6 Central Pontine Myelinolysis

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INTRODUCTION

Central pontine myelinolysis (CPM) was originally described by Adams and colleagues in 1959. He first detailed the entity in a group of malnourished and alcoholic patients. Further studies and advancement in medicine have shown that CPM most commonly results from the rapid correction of serum sodium in hyponatremic patients. The pathophysiology of CPM is currently not fully understood. However, it has been shown that CPM results from the physiologic imbalance of osmoles within the brain. Many other conditions associated with disorders of solute metabolism, including inappropriate antidiuretic hormone secretion syndrome, malnutrition, psychogenic polydipsia, liver transplantation, and dialysis disequilibrium syndrome, share the common finding of alterations in cellular volume control. The imaging findings of CPM correspond to locations within the brain (in this case the pons) that are most susceptible to osmotic stress, as do the findings of extrapontine myelinolysis (EPM). Together, CPM and EPM constitute the osmotic demyelination syndromes (ODSs).

The central pons is the most commonly identified site of involvement in ODSs. A necropsy series of 58 cases identified isolated central pontine involvement in 50% of cases. The other 50% of cases had either central pontine with extrapontine (30%) or isolated extrapontine (20%) involvement (Fig. 6.1). Histologic sites of EPM have been described within the cerebellum, lateral geniculate body, external capsule, extreme capsule, hippocampus, putamen, cerebral cortex/subcortex, thalamus, and caudate, in descending order of frequency. Importantly, extrapontine involvement is usually symmetric.

Myelinolysis results in preservation of local neurons and axons in the effected sites without an inflammatory reaction, as evident by paucity of lymphocytes on histologic specimens. These findings help to differentiate myelinolysis from multiple sclerosis or infarction. Histologic specimens have also demonstrated splitting and

vacuolization of myelin sheaths, which are subsequently taken up by macrophages.

IMAGING PATTERN

Classically, CPM demonstrates T2 hyperintensity within the central pons, with peripheral pontine sparing, as well as sparing of the corticospinal tracts. This results in a "trident" or "bat wing" appearance on axial images (Fig. 6.2).

EPM also causes T2 hyperintensity but in typically symmetric extrapontine locations (listed previously) (Fig. 6.3).

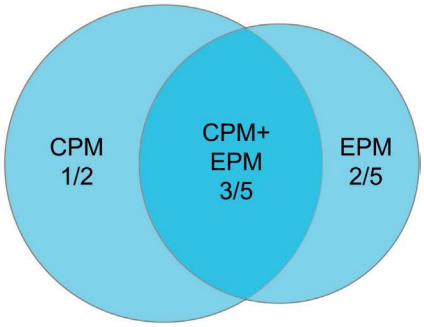

Figure 6.1. Relative proportions of central pontine myelinolysis *(CPM)*, extrapontine myelinolysis *(EPM)*, and CMP with EPM. *(From: Martin RJ. Central pontine and extrapontine myelinolysis: the osmotic demyelination syndromes.* J Neurol Neurosurg Psychiatry. *2004;75[suppl 3]:iii22–iii28.)*

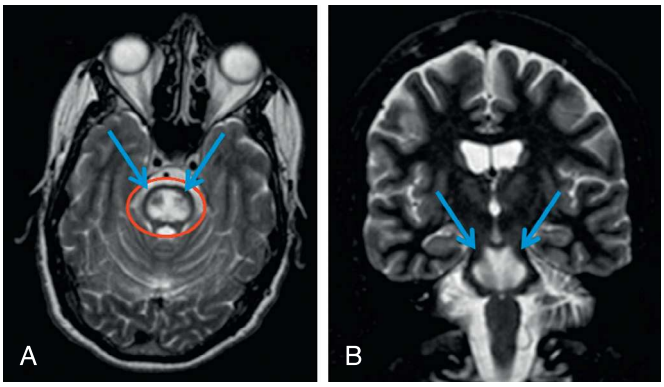

Figure 6.2. Central pontine myelinolysis—axial and coronal T2-weighted images show T2 hyperintense signal involving the central pons with peripheral pontine sparing *(red circle)* and sparing of the corticospinal tracts *(blue arrows)*. This pattern of involvement results in a T2 "bat wing" or "trident" appearance on axial imaging.

