glycol plate and fibrin glue.

The patient was extubated on the first post-operative day. Neurologic exam at that time was notable for right ophthalmoplegia, left sixth nerve palsy, and sluggishly reactive pupils. He briskly followed commands with his right side but had extensor posturing on the left. Post-operative MRI revealed gross total resection of tumor, and MR angiography revealed restoration of flow in the previously stenotic right cavernous ICA (Figure 4A). Diffusion-weighted and FLAIR images demonstrated evolution of right-sided infarction in the centrum semiovale, corona radiata, and subcortical white matter and scattered punctate foci of restricted diffusion bilaterally, consistent with completed watershed and embolic infarcts on the right and embolic infarcts on the left (Figure 4B-C). Most of the right ACA and MCA territory seen to be at risk on pre-operative imaging remained viable, and perfusion imaging now identified no tissue at risk of infarction (Figure 4D-E and Figure 5).

The patient improved clinically over the next few days; by the time of hospital discharge on post-operative day four, he was alert and oriented, was following commands, and had recovered antigravity strength in his left lower extremity, as well as some movement of his right extra-ocular movements. Upon discharge, he was admitted to an acute rehabilitation facility, and was subsequently discharged to home two weeks later. At six-week follow-up, he had recovered nearly full strength in in left lower extremity, with the exception of only antigravity strength in his left hip flexor. His left upper extremity remained paretic, with only trace activation of muscle groups on examination. He had a partial 6<sup>th</sup> nerve palsy, but his cranial nerves were otherwise

intact. He was able to ambulate with the assistance of a cane, and he reported independence in his activities of daily living.

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## Discussion

Pituitary apoplexy associated with cerebral infarction is a rare clinical entity reported 27 times in the literature<sup>5-7</sup>. There are two primary mechanisms by which pituitary apoplexy may lead to cerebral infarction – compression of the intracavernous or supraclinoid ICA by an expanding sellar/suprasellar mass and vasospasm. Focusing specifically on the former, 18 cases have been reported, making this the 19<sup>th</sup> reported case. This is the first reported case in which perfusion imaging was used to identify a cerebral territory at risk of infarction and to guide the decision to emergently decompress an apoplectic sella.

Historically, pituitary apoplexy has been considered a neurosurgical emergency, requiring expedited surgical decompression of the sella to salvage visual and endocrine function<sup>4,8,9</sup>. More recently, however, several case series have supported a role for conservative management in select cases<sup>10-14</sup>. In the largest of these, Bujawansa et al (2015) reported equivalent ophthalmologic and endocrinologic outcomes from a conservative treatment strategy for patients with mild and non-progressive visual disturbance<sup>14</sup>. Other clinical features, including level of consciousness, cranial nerve palsies, and endocrine disturbances, were not found to influence outcome significantly, regardless of treatment strategy. The role of cerebral infarction in determining surgical versus conservative management was not addressed.

Banerjee et al (2015) published a comprehensive review of all case reports of pituitary apoplexy associated with cerebral infarction in the literature at the time of their report. In these 25 cases, vascular compression was implicated in 17 and vasospasm in eight. A comprehensive analysis of these cases revealed a trend toward better outcomes with surgery in patients with vascular compression and with conservative management in patients with vasospasm. Importantly, however, the authors state that the available evidence does not support cerebral infarction alone as an indication for surgery in pituitary apoplexy, but rather, that the indications for surgery in this unique clinical scenario are no different than those for pituitary apoplexy alone. More specifically, they recommend surgical intervention only in the setting of clinically significant or worsening visual field deficit or deteriorating mental status, regardless of the presence of cerebral infarction. Nevertheless, given the small sample size and varied quality of evidence evaluated, the authors appropriately recognize the limitation of their analysis<sup>5</sup>.



In the case reported here, the rationale for surgical intervention was threefold: worsening visual disturbance, deteriorating mental status, and ischemic cerebrum at risk of infarction. Although the previously cited criteria for surgical intervention in pituitary apoplexy were present and the perfusion imaging data thus were not independently determinant of choice of surgery, this case nonetheless documents that perfusion imaging may strengthen the rationale for emergent surgical decompression intended to salvage ischemic tissue at risk of cerebral infarction following pituitary apoplexy. Further investigation is warranted to evaluate the utility of cerebral perfusion imaging in the management of the subset of pituitary apoplexy patients with associated cerebral infarction and otherwise borderline indications for surgical intervention. In addition, future studies should aim to evaluate the relative utility of CT versus MRI perfusion imaging, as both imaging modalities have demonstrated diagnostic utility in the setting of acute ischemia<sup>15-17</sup>, but neither has been specifically studied in the context of pituitary apoplexy.

