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Case Report

Bilateral cerebellar hemorrhagic infarcts as an early presentation following opioid-induced toxic encephalopathy in an adult patient

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ABSTRACT

In the midst of the national opioid crisis, it is necessary for emergency physicians and radiologists to be familiar with presentations of opioid-related complications. We describe a case report of a 51-year-old female who developed bilateral cerebellar hemorrhages following opioid and benzodiazepine overdose. Malignant cerebellar edema is a rare but recognized complication following opiate overdose in children or chronic heroin toxicity. However, acute cerebellar involvement is rarely reported in adults. We feel that clinicians and radiologists should keep in mind the possibility of opioid toxic encephalopathy in their differential for adults with acute bilateral cerebellar infarcts and/or hemorrhages.

Introduction

Being able to quickly recognize the features of various toxidromes has been emphasized as an important skill for physicians in the current opioid epidemic. Early recognition can be lifesaving. The opioid toxidrome commonly includes symptoms such as respiratory depression, bradycardia, sedation, miosis, and decreased bowel sounds. Along with clinical symptoms, certain imaging features can be associated with this toxidrome, such as ischemic stroke, heroin-induced leukoencephalopathy, and hypoxic ischemic injury [1]. We present a rare case of opioid toxicity resulting in bilateral cerebellar hemorrhages in an adult.

Abbreviations: DWI, diffusion-weighted imaging; FLAIR, fluid-attenuated inversion recovery; MRI, magnetic resonance imaging; SWI, susceptibility-weighted imaging.

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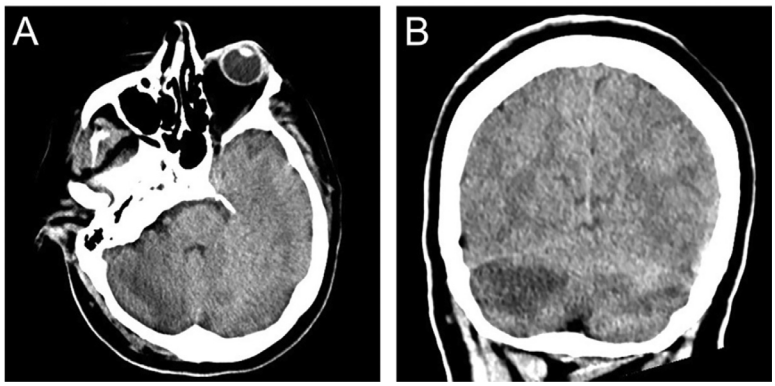

Fig. 1 – Initial head CT. (A) Axial and (B) coronal head CT images demonstrate bilateral cerebellar hypodensities.

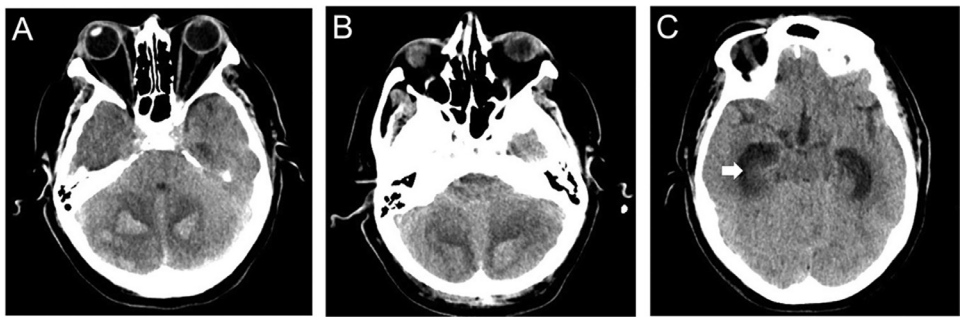

Fig. 2 – Head CT on day 2. (A and B) Multifocal hemorrhages in the bilateral cerebellar hemispheres and effacement of the fourth ventricle. (C) Dilatation of bilateral lateral ventricles with transependymal resorption, suggestive of acute hydrocephalus. Note the hypoattenuation of the right hippocampus (arrow).

