Variability of Neuroimaging and Clinical Outcomes in Opioid Associated Neurotoxicity Syndromes

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Teaching Points (part 1)

- Recognition of Opioid Associated Neurotoxicity Syndromes
  - Opioid toxicity, particularly Fentanyl, is associated with syndromes such as CHANTER, POUNCE and OAA.
- Clinical and Imaging Findings
    - Neuroimaging findings include restricted diffusion in the cerebellum, hippocampi, and/or the basal ganglia on MRI.
    - Hydrocephalus and cerebellar tonsillar herniation may occur.
    - Several cases demonstrated coexisting cortical ischemic infarcts.

Teaching Points (part 2)

- Prognosis
    - Several patients recovered with minimal residual deficits
    - Restricted diffusion on MRI does not indicate irreversible damage, signaling that early recognition and intervention could improve outcomes.
- Clinical Management
    - External ventricular drainage for hydrocephalus shows benefits.
    - Prompt diagnosis can result in early intervention potentially improving outcomes.

Patient Presentation/Associated Drugs

- Patient Presentation
    - Patients with OANS can present with depressed neurological function such as a decreased GCS (≤ 8).
    - Patients can present as typical opioid overdose cases (respiratory depression and hypoxia).
    - Many patients have a history of opioid use, particularly fentanyl.
    - Other complications can include hydrocephalus, cerebellar tonsillar herniation, cortical ischemic infarcts, and/or cardiac arrest.
- Associated Drugs
    - All opioids, especially Fentanyl.

Progression of Disease

- Neurologic Depression
- Edema and Diffusion Restriction
- Hydrocephalus and Herniation
- Recovery
  - Mild cases may result in partial recovery with minor neurologic deficits such as mild memory impairment or coordination problems.
  - Severe cases may result in coma or permanent neurologic damage (ataxia, cognitive impairment, dysarthria).
  - Mortality is also a possibility if herniation and hydrocephalus are not properly addressed.

Imaging Findings (MRI)

- MRI
  - Restricted diffusion (RD) in the cerebellum, hippocampus, and basal ganglia (putamen or globus pallidus).
  - Edema in the cerebellum and hippocampus coexisting with RD.
  - Hyperintense areas may indicate cortical ischemic infarcts.
  - Hydrocephalus may be appreciated through ventricular enlargement and brain structure displacement.

Imaging Findings (CT)

- CT
  - Diffuse hypodensity in corresponding regions.
  - Hydrocephalus may be observed (ventricular dilation).
  - Herniation may be observed through mass effect.

	Cerebellum	Hippocampi	Basal ganglia	Cerebral cortex
CHANTER	+	+	+	±
POUNCE	+	±	-	±
OAA	-	+	-	±

Figure 1. Summarization of typical locations of edema-like signal and restricted diffusion on imaging in CHANTER, POUNCE, and OAA syndromes. “+” means typically present. “±” means may or may not be present. “-” means typically absent.