## Conclusion

Identification of cerebrum at risk of infarction by perfusion imaging has recently been shown to improve outcomes in patients with acute ischemic strokes<sup>18-22</sup>. In this unique case, perfusion imaging data contributed to the decision to emergently decompress the sella in a patient with pituitary apoplexy associated with cerebral infarction and a large ischemic penumbra. Expedited surgical intervention facilitated reperfusion and salvage of the significant territory at risk. In the context of recent claims that cerebral infarction alone is not an indication for emergent surgery in pituitary apoplexy, this case suggests that perfusion imaging may identify a subset of patients with apoplexy-associated cerebral infarction in whom emergent surgical decompression of the sella is strongly indicated.

**Figure 1.** A) Axial CT images of the head obtained soon after presentation reveal a well-circumscribed expansile sellar and suprasellar mass. B) Sagittal T1-weighted MRI images several hours later confirm a large, heterogeneously-enhancing sellar and suprasellar hemorrhagic mass. C) Coronal images at the level of the cavernous sinus reveal mild compression of cavernous carotid flow void on the left and absence of the flow void on the right.

**Figure 2.** A) Diffusion-weighted MRI images demonstrate scattered punctate areas of restricted diffusion in the right cerebral hemisphere, consistent with both embolic and watershed infarcts. B) Coronal CT angiogram images show laterally-displaced ICAs with severe compression-related narrowing of the right cavernous ICA. C) CT perfusion reveals an increased  $T_{\max}$  throughout the right ACA and MCA distributions and associated decrease in D) CBV and E) CBF, predominantly in the watershed region of the right hemisphere, consistent with a small area of core infarct surrounded by a large ischemic penumbra.

**Figure 3.** Intraoperative endoscopic images demonstrate A) erosion of the sellar floor by the sellar tumor, and B) tumor tissue encountered immediately upon opening the dura.

**Figure 4.** A) Post-operative sagittal MRI reveals gross total resection of intrasellar and suprasellar tumor. Post-operative MR angiography demonstrates decompression of and restoration of blood flow through the previously occluded right cavernous ICA. B) Diffusion-weighted and C) FLAIR images demonstrate evolution of right-sided infarcts throughout the centrum semiovale, corona radiata and subcortical white matter, as well as scattered punctate foci of restricted diffusion, consistent with completed watershed and embolic infarcts on the right and embolic infarcts on the left. D and E) Perfusion images demonstrate resolution of prolonged right-hemispheric  $T_{\max}$ .