Conventional CT and MR imaging findings typically lag behind the clinical manifestations of CPM. Although CT may show late low-attenuation changes in the central pons in some cases, serial MR imaging is the most appropriate method to evaluate patients with clinically suspected CPM. One case series of two patients proposes that T2 hyperintensity in extrapontine locations may predate central pontine T2 hyperintensity in some patients.

TEMPORAL EVOLUTION: OVERVIEW

Variable imaging features may be evident in osmotic demyelination, depending on when the process is imaged. In particular, the acute, subacute, and chronic imaging characteristics differ. Furthermore, some variable imaging features, including the diffusion-weighted imaging (DWI) and postcontrast imaging characteristics, may be present or absent according to phase.

Acute Phase

Several reports have suggested that DWI images might facilitate the early diagnosis of CPM. However, the exact frequency and onset in time of the appearance of these abnormal findings in relation to symptoms is still unclear.

When present, DWI signal hyperintensity may begin to appear within 24 to 72 hours after onset of symptoms. ADC signal varies from hypointensity (restricted diffusion) when intramyelinolytic cytotoxic edema predominates to hyperintensity if vasogenic edema related to myelin destruction predominates. These competing processes result in variable DWI and ADC signal profiles that may differ between patients and may differ during the course of the disease in an individual patient as the balance of cytotoxic and vasogenic processes shifts.

Several case reports, such as that of Ruzek et al., have shown that early DWI changes are a common finding in CPM/EPM. However, others have reported that these signal changes may not regularly precede tissue changes described on conventional MRI sequences. One report suggests that DWI can be normal in the acute stage of CPM, even within 1 week after the onset of symptoms. Graff-Radford et al. reported that 21% of their patients showed no abnormalities on early MRI; however, all patients had characteristic pontine signal abnormality on T2-weighted images on repeat imaging. This finding is in agreement with a more recent report that early MRIs were normal in 25% of cases.

Early in the diagnosis of CPM/EPM, faint hyperintensity on T2-weighted and fluid-attenuated inversion recovery (FLAIR) imaging in characteristic locations may be the only finding. T1-weighted images usually show normal to hypointense T1 signal. Postcontrast enhancement due to blood-brain barrier disruption may also occur at this stage.

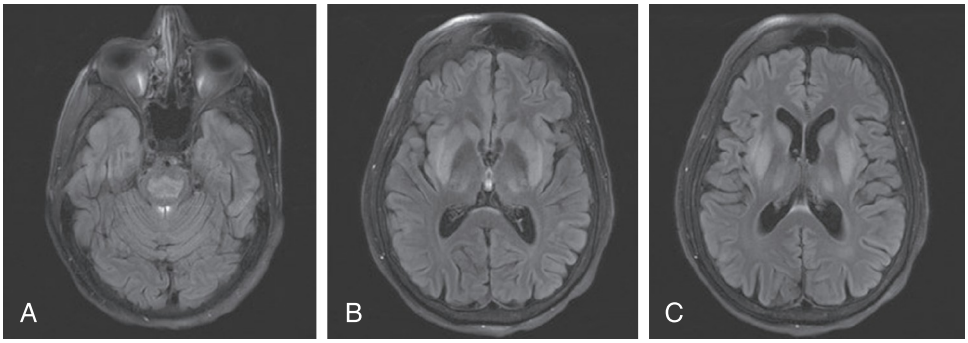

Figure 6.3. Central pontine and extrapontine myelinolysis—axial FLAIR images at the level of the pons (A) and basal ganglia (B and C) demonstrating classic central pontine pattern of involvement, as well as multiple symmetric sites of extrapontine involvement including the basal ganglia, thalami, and external capsules in a patient with history of alcohol abuse presenting with hyponatremia.

