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Case Report

Opioid-induced toxic leukoencephalopathy in a child: A case report

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ABSTRACT

In environments, where opioids are used increasingly for recreational purposes, children are more at risk for both accidental and non-accidental intoxications. In toxic doses, opioids can cause lethal leukoencephalopathy. Here, we report a case of an 8-year-old male child who presented with altered mental status following accidental morphine overdose and was managed with cardio respiratory support, naloxone, and supportive therapy.

Keywords: Opioid toxicity, Leukoencephalopathy, Naloxone

INTRODUCTION

Opioids include a large number of natural alkaloid compounds and related synthetic compounds. These agents are highly addictive and can lead to physiological dependence with development of tolerance and withdrawal. Overdose of opioids in pediatric age group is related to easy access to pain medications or when illicit drugs are used in household by someone else.[1] Opioid-induced neurotoxicity is a multifactorial syndrome with wide spectrum of symptoms including confusion, delirium, delusions, hallucination, and seizure.[2] The life-threatening complications of opioid overdose are hypoxia, anaphylaxis, pulmonary edema, acute respiratory acidosis, and aspiration pneumonitis.[3] However, both immediate and delayed effects of opioid overdose can be well tackled with prompt diagnosis and management, with encouraging outcome in such patients. This case report highlights opioid-induced toxic leukoencephalopathy in an otherwise unusual age group.

CASE REPORT

An 8-year-old male child presented to the emergency department with difficulty in breathing since the past few hours. On examination, the child was non-arousable, bradypneic with shallow respiration and pulse oxygen saturation of 30% on room air, feeble peripheral pulse, BP recorded was 84/46, and minimal arterial pressure of MAP-60. Neurological examination revealed 1 mm miotic pupils bilaterally, global hypertonic and hyperreflexia. The child was undernourished with weight 20 kg and height 124 cm. He was reared up in social setting premises of spiritual guru in whom family had faith. History also revealed absence of any preexisting systemic illness or infection. Thus, the child was intubated immediately and normal saline bolus was given for managing shock. Then, the child was shifted to pediatric intensive care unit and assisted

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ventilation was started. Arterial blood gas analysis revealed combined metabolic and respiratory acidosis (pH 7.15, $PaCO_2$:50.5, PaO_2:103, and HCO_3-16). After few hours, the child had endotracheal bleeding, and chest X-ray was done. It was suggestive of pulmonary edema, which was managed conservatively. Additional laboratory evaluations like liver function test revealed mild transaminitis and complete blood count showed leucocytosis.Dilated fundus examination showed bilateral disc edema with flame shaped hemorrhage superior to the optic nerve head in the left eye [Figure 1a and b]. Urine sample was sent for toxic substance screening. Injection dexamethasone (0.6 mg/Kg/day), ceftriaxone (100 mg/Kg/day), vancomycin (45 mg/Kg/day), acyclovir (20 mg/Kg 8 hourly), and one dose of naloxone (0.1 mg/Kg/dose) were administered. A broad differential diagnosis of respiratory failure of unknown origin was kept with suspicion of possible allergic reaction or opioid overdose or meningitis. Meantime, the child developed generalized tonic clonic seizures, which was managed with intravenous injection levetiracetam (20–40 mg/Kg/day).

On the 2nd day of admission, 2D MRI brain using axial T2W, FLAIR, and diffusion-weighed and T1 sequences on a 1.5 T 18-channel MRI scanner revealed findings suggestive of leukoencephalopathy. The report revealed symmetrical areas of altered signal intensity showing diffusion restriction of DW/ADC diffusely involving the subcortical white matter in bilateral cerebral hemispheres (involving perirolandic subcortical white matter, frontal, parietal, occipital, and temporal subcortical white matter). Periventricular white matter, corpus callosum, basal ganglia, and brain stem were spared [Figure 2]. Urine toxicology report came to be positive for morphine for which stat dose (0.1 mg/kg I.V. push) of naloxone was given, followed by naloxone infusion for 5 h. After 48 h, the child showed improