

Pediatric Acute Opioid Induced Leukoencephalopathy with Malignant Cerebellar Edema

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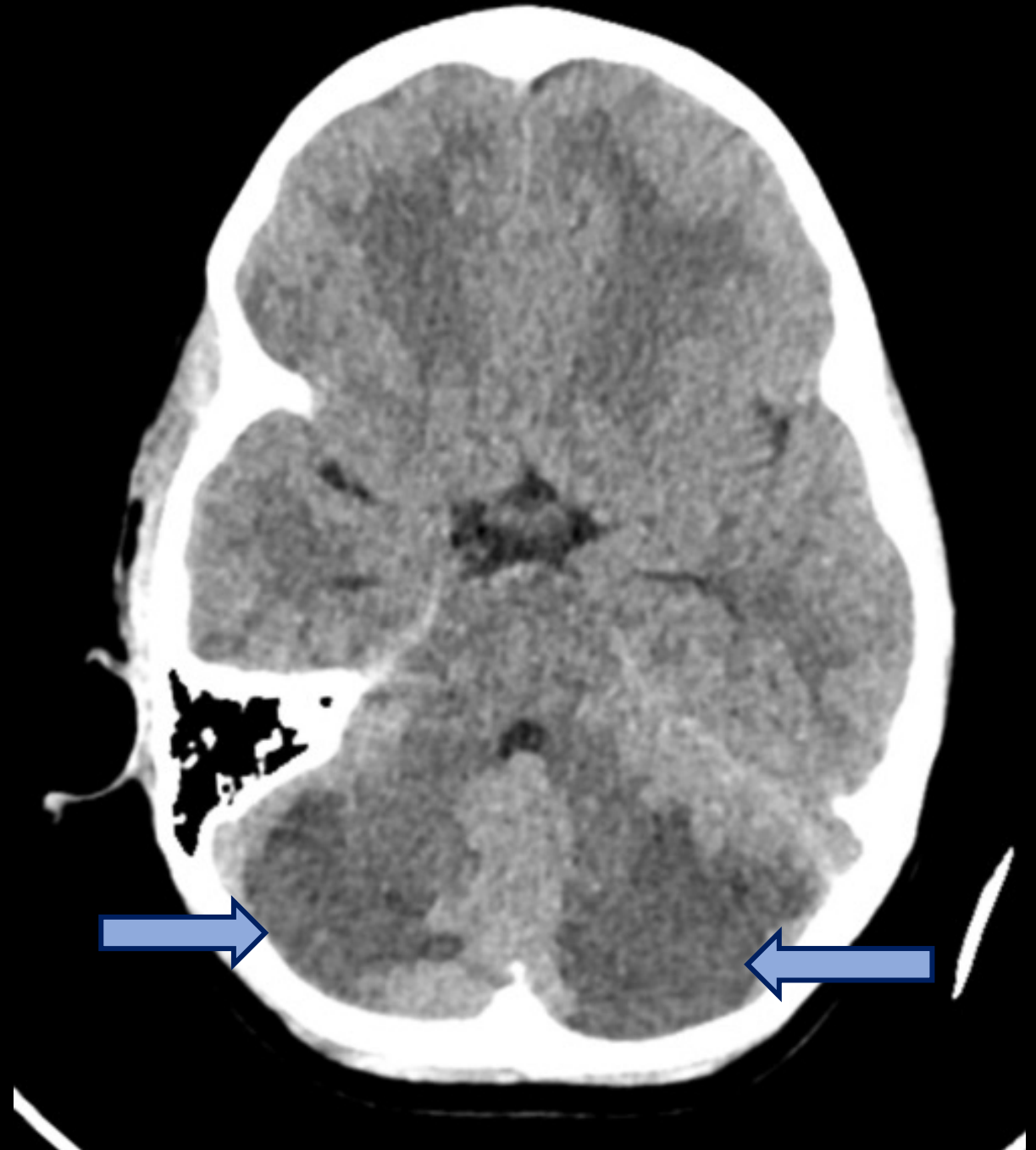
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History

- 4-year-old male with no known past medical history
- Reportedly normal day prior to presentation
- Found in bed by mother in morning with tonic seizure activity and EMS called
- Decompensated prior to hospital arrival, intubated for airway protection and started on 2 pressors for shock of unknown etiology
- No external evidence of trauma and occult trauma workup negative
- Concern raised for ingestion as mother was known substance abuser
- Urine drug screen was negative

CT Head without contrast

- Initial CT head without contrast revealed symmetric hypoattenuation in the cerebellar hemispheres and middle cerebellar peduncles sparing the midline and lateral portion, concerning for infarcts