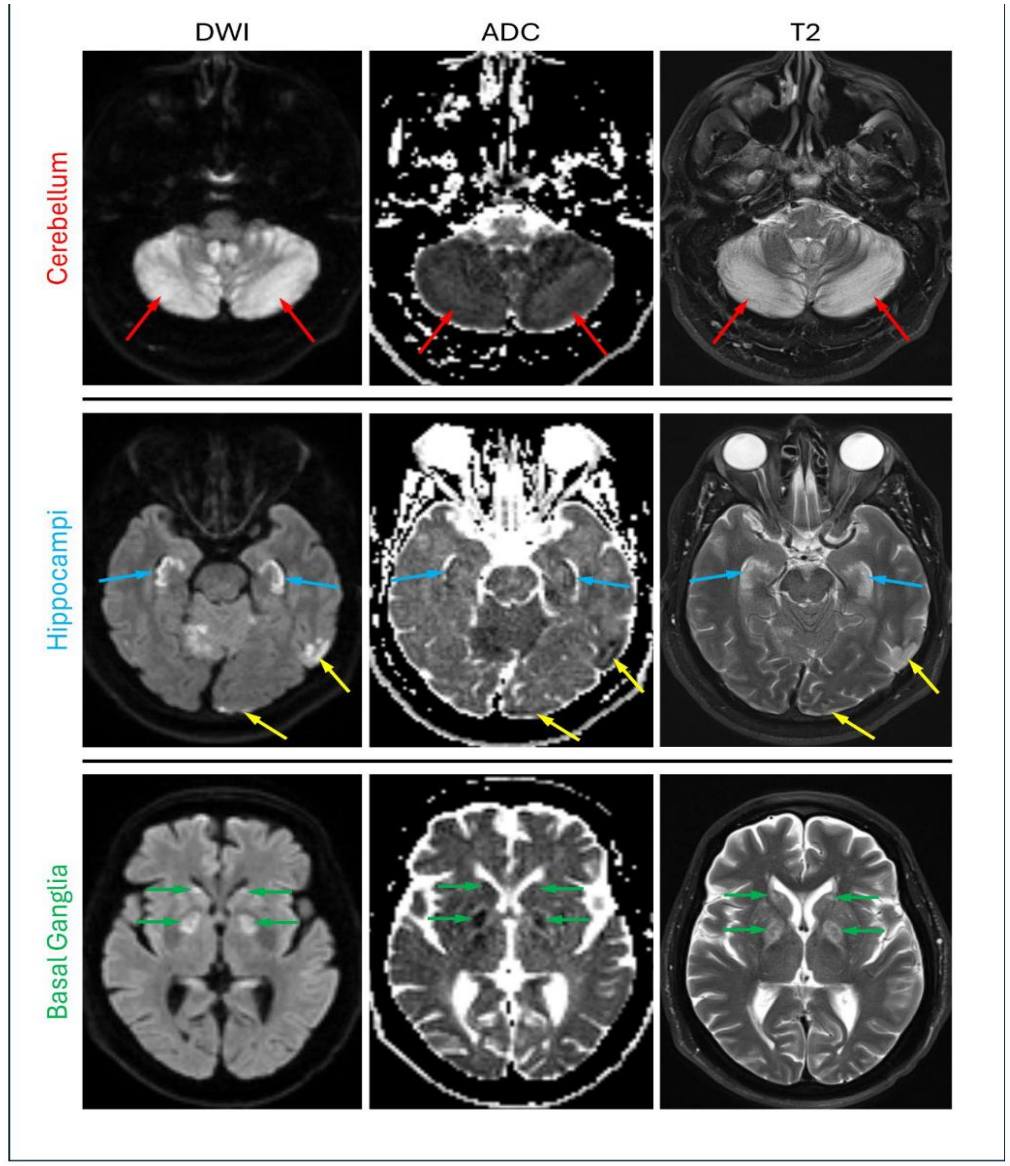

Figure 2. MRI case example of CHANTER syndrome in a 58-year-old male patient with representative DWI, ADC, and T2 axial images. Areas of restricted diffusion and T2 signal hyperintensity are demonstrated in the cerebellum (red arrows), hippocampi (blue arrows), and basal ganglia (green arrows). In addition, there are areas of similar signal abnormality involving the posterior left cerebral cortex (yellow arrows).

