Imaging of Important Causes of Brain Stem Enlargement: Beyond the Low-Grade Glioma

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After participating in this activity, the diagnostic radiologist should be better able to diagnose by imaging the many important causes of brain stem enlargement in addition to the more common low-grade glioma.

Key words: Brain Stem Enlargement, Imaging of Glioma Mimics

The brain stem is a critical part of the central nervous system (CNS); it houses the cranial nerve nuclei and cardio-pulmonary centers, and serves as a conduit for descending tracts into the spinal cord. The brain stem is located in the posterior fossa, and anatomically is composed of the midbrain (most rostral part of the brain stem), pons, and medulla. Gliomas are the most common cause of brain stem enlargement. However, a variety of other pathologic processes such as infection, metastasis, inflammation or demyelination, hemorrhagic lesions, posterior reversible encephalopathy syndrome, and hypertrophic olivary degeneration also may involve the brain stem, and occasionally cause diagnostic dilemmas. In some instances, combining the clinical presentation with the radiologic findings may even obviate the need for biopsy of this critical region of the central nervous system.

Imaging Findings

Brain Stem Glioma. The low-grade brain stem glioma is the most common primary brain stem neoplasm. These lesions most commonly occur in the pons, and typically exhibit a diffusely infiltrating pattern of growth. In some cases, brain stem gliomas will show an exophytic growth pattern, which is quite specific for this lesion. Another characteristic imaging feature of brain stem gliomas is the tendency to engulf the basilar artery as the lesion grows. Brain stem gliomas are usually slow-growing lesions, especially in the tectal region; however, gradual compression of the aqueduct of Sylvius or fourth ventricle with resultant hydrocephalus may be encountered. Occasionally, cysts, necrosis, or hemorrhage may occur within the gliomas. Calcification, however, is quite rare and should prompt consideration of an alternative diagnosis. On MRI, brain stem gliomas are usually T1-hypointense with corresponding T2-weighted/fluid-attenuated inversion recovery (FLAIR) hyperintensity, with the area of abnormal T2-weighted/FLAIR hyperintensity more extensive than the area of abnormal T1-hypointense signal (Figure 1). On contrast-enhanced MRI, low-grade gliomas show minimal to no enhancement with the exception of an exophytic component, which can enhance prominently. Higher grade brain stem gliomas will show more extensive enhancement. A pertinent clinical feature of brain stem gliomas is that they occur primarily in the pediatric population.

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Abscess. Pyogenic abscesses may present as solitary brain stem lesions—a classic example is an abscess caused by *Listeria monocytogenes*. Similar to abscesses elsewhere in the brain, the MR appearance of a brain stem pyogenic abscess is quite characteristic with most abscesses presenting as ring-enhancing lesions with restricted diffusion centrally within the lesion (Figures 2 and 3). Vasogenic edema and mass effect are common, and the rim of the abscess may show T1-hyperintensity and T2-hypointensity presumably related to the presence of free radicals or collagen. Diagnostic confusion may arise when abscesses in the brain stem fail to show central restricted diffusion. This is especially true in abscesses caused by *Toxoplasma gondii*, the most common space-occupying central nervous system mass lesion in patients with AIDS. Although toxoplasmosis abscesses usually show ring enhancement and are associated with vasogenic edema and mass effect, there can be a conspicuous absence of central restricted diffusion. Instead, a classic finding that may be seen in toxoplasmosis abscesses, but not in gliomas, is the so-called target sign, in which a small eccentric nodule is present along the inner margin of the ring-enhancing lesion. Another finding that may be seen in the toxoplasmosis abscess is T1-hyperintense borders, presumably related to subacute mural hemorrhage. The T1-hyperintense rim may also cause a targetoid appearance of peripheral restricted diffusion on diffusion-weighted imaging, also possibly related to mural hemorrhage. A clinical distinguishing factor is that toxoplasmosis usually is seen in patients with AIDS, and most patients will have positive polymerase chain reaction testing of peripheral blood samples for *T. gondii*.

Metastases. Metastases are the most common supratentorial and infratentorial neoplasm in adults, and rarely may present as a solitary brain stem mass. Also rarely, a solitary brain stem metastasis can represent the first sign of malignancy in a patient. About 20% of patients with cancer will develop cerebral metastases. The most common primary tumor that metastasizes to the brain is lung cancer. Aggressive primary brain malignancies such as glioblastoma multiforme also may occur as an isolated lesion in the brain stem, but they are far less common than metastatic disease (Figure 4).