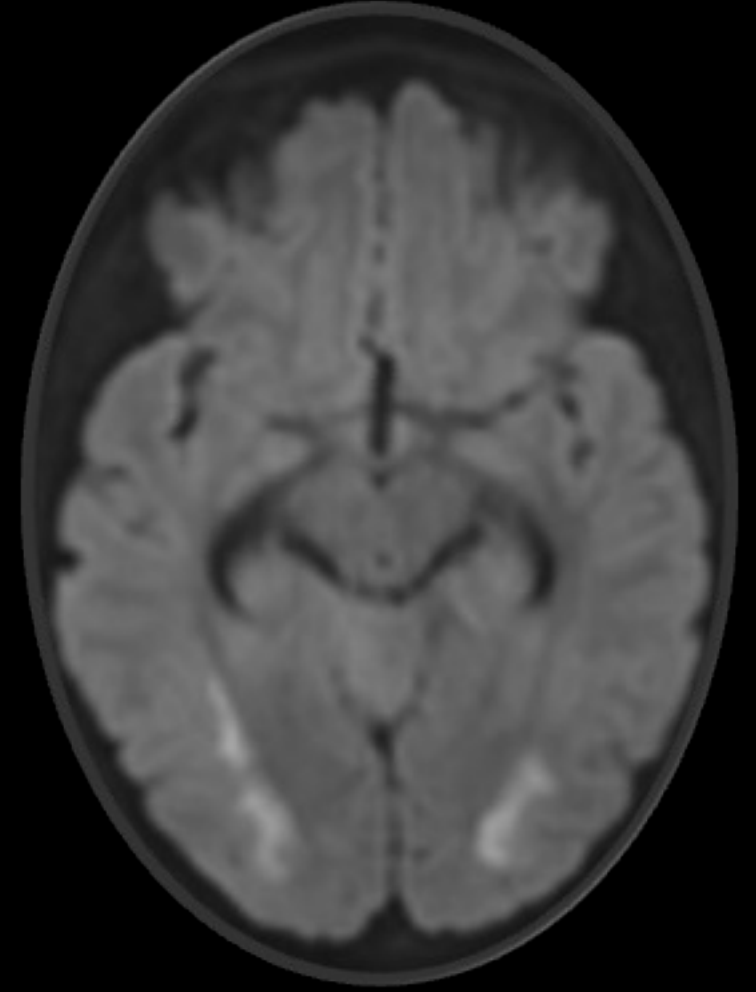
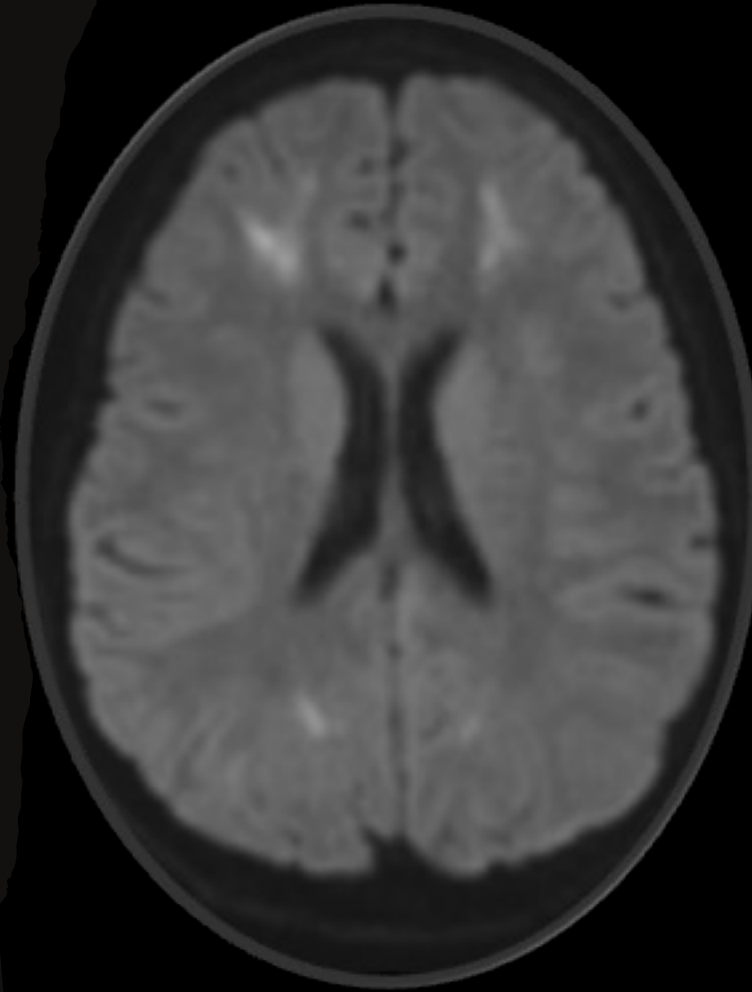


MRI Brain

Follow-up MRI Day 2 shows corresponding symmetric **diffusion restriction**, **T2 hyperintense signal**, and **internal petechial hemorrhage** on SWI.