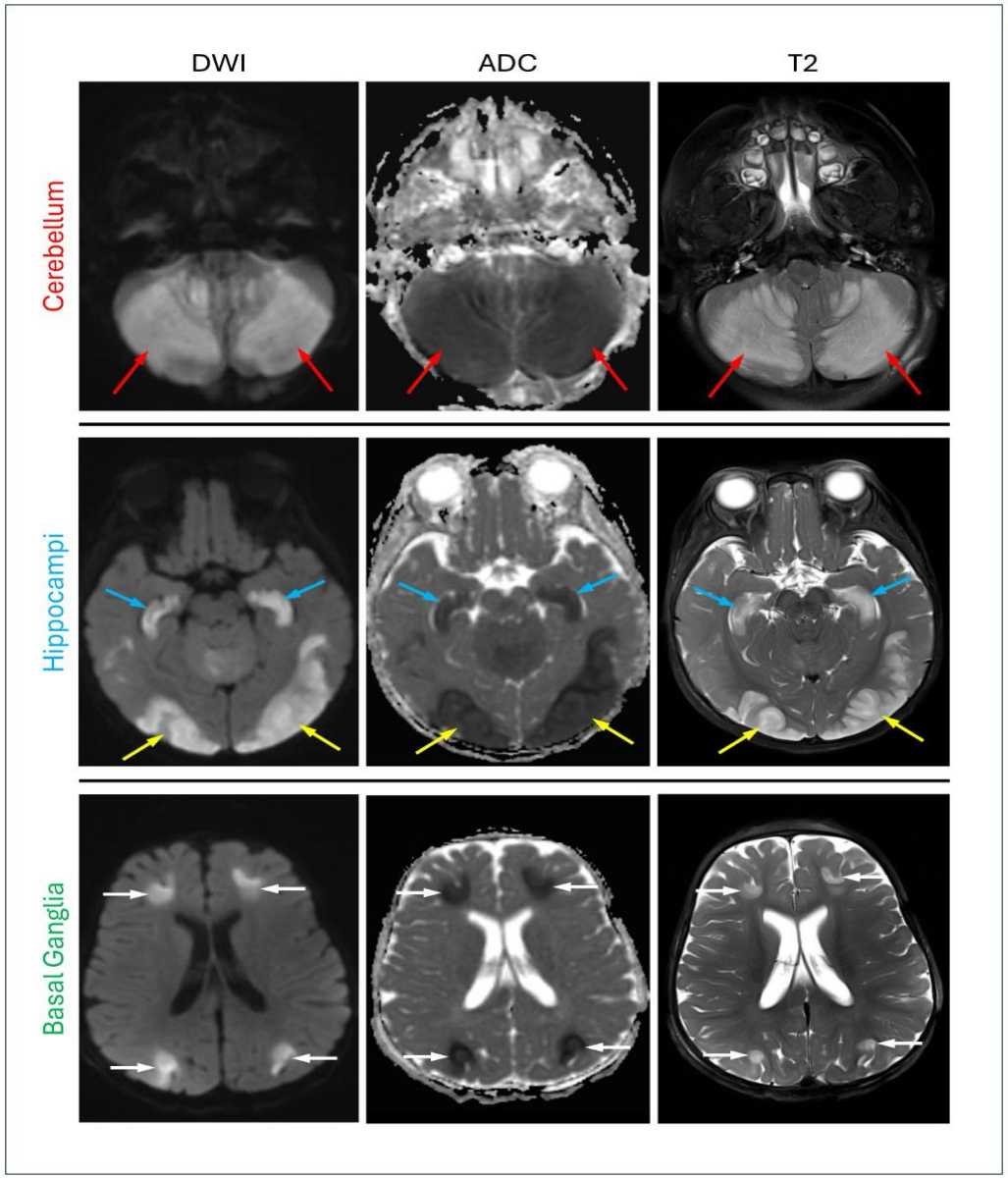

Figure 3. MRI case example of POUNCE syndrome in a 12-month-old female patient with representative DWI, ADC, and T2 axial images. Areas of restricted diffusion and T2 signal hyperintensity are demonstrated in the cerebellum (red arrows) and hippocampi (blue arrows). In addition, there are areas of similar signal abnormality involving the posterior cerebral cortex (yellow arrows) and bilateral cerebral white matter (white arrows).