Brain stem metastatic lesions can demonstrate variable signal intensity on T1-weighted, T2-weighted, FLAIR, and...
gradient MR images depending on tumor histology. Metastatic lesions usually enhance, either homogeneously or in a ring-enhancement pattern (Figure 5). Vasogenic edema out of proportion to the size of the lesion is another feature of a metastatic lesion. In any patient with a solitary ring-enhancing lesion in the brain stem, further work-up with contrast-enhanced CT of the chest, abdomen, and pelvis is required to search for a primary malignancy. An important clinical feature that can distinguish metastasis from glioma is the age of the patient; gliomas tend to occur in children whereas brain metastases occur mostly in adults. Given the high prevalence of metastatic disease in adults, metastasis should always be considered in the differential diagnosis of a brain stem mass.

**On MRI, brain stem metastatic lesions usually enhance, either homogeneously or in a ring-enhancement pattern.**

**Demyelinating Diseases.** Demyelinating diseases are common in the United States, and certain forms can cause isolated brain stem involvement with confusing imaging findings, even resulting in unnecessary biopsy in some cases. Acute disseminated encephalomyelitis (ADEM) in particular has a high rate of brain stem involvement (up to 50% in some studies), and isolated cases involving the brain stem have been reported. On MRI, ADEM typically shows perilesional edema and mass effect. An imaging feature that can distinguish ADEM from gliomas is the presence of an incomplete ring of peripheral enhancement, a finding that is characteristic of demyelinating processes such as ADEM. Isolated brain stem ADEM is a challenging diagnosis to make, and one that often is only made in retrospect as new lesions do not occur in monophasic ADEM.

The tumefactive form of multiple sclerosis also may be difficult to distinguish from a glioma. On MRI, tumefactive
lesions from glioma is CT hypoattenuation corresponding to the areas of MR enhancement in tumefactive demyelinating lesions; this finding is reportedly highly specific for tumefactive demyelinating lesions. Absence of recurring episodes of demyelination usually will distinguish monophasic ADEM from multiple sclerosis.

Acute demyelinating encephalomyelitis (ADEM) has a high rate of brain stem involvement (50% in some studies); occasionally ADEM is isolated to the brain stem.

Vascular Lesions. Cavernomas. Cavernomas are vascular lesions that often occur in the brain stem, most commonly the pons; and they may only come to clinical attention incidentally during work-up for a different reason. Multiple cavernomas are present in about 50% of cases. Characteristic MRI findings of cavernomas include a rim of hypointensity most pronounced on T2-weighted imaging and susceptibility-weighted sequences as a result of hemosiderin staining of adjacent brain parenchyma from prior episodes of subclinical hemorrhage (Figure 8). Larger lesions may have a heterogeneous appearance with areas of central T1- and T2-hyperintensity (so-called popcorn appearance), related to subacute blood products. Surrounding T2-hyperintensity may be seen with vasogenic edema associated with acute hemorrhage, whereas T1-hyperintensity within the lesion may reflect methemoglobin from subacute hemorrhage. Cavernomas may be associated with multiple sclerosis usually presents as a large white matter lesion with no significant mass effect or edema (Figures 6 and 7). One finding that may distinguish tumefactive demyelinating

Figure 6. Brain stem multiple sclerosis. Axial, T2-weighted MR image at the level of the pons shows increased signal in the left pons (arrow). This 45-year-old woman had known multiple sclerosis and presented with new right leg weakness, corresponding to the area of MR signal abnormality seen in the pons, which was a new finding compared with prior MR studies.

Figure 7. Multiple sclerosis. Sagittal, FLAIR MR image of the same patient in Figure 6 shows multiple lesions at the callosal-septal region compatible with multiple sclerosis.

Figure 8. Cavernoma. Axial, T2-weighted MR image shows a well-circumscribed mass in the pons with heterogeneous T2-hyperintense signal centrally and a thin rim of surrounding T2-hypointensity, findings classic for a cavernoma. Surrounding the lesion is an area of T2-hyperintensity within the pons, reflecting vasogenic edema (arrow).
with developmental venous anomalies, which are normal variations in the drainage of the white matter. Developmental venous anomalies usually occur in the vicinity of the cavernomas. The MR signal characteristic of cavernomas is a key imaging feature that should distinguish these lesions from a glioma.

On T2-weighted MR images, cavernomas of the brain stem, usually involving the pons, show a thin rim of hypointensity about the lesion.