Subacute Phase

Multiple case reports, such as that of Cramer et al., show development of increasing T2 hyperintensity within the central pontine region a week after the development of symptoms, with variable expansion of the pons. DWI images may still show increased signal with corresponding decreased signal on the ADC map. Alternatively, follow-up imaging may show normalized or elevated ADC values, suggesting the disappearance of cytotoxic edema in the later phases despite persistent increased signal on T2-weighted images due to vasogenic edema and/or gliosis. Similarly, enhancement should resolve in the subacute period.

Chronic Phase

Usually, the degree and extent of pontine hyperintensity on T2-weighted images decrease a few weeks after the onset of symptoms. Case reports have shown that the milder the signal on T2-weighted images beyond the subacute phase, the better the long-term outcome.

The classic configuration of "trident" or "bat wing" pontine T2 hyperintense signal abnormality with sparing of the corticospinal tracts and peripheral pons persists, although the lesion is smaller in size compared with initial imaging due to volume loss. Corresponding T1 hypointensity without enhancement typically also persists.

These findings are summarized in Table 6.1, as well as in two MRI cases of CPM (Figs. 6.4 and 6.5).

MIMICS AND DIFFERENTIAL DIAGNOSIS

1. Chronic ischemic changes from microangiopathic disease: These lesions may involve a similar location as CPM but typically do not have restricted diffusion and do not spare the corticospinal tracts. In addition, this entity almost always has associated supratentorial white matter changes (Fig. 6.6).
2. Acute pontine infarct, acute disseminated encephalomyelitis, and demyelination: These lesions may have a similar appearance to CPM but typically are asymmetric and may not spare the peripheral pons and corticospinal tracts (Fig. 6.7).
3. Paraneoplastic processes: These lesions are rare; however, they may be central in the pons and effect extrapontine sites. These lesions will typically resolve with treatment of the associated primary cancer (Fig. 6.8).
4. Brainstem hemorrhage: These hemorrhages demonstrate signal characteristics and evolution as described in the hemorrhage chapter (see Chapter 1) and usually produce susceptibility effects consistent with blood products (Fig. 6.9).
5. Gliomas: typically seen in the pediatric population, with marked pontine expansion that engulfs the basilar artery.

TABLE 6.1 Summary of Central Pontine Myelinolysis Evolution on Imaging

MR Sequence	Acute CPM	Subacute CPM	Chronic CPM
DWI	↑ or —	↑↑	—
ADC	↓ or—or ↑	↓ or—or ↑	↑
T2/FLAIR	↑ or —	↑↑	↑
T1	↓ or —	↓↓	↓

ADC, Apparent diffusion coefficient; *CPM*, central pontine myelinolysis; *DWI*, diffusion-weighted imaging; *FLAIR*, fluid-attenuated inversion recovery.