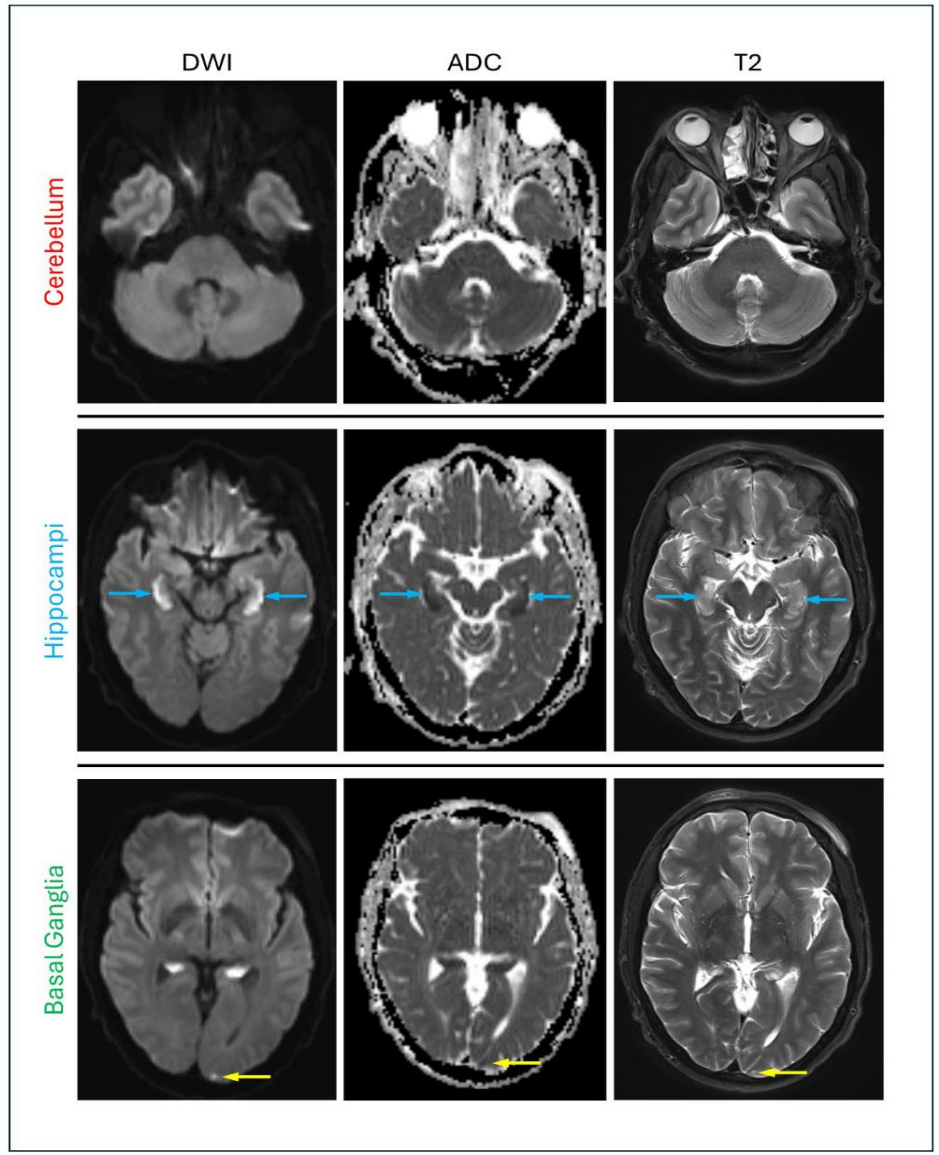

Figure 4. MRI case example of CHANTER syndrome in a 52-year-old male patient with representative DWI, ADC, and T2 axial images. Areas of restricted diffusion and T2 signal hyperintensity are demonstrated in the hippocampi (blue arrows). In addition, there are areas of similar signal abnormality involving the posterior left cerebral cortex (yellow arrows).