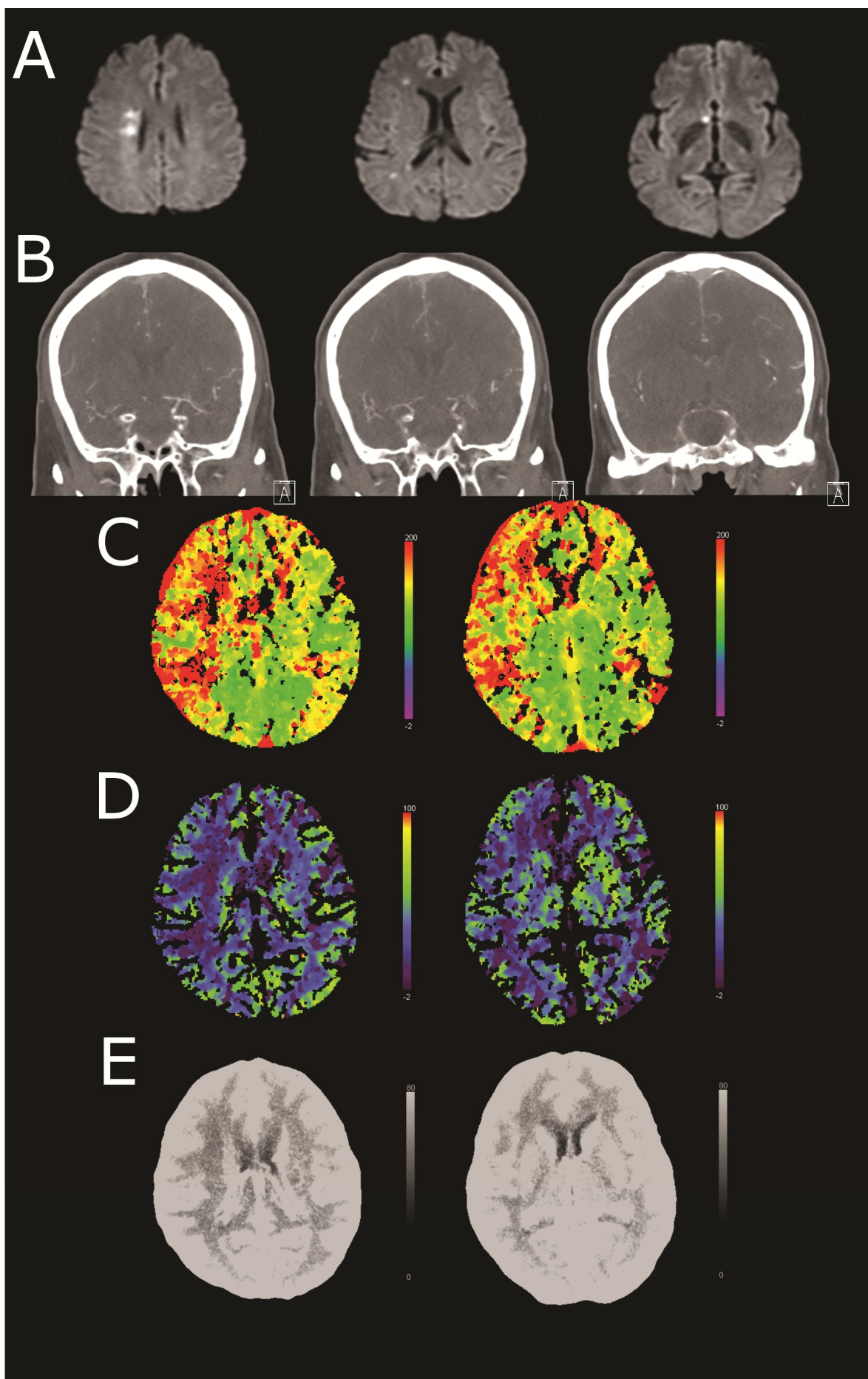
**Figure 5.** RAPID Summary demonstrating salvage of the ischemic penumbra that had been seen on pre-operative imaging.

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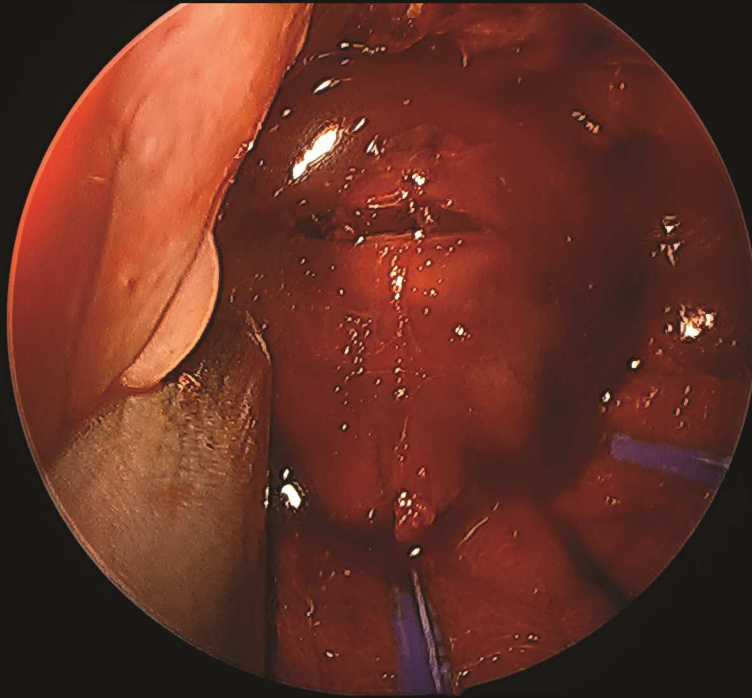
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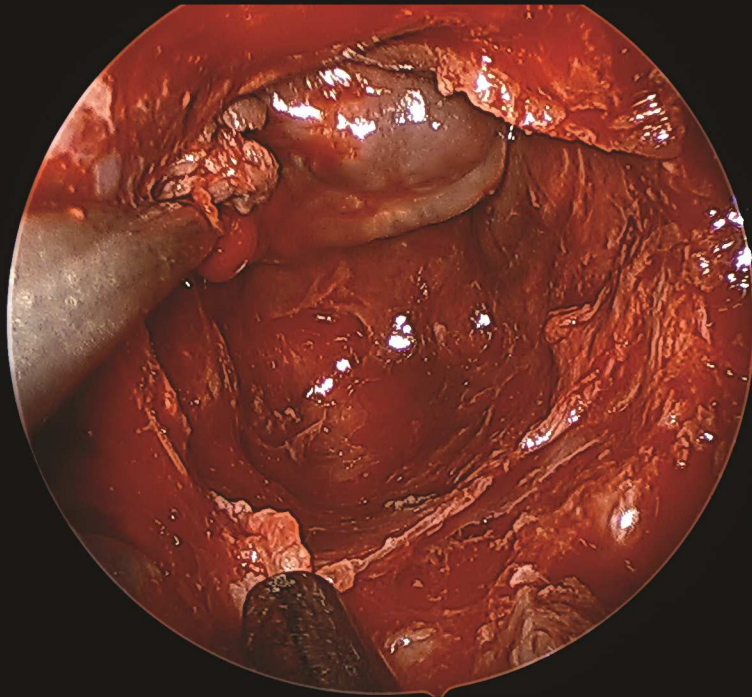