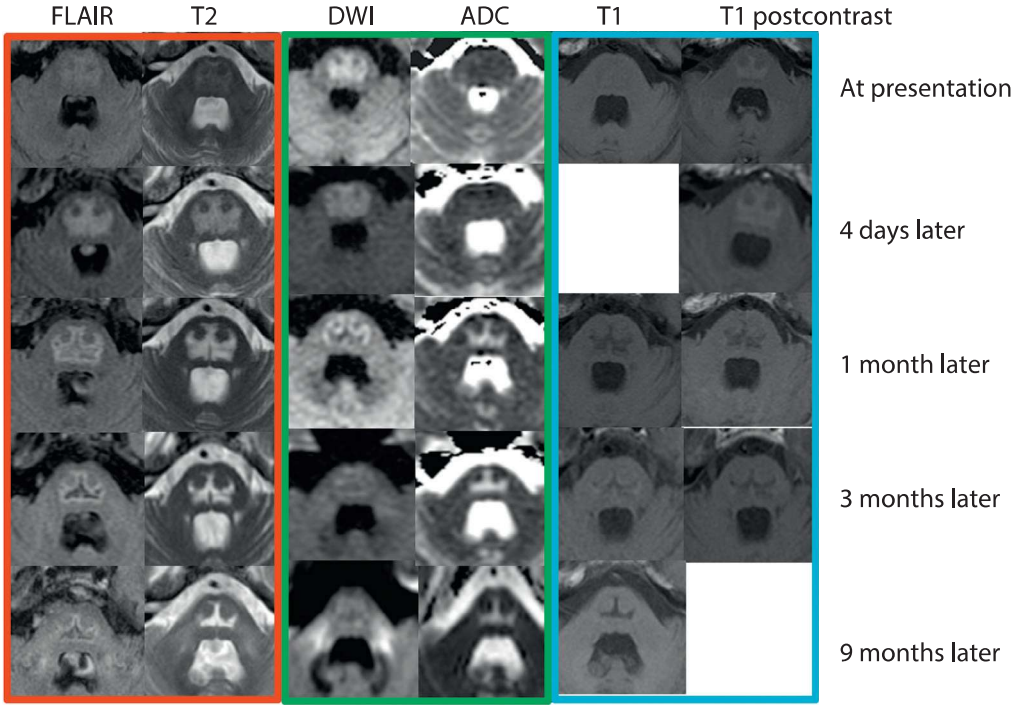

Figure 6.4. Mental status change following orthotopic liver transplant. T2 and FLAIR images demonstrate an initial increase in abnormal signal between presentation and the 4-day follow-up study with progressive decrease in signal and size of abnormality involving the central pons over time *(red box)*. Diffusion-weighted imaging *(DWI)* and apparent diffusion coefficient *(ADC)* images demonstrates mildly restricted diffusion early that is replaced by T2 "shine-through" effect in later stages *(green box)*. In addition, active wallerian degeneration is seen to involve the middle cerebellar peduncles at 9-month follow-up related to pontocerebellar disconnection. T1 and T1 postcontrast images demonstrate subtle early-phase enhancement that resolves in later stages *(blue box)*. There is progressive decrease in size of T1 hypointensity corresponding to sites of T2 signal abnormality in the later stages suggesting volume loss.

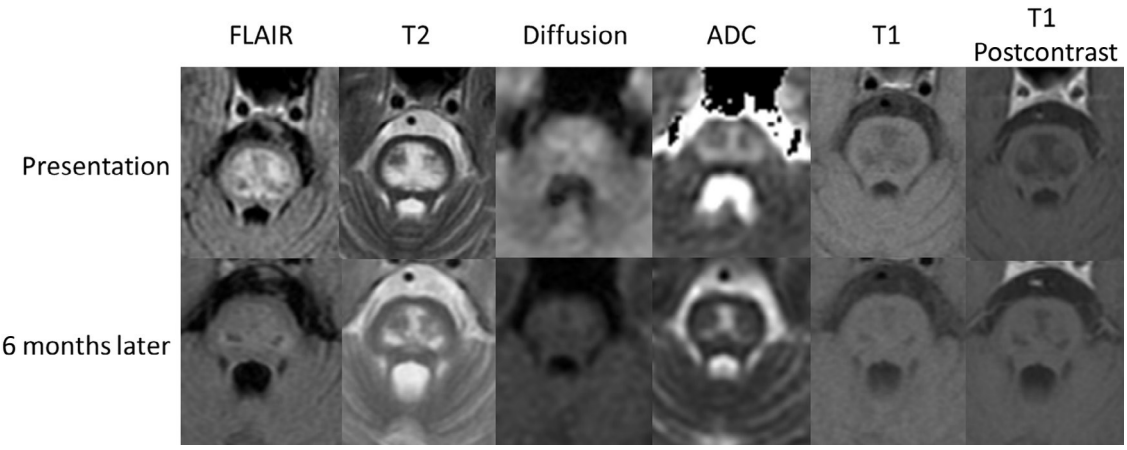

Figure 6.5. Acute and chronic phases of central pontine myelinolysis. *Left to right:* Axial FLAIR, T2, diffusion, apparent diffusion coefficient *(ADC)*, T1, T1 postcontrast. There is "trident" T2 hyperintensity and T1 hypointensity sparing the peripheral pons and corticospinal tracts. There is subtle DWI hyperintensity with ADC hyperintensity at presentation. Six months later, there is diminished T2 and ADC hyperintensity and T1 hypointensity, pontine volume loss, and resolved DWI hyperintensity. No contrast enhancement is seen at either time point.