**Posterior Reversible Encephalopathy Syndrome.** Posterior reversible encephalopathy syndrome (PRES) is a type of encephalopathy characterized by widespread areas of vasogenic edema in the brain, with a predilection for the parietal and occipital lobes. The pathophysiology of PRES is thought to be related to sparse sympathetic innervation of the posterior circulation, which results in impaired vascular autoregulation and vulnerability to sudden or sustained increases in blood pressure. On MRI, confluent areas of cortical and subcortical vasogenic edema in the distribution of the posterior circulation (occipital lobes, brain stem) are characteristic of PRES (Figure 9). The areas of abnormal T2-weighted/FLAIR signal abnormality related to uncomplicated PRES usually do not enhance or show restricted diffusion, but if untreated these lesions may go on to infarction or hemorrhage. Isolated brain stem involvement by PRES is a rare but a well-recognized occurrence, and PRES is reported to occur in the brain stem in about 13% of patients.\(^6\) Isolated brain stem involvement in PRES can be confused with a glioma on MRI. Clinical findings that would support the diagnosis of PRES include a history of renal transplantation or exposure to cyclosporine used to inhibit rejection after any organ transplant, untreated hypertensive urgency (i.e., systolic pressure >180 mm Hg and diastolic pressure >120 mm Hg without significant signs of end-organ damage), and eclampsia.

Osmotic demyelination in the brain stem, presumably because of serum sodium abnormalities, could potentially have a similar appearance to PRES and gliomas, but characteristic sparing of the corticospinal tracts in the pons, lack of mass effect, and the clinical history should readily distinguish osmotic demyelination from PRES and a brain stem glioma (Figure 10).

On MRI, confluent areas of vasogenic edema in the distribution of the posterior circulation (occipital lobes and brain stem) are characteristic of PRES.

**Hemorrhage.** Hemorrhage in the brain stem is seen most commonly in the setting of hypertension, with the pons being the most common location in the brain stem. Brain stem hemorrhage also may be seen in the setting of trauma. The diagnosis of acute hemorrhage is usually straightforward on CT (Figure 11), and is usually not confused with a brain stem glioma (unless the glioma is hemorrhagic, which can occur).

Patients who present with a resolving hematoma on MR
imaging may pose some difficulty, as resolving hematomas may be associated with ring enhancement and restricted diffusion at the periphery of the lesion. Follow-up imaging is helpful in these cases, as hemorrhage resolves whereas a tumor does not.

**Infarction.** Acute pontine infarction is usually a straightforward diagnosis, with restricted diffusion (Figure 12) and abnormal T2-weighted/FLAIR-hyperintense signal seen within the pons. Depending on the timing of the MR scan during the patient’s clinical course, subacute infarction may produce a slightly more challenging picture. There may be brain stem expansion and mass effect from edema, lack of restricted diffusion, and enhancement may occur after gadolinium administration. Hemorrhagic transformation can occur, further confusing the MRI findings. Short-term follow-up MRI will be helpful as infarcts show gradual resolution of edema, mass effect, and enhancement whereas gliomas remain stable or progress. An important clinical clue is the neurologic status of the patient. Massive brain stem infarction is not a subtle clinical diagnosis, and most patients are comatose or nearly so. In contradistinction, patients with brain stem gliomas may have headaches, mental status changes, and long-tract signs, but overall experience a more gradual decline in their neurologic status.

**Hypertrophic Olivary Degeneration.** A unique form of transsynaptic degeneration seen in the brain stem is hypertrophic olivary degeneration, in which disruption of the dentato-rubro-olivary pathway produces hypertrophy of the inferior olivary nucleus (Figure 13). The 3 components of the dentato-rubro-olivary pathway (the triangle of Mollaret) are the inferior olivary nucleus, red nucleus, and dentate nucleus of the cerebellum. MR findings in hypertrophic olivary degeneration include enlargement of the inferior olivary nucleus with abnormal T2-weighted/FLAIR-hyperintense signal. Enhancement is not usually a feature of hypertrophic olivary degeneration. Clinically, patients may present with ocular or palatal myoclonus and tremor. Remote hemorrhage or encephalomalacia in the expected location/pathway of the dentato-rubro-olivary pathway may be seen in addition to an enlarged inferior olive, and these additional findings increase the diagnostic confidence for hypertrophic olivary degeneration.

**Extra-axial Masses.** Occasionally, large extra-axial masses in the posterior fossa may cause apparent brain stem enlargement if there is mass effect on and edema within the brain stem, particularly on CT. MRI often is helpful in delineating a sharp demarcation between the extra-axial mass and the brain stem, especially on contrast-enhanced sequences (Figure 14).
Conclusion

This CME activity emphasizes that knowledge of diseases that can enlarge the brain stem and potentially can be confused with a glioma will aid the radiologist in making the correct diagnosis and minimize the risk to the patient by directing the clinical team toward the most appropriate next step of management. Table 1 emphasizes the key imaging and clinical features of the various lesions causing brain stem enlargement.