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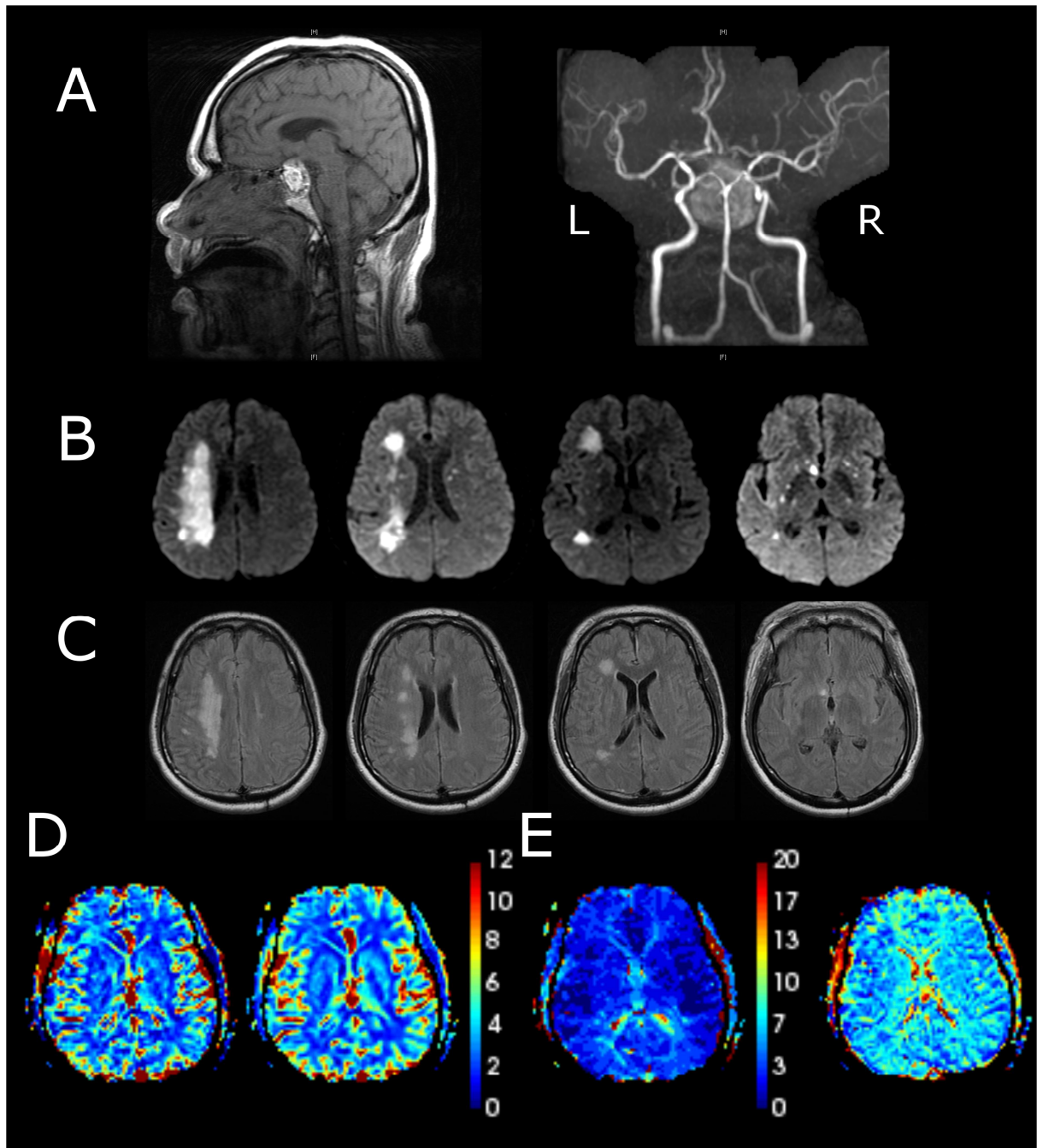