MRI Brain

Diffusion restriction also present in the bilateral frontal, parietal, and occipital deep and subcortical white matter.



Management

- Initially received naloxone without improvement
- Underwent decompressive suboccipital craniectomy with partial cerebellar resection for elevated ICP and concern for impending herniation
- Due to a negative UDS, an extensive workup for genetic metabolic diseases and congenital myopathies (due to elevated CK) was initiated and found to be negative, including inpatient muscle biopsy
- Protracted hospital course complicated by sepsis and multi-drug resistant pneumonia and profound electrolyte abnormalities managed medically
- Neurorehabilitation with PT/OT

Outcome

- Removed from mother's care by child protective services
- Discharged to caregiver after 1 ½ month hospital stay
- Close follow-up with PT/OT, pediatric, neurosurgery
- Significant ongoing gait instability
- Can now stand with assistance and regaining some independence
- Ongoing investigation of environmental neglect and drug exposure precipitating illness

Acute Opioid-induced Leukoencephalopathy: Clinical Presentation

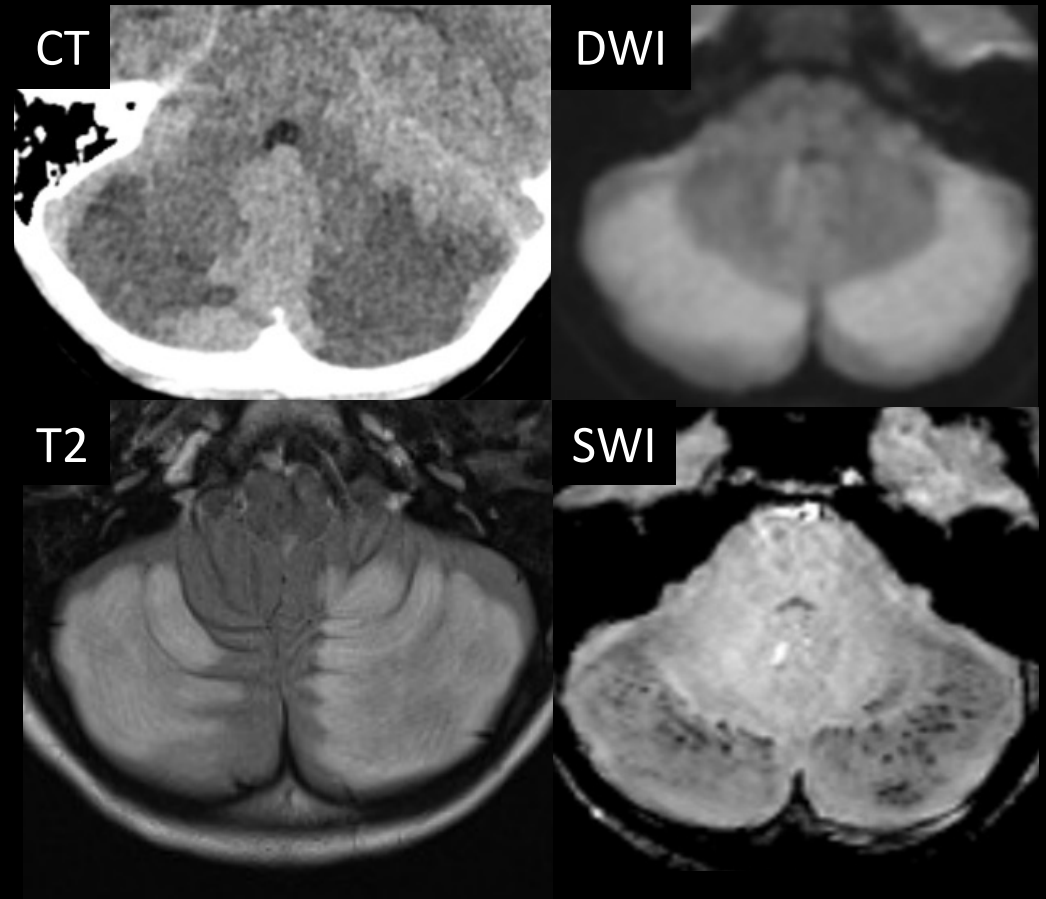
- Heterogenous, ranging from mild mental status or psychomotor changes, to coma and death
- Commonly complicated in the acute phase by elevated ICP, hydrocephalus and tonsillar herniation depending on cerebellar involvement, which necessitates neurosurgery intervention
- Reported cases of this condition have largely been in the pediatric and young adult age groups
- Classically associated with heroin or methadone, but has occurred with fentanyl and other commonly used opioids