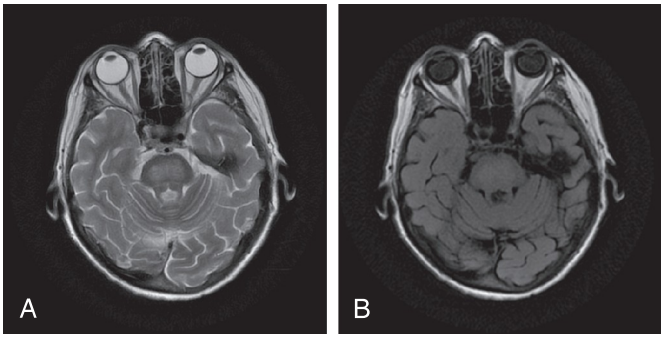

Figure 6.6. Small vessel microangiopathic changes of the pons. (A) Axial T2 and (B) axial FLAIR. Chronic microangiopathic changes involving the central pons in an asymptomatic patient. Supratentorial chronic microangiopathic changes were also seen. Note involvement of the corticospinal tracts.

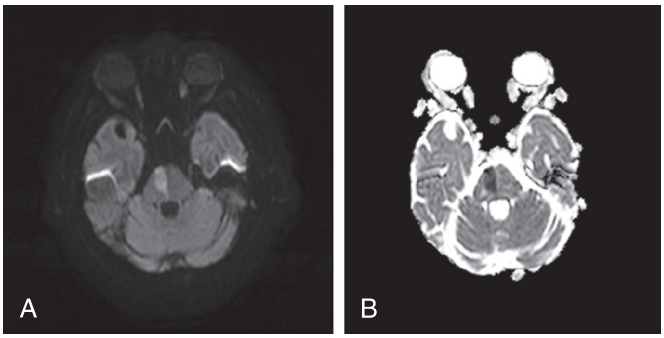

Figure 6.7. Acute pontine infarct (A) axial DWI and (B) axial ADC. The patient presented with acute left-sided weakness and slurred speech. An acute right paramedian pontine infarct demonstrates restricted diffusion on DWI and ADC images. Note asymmetry of the lesion compared with central pontine myelinolysis.