References


Table 1. Key Imaging and Clinical Features of Lesions Causing Brain Stem Enlargement

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Key Imaging and/or Clinical Discriminators</th>
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<tbody>
<tr>
<td>Glioma</td>
<td>Exophytic growth pattern</td>
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<td></td>
<td>May engulf basilar artery</td>
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<td></td>
<td>Usually occurs in pediatric population</td>
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<tr>
<td>Pyogenic abscess</td>
<td>Ring-enhancing lesion with central restricted diffusion</td>
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<td>Patients may be febrile, with history of endocarditis or IV drug use</td>
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<tr>
<td>Toxoplasmosis abscess</td>
<td>No central restricted diffusion</td>
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<td>“Target sign” on contrast-enhanced MRI</td>
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<tr>
<td>Metastasis</td>
<td>May have a remote or current history of malignancy</td>
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<td></td>
<td>Concurrent scanning of thorax may reveal unsuspected primary tumor</td>
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<tr>
<td>Demyelinating disease</td>
<td>Incomplete ring of enhancement on contrast-enhanced MRI</td>
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<td></td>
<td>CT hypoattenuation of enhancing MR lesions in tumefactive demyelination</td>
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<tr>
<td>Cavernoma</td>
<td>T2-hypointense rim is characteristic</td>
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<td></td>
<td>Patients may be associated with a developmental venous anomaly</td>
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<tr>
<td>PRES</td>
<td>Confluent subcortical/cortical vasogenic edema in posterior circulation</td>
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<td>History of hypertensive urgency, eclampsia, organ transplant</td>
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<tr>
<td>Osmotic demyelination</td>
<td>Abnormal T2-weighted/FLAIR-hyperintense signal in pons that spares descending corticospinal tracts</td>
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<td></td>
<td>Patients may have evidence of serum sodium abnormalities</td>
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<tr>
<td>Hypertrophic olivary degeneration</td>
<td>Enlarged inferior olivary nucleus with abnormal T2-weighted/FLAIR signal</td>
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<td>Evidence of remote injury may be present in dentate or red nuclei</td>
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PRES, posterior reversible encephalopathy syndrome.

Figure 15. See quiz question 4.
CME QUIZ: VOLUME 38, NUMBER 8

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1. Which one of the following is the most common intra-axial malignancy of the posterior fossa in adults?
   A. Medulloblastoma
   B. Glioblastoma multiforme
   C. Ependymoma
   D. Metastasis
   E. Meningioma

2. A 26-year-old man with AIDS develops a brain stem pyogenic abscess caused by Toxoplasma gondii. The MR features of his abscess may be expected to include a mass lesion with all of the following, except
   A. central restricted diffusion
   B. mass effect
   C. associated vasogenic edema
   D. ring enhancement

3. Which one of the following is the probable cause of posterior reversible encephalopathy syndrome?
   A. Untreated hypertensive urgency
   B. Hyponatremia
   C. Hypercalcemia
   D. Dehydration
   E. Hypothyroidism

4. Figure 15 on page 7 is an axial, T2-weighted head MR image of a 45-year-old man for evaluation of recent severe head trauma. In addition to the obvious lesion in the pons, what other lesion should be suspected in this patient?
   A. Dural arteriovenous fistula
   B. Brain stem glioma
   C. Developmental venous anomaly
   D. Intracranial aneurysm
   E. Frontal sinus osteoma

5. The most likely cause of vasogenic edema in the pons that spares the descending corticospinal tracts is
   A. ischemia or infarction
   B. osmotic demyelination
   C. metastatic disease
   D. pyogenic abscess
   E. necrotic tumor

6. Which one of the following is the most likely cause of a brain stem lesion that exhibits an exophytic growth pattern that engulfs the basilar artery on MRI?
   A. Abscess
   B. Metastasis
   C. PRES
   D. Glioma
   E. Infarction

7. Which one of the following brain structures is involved in hypertrophic olivary degeneration?
   A. Corpus callosum
   B. Mammillary body
   C. Pineal gland
   D. Inferior olivary nucleus
   E. Hypothalamus

8. Which one of the following is the most common primary brain stem neoplasm in children?
   A. Glioblastoma multiforme
   B. Ependymoma
   C. Low-grade glioma
   D. Astrocytoma
   E. Medulloblastoma

9. The cause of the central restricted diffusion on MRI of an abscess in the brain stem is
   A. necrosis
   B. pus
   C. vasogenic edema
   D. calcification
   E. gas

10. Which one of the following is the most common primary malignancy in adults that metastasizes to the brain stem?
    A. Kidney
    B. Colorectal
    C. Lung
    D. Breast
    E. Liver