Take home points

- Leukoencephalopathy secondary to opioids is more rare than hypoxic brain injury, but can be just as devastating
- Many opioids, such as fentanyl, do not appear on urine drug screen, increasing the need for high indices of suspicion in suspected exposure-induced illness
- With increasing risk of accidental exposure in pediatric populations with the current opioid crisis, being mindful of opioid induce toxic leukoencephalopathy will become increasingly necessary
- Cerebellitis pattern that occurs can lead to hydrocephalus and tonsillar herniation, necessitating surgical posterior fossa decompression.

Take home points

- This is a case example of this **characteristic imaging pattern** of cerebellar diffusion restriction and edema with sparing the lateral cerebellum and areas of internal petechial hemorrhage *plus* cerebral white matter diffusion ischemia, which is reported on numerous case reports/series of opioid-induced leukoencephalopathy.
 - See tables on following slides
- **We propose that this pattern appears to be unique for pediatric opioid-induced leukoencephalopathy and advocate for increased awareness of its appearance**
- A do-not-miss diagnosis, even with a negative urine drug screen!



Opioid induced toxic leukoencephalopathy case reports

| | | | |
|--|---------|-------------------------|---|
| Nanan R. <i>et al. Neuroradiology.</i> 42, 845–848 (2000) | 14 yo F | Morphine | T2/FLAIR hyperintensities of supratentorial and cerebellar white matter |
| Anselmo M. <i>et al. J. Child Neurol.</i> 21, 618–620 (2006) | 3 yo M | Methadone | T2/FLAIR hyperintensities of hippocampus and cerebellar hemispheres with cerebellar edema |
| Mills F. <i>et al. Pediatr. Radiol.</i> 38, 227–229 (2008) | 3 yo F | Methadone | T2/FLAIR hyperintensities in cerebellar hemispheres with massive cerebellar edema and bilateral watershed cerebral infarcts |
| Riascos R, <i>et al. Emerg Radiol.</i> 15, 67-70 (2008) | 22 mo M | Methadone | Bilateral cerebellar hypoattenuation |
| Bellot B, <i>et al. Paediatr Neurol.</i> 15, 368–71 (2011) | 2 yo M | Buprenorphine | T2/FLAIR hyperintensities in bilateral cerebellar and cerebral white matter with associated cerebellar edema |
| Metkees M, <i>et al. Pediatr. Radiol.</i> 52, 256–7 (2015) | 15 yo F | Methadone | Bilateral T2/FLAIR hyperintensities in supratentorial white matter |
| Reisner A. <i>et al. J. Neurosurg. Pediatr.</i> 16, 752–757 (2015) | 2 yo F | Morphine, hydromorphone | Diffuse T2/FLAIR hyperintensities in cerebral and cerebellar white matter with cerebellar edema and petechial hemorrhages. |
| Duran, D. <i>et al. Front. Neurol.</i> 8, 362 (2017) | 10 mo F | Oxycodone | Severe bilateral cerebellar hypoattenuation and T2 cerebellar white matter intensity with massive cerebellar edema |

Opioid induced toxic leukoencephalopathy case reports cont.

| | | | |
|---|----------------|-------------------------------------|--|
| Chen CH, et al. <i>Neuroradiol. J.</i> 32, 386–391 (2019) | 3 yo F | Hydromorphone hydrocodone; fentanyl | T2/FLAIR hyperintensities of cerebellar and supratentorial white matter and massive cerebellar edema |
| Tiong SC, et al. <i>J. Radiol. Case. Rep.</i> 13, 1–9 (2019) | 2 yo F, 3 yo M | Methadone | Both cases demonstrated bilateral cerebellitis |
| Wheaton T, et al. <i>Heliyon</i> 5, e03005 (2019) | 4 yo M | Oxycodone | Diffuse T2/FLAIR hyperintensities involving cerebellar and cerebral white matter with associated massive cerebellar edema and hemorrhagic conversion |
| Haghighi-Morad M, et al. <i>BMC Med Imaging.</i> 20, 6 (2020) | 23 mo – 33 yo | Methadone | Cases presented with a mix of cerebral and cerebellar white matter T2/FLAIR hyperintensities |
| Repple J, et al. <i>BMC Neurol.</i> 21, 85 (2021) | 19 yo M | Methadone | T2/FLAIR hyperintensities of bilateral basal ganglia and cerebellar white matter with associated edema |