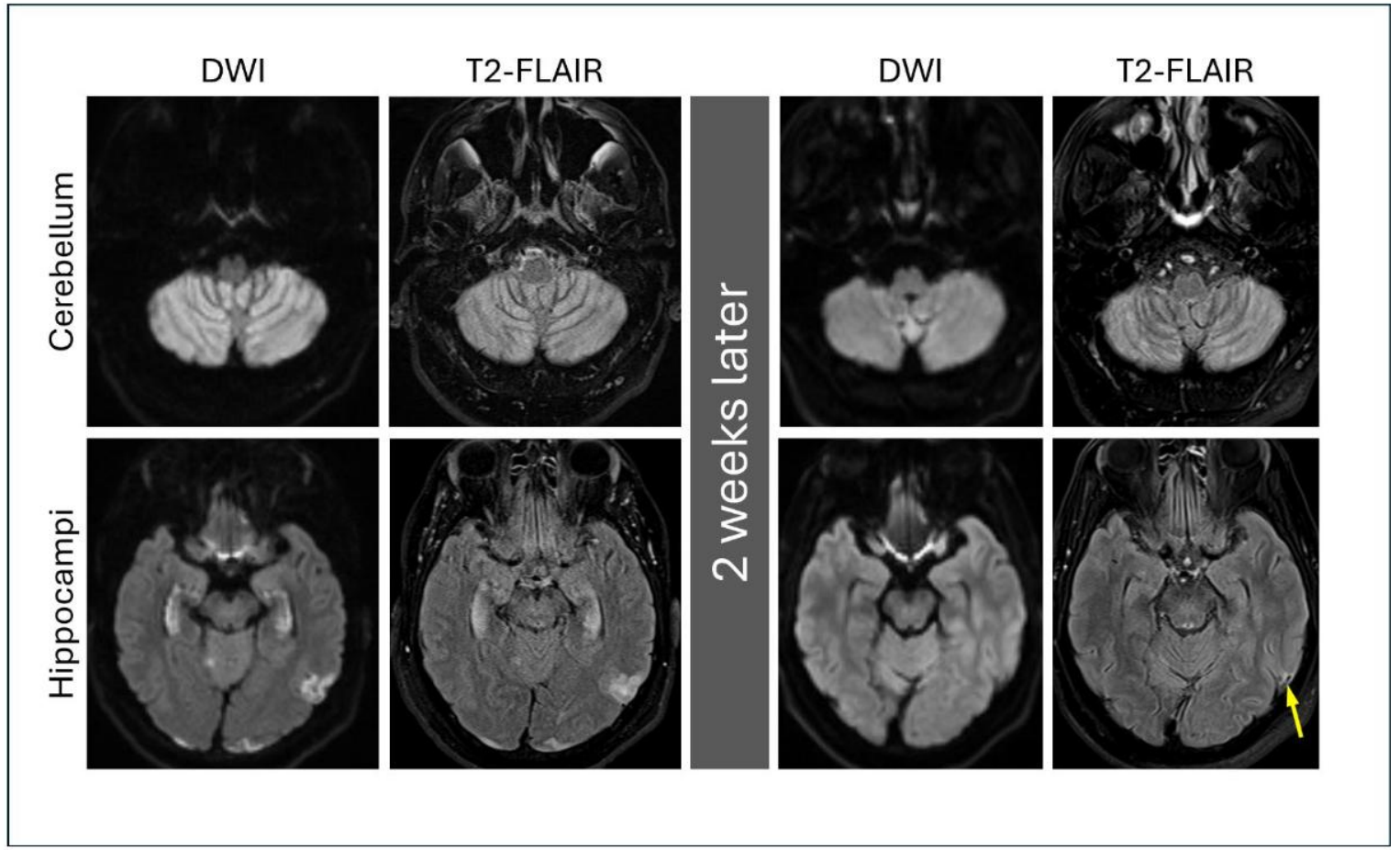

Figure 5. Progression of MRI findings in CHANTER syndrome in the same 58-year-old male patient from Figure 2. Representative DWI and T2-FLAIR axial images are shown at baseline (left) and after 2 weeks (right). Areas of restricted diffusion and T2-FLAIR signal hyperintensity in the cerebellum, hippocampi, and posterior cerebral cortex are less conspicuous on followup imaging with only a small area of developing gliosis in the posterior left temporal cortex (yellow arrow).

Outcomes

- 2 Patients died due to brain herniation and hydrocephalus.
- 3 patients developed cerebellar tonsillar herniation.
- 2 patients developed hydrocephalus.
- 3 patients with CHANTER, 1 patient with POUNCE, and the patient with OAA were discharged with only minor residual neurologic deficits.
  - Minor deficits included memory impairment, ataxia, or mild cognitive impairments.