Case Report

A 51-year-old female with a history of hypertension, type 2 diabetes mellitus, chronic kidney disease, and opioid and benzodiazepine use disorder was found unresponsive and apneic at home. The opiate and benzodiazepine toxicology screens were positive at the emergency room. She had persistent decreased level of consciousness despite naloxone. Initial CT of the head on arrival demonstrated bilateral multifocal cerebellar hypoattenuations (Fig. 1).

The next day, the patient developed hypertension as well as tachycardia and tachypnea. The follow-up head CT showed progression of cerebellar edema and hemorrhagic conversion in the cerebellar hypoattenuations as well as new right hippocampal hypoattenuation (Fig. 2). The mass effects of cerebellar edema and hemorrhages effaced the fourth ventricle and caused acute obstructive hydrocephalus. She was taken to the operating room for suboccipital craniectomy and temporary extra-ventricular drain placement. CT angiography of the head did not find any evidence of vascular malformation or venous thrombosis. An MRI of the head showed extensive edema and multifocal hemorrhages in bilateral cerebellums as well as diffusion restriction of the right hippocampus (Fig. 3). She was extubated in the operating room, and her postoperative course was uncomplicated. She was discharged to continued home health care after 2 weeks with mild dizziness and unsteady gait.

Discussion

The most common acute neuroimaging findings of opioid-related complications include infectious conditions, ischemic stroke, heroin-induced leukoencephalopathy, and hypoxic ischemic injury [1]. This case highlights a rare presentation of cerebellar hemorrhages in an adult following opioid toxicity. Malignant cerebellar edema has been commonly linked with the well-known heroin-induced leukoencephalopathy, which is associated with heroin inhalation known as “chasing the dragon.” Typical heroin-induced leukoencephalopathy is characterized by bilateral extensive confluent symmetric cerebral and cerebellar white matter changes [2]. Compared to our case, heroin-induced leukoencephalopathy usually presents over weeks to months after prolonged exposure, and gray matter structures are usually spared [2]. Histopathological examinations have revealed oligodendrocyte apoptosis and spongiform degeneration in the white matter [3,4]. Of note, the patient in our case had no previous history of heroin use.

Apart from heroin-induced leukoencephalopathy, malignant cerebellar edema in adults following exposure to other