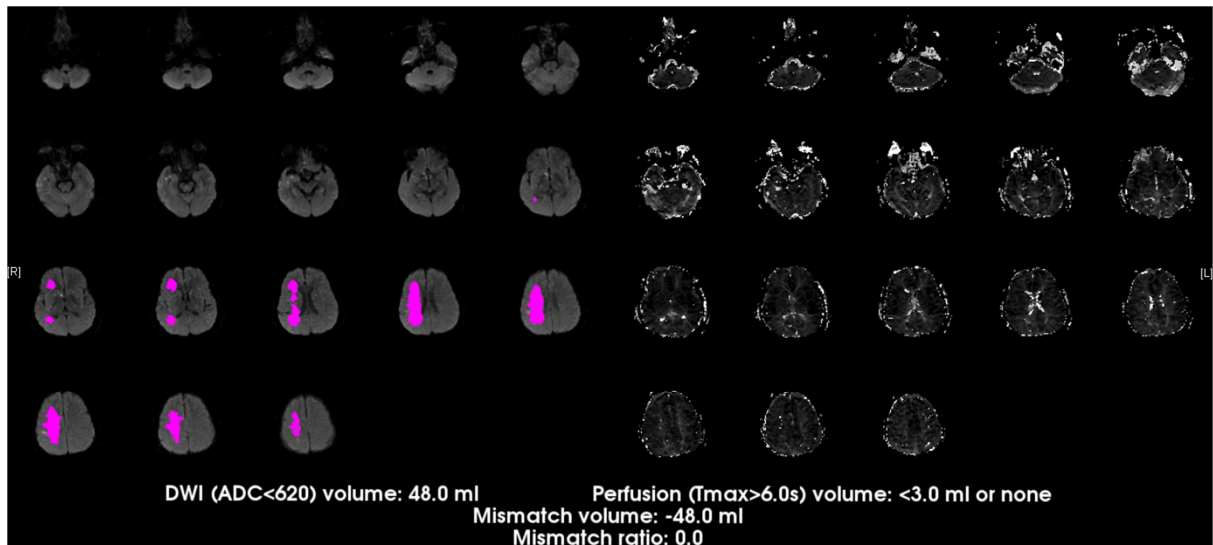
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## Abbreviation List:

ICA, internal carotid artery

CTA/P, CT angiogram and perfusion

$T_{\max}$ , time-to-peak

ACA, anterior cerebral artery

MCA, middle cerebral artery

CBV, cerebral blood volume

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**Highlights:**

1. Although pituitary apoplexy has historically been considered a surgical emergency, recent literature supports a conservative management approach in select patients.
2. In rare cases, pituitary apoplexy may be associated with cerebral infarction. The underlying mechanism may be either vasospasm or direct vascular compression.
3. In patients with pituitary apoplexy associated with compression of the adjacent internal carotid artery, perfusion imaging may be utilized to evaluate for ischemic penumbra, which would justify emergent surgical decompression in order to salvage ischemic tissue at risk of cerebral infarction.