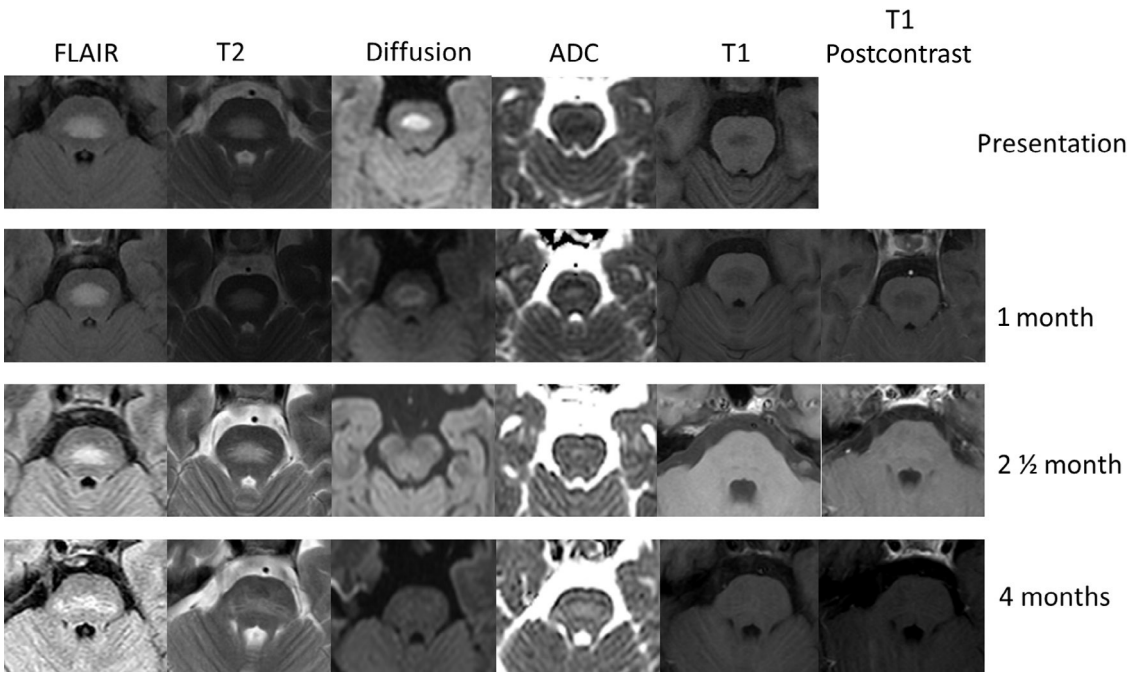

Figure 6.8. Paraneoplastic encephalopathy patient with a history of ovarian carcinoma presenting with encephalopathy with marked improvement in mental status following chemotherapy. (Row 1) At presentation, central pontine T2 hyperintense signal with restricted diffusion and T1 hypointensity. The "trident" or "bat wing" morphology of central pontine myelinolysis is absent, although the corticospinal tracts are spared. (Row 2) At 1-month follow-up, there is slight increase in extent of the T2 abnormality within the central pons with peripheral restricted diffusion and central T2 "shine-through" effect. No enhancement is seen. (Row 3) At 2.5-month follow-up, there is decrease in the size of the T2 hyperintense lesion. Restricted diffusion and T1 hypointensity have resolved. There is a small focus of elevated diffusion (hyperintense on the ADC map). No enhancement is seen. (Row 4) At 4-month follow-up, the T2 hyperintense lesion is smaller in the anterior posterior dimension but longer in the transverse dimension. There is increased facilitated diffusion. No abnormality is identified on T1-weighted images, and there is no abnormal enhancement.

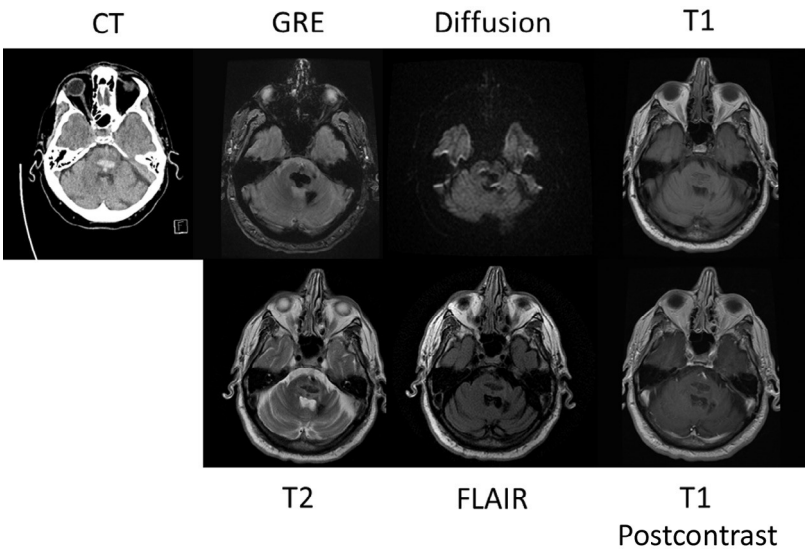

Figure 6.9. Acute pontine hemorrhage—CT shows hyperdense acute hemorrhage in the central pons. The hemorrhage is mildly hypointense on T1 and markedly hypointense on FLAIR and T2-weighted images, consistent with deoxyhemoglobin. Mild surrounding hyperintense edema is seen on FLAIR and T2-weighted images. There is no abnormal enhancement to suggest an underlying mass lesion. Deoxyhemoglobin causes local susceptibility effects, which results in low signal on DWI. There is also a more chronic hemorrhage with hemosiderin (T1 and T2 hypointense with susceptibility and no surrounding edema) in the medial left cerebellum.

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