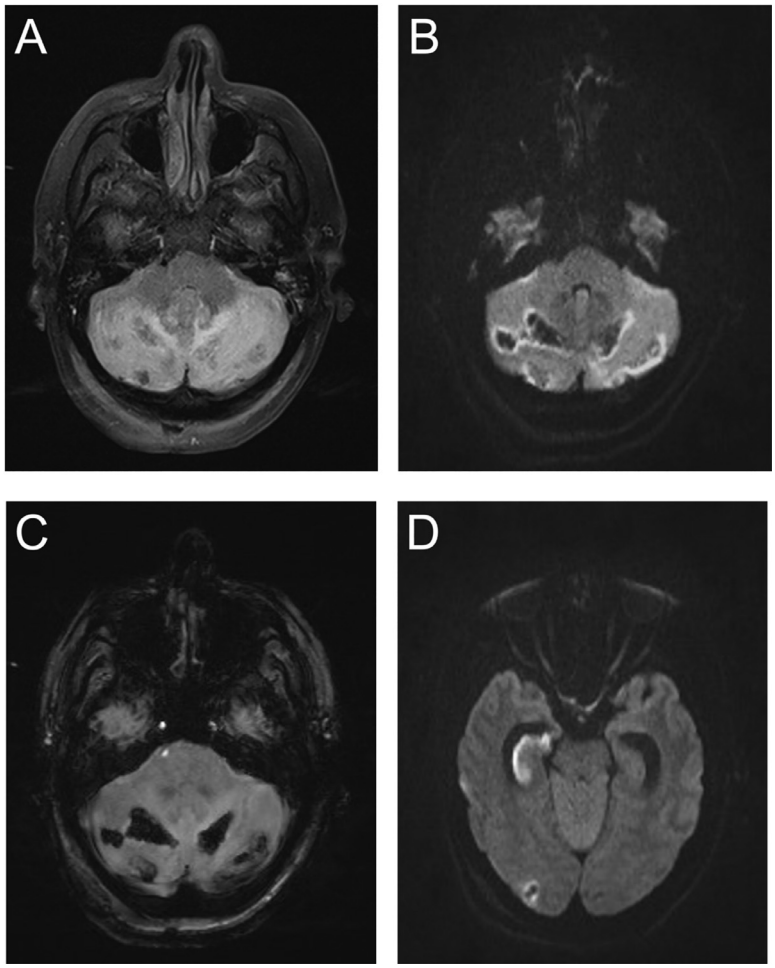

Fig. 3 – Brain MRI on day 2 status post suboccipital craniectomy and ventricular shunt placement. (A) FLAIR shows extensive bilateral cerebellar edema as well as multifocal isointense to hypointense acute hemorrhages. (B) Axial DWI shows restricted diffusion in the bilateral cerebellar hemispheres. Note signal drops due to susceptibility artifacts of cerebellar hemorrhages. (C) Axial SWI shows multifocal hemorrhages in the cerebellum bilaterally. (D) Axial DWI shows acute cytotoxic edema in the right hippocampus. Note an additional small hemorrhage in the right occipital lobe.

opioids is rare and appears differently than in pediatric cases of opioid toxicity [5-7]. One explanation for this discrepancy is that the profile of opioid receptor expression in the cerebellum differs between infants and adults. Both the binding affinity and capacity of μ receptors are higher in the developing cerebellum than in the adult cerebellum. The binding capacity of these receptors in the newborn cerebellum is twice that of the receptors in the adult cerebellum [8]. This may explain why cerebellar involvement has been seen in more pediatric cases of opioid overdose than in adult cases. In a review of pediatric opioid leukoencephalopathy, nearly all of the reported non-heroin cases (11/12) presented with cerebellar involvement [7]. Reported causative agents included morphine, hydromorphone, methadone, buprenorphine, and oxycodone [7]. Kim et al. named this syndrome with bilateral cerebellar edema following opioid overdose as pediatric opioid use-associated neurotoxicity with cerebellar edema (POUNCE) syndrome [6]. Several mechanisms have been proposed for the effects of opioids with regards to cerebellar involvement, including oligodendrocyte toxicity, demyelination, increased blood-brain barrier permeability and edema, neuronal damage through mitochondrial insult, and apoptotic upregulation.

In adults, malignant cerebellar edema in nonheroin opioid toxic encephalopathy is even rarer. In a summary of 7 reported oxycodone-induced leukoencephalopathy in the adults, less than half (n = 3) presented with cerebellar involvement [9]. Jasne et al. reported a rare constellation of neuroimaging findings following exposure to opioids or other drugs of abuse in the adults [10]. They reported a distinct pattern of cerebellar, hippocampal, and basal ganglia restricted diffusion, which they labeled as CHANTER (Cerebellar Hippocampal and Basal Nuclei Transient Edema with Restricted diffusion) syndrome. All of these patients presented with severe cerebellar edema which led to obstructive hydrocephalus requiring aggressive medical and surgical management. Although our case had no basal ganglia involvement, she presented with bilateral

cerebellar edema with acute obstructive hydrocephalus as well as right hippocampal cytotoxic edema. We believe our case is on the spectrum of CHANTER syndrome and may be caused by a similar mechanism related to mitochondrial failure with anoxic injury precipitated by opiates. Nevertheless, our case had cerebellar hemorrhages and irreversible damages, which is atypical in the context of transient cerebellar edema in CHANTER syndrome [10].

In patients with CHANTER syndrome, prognosis is very good despite early obstructive hydrocephalus. Similarly, our case recovered soon after decompression of cerebellar hemorrhages and extraventricular shunt placement. This highlights the importance of early neurosurgical consultation. Early identification and treatment of this syndrome is critical. Further work is needed to identify the risk factors and mechanisms by which this syndrome presents in individuals with a history of drug abuse.

In conclusion, we report a unique case of bilateral multifocal cerebellar hemorrhages following acute opioid overdose. Cerebellar involvement in opioid overdose is rarely reported in the adult population. We feel that clinicians and radiologists should be cognizant of opioid-induced toxic encephalopathy in their differential for adults with acute bilateral cerebellar infarcts and/or hemorrhages.

Patient consent

Unable to reach patient for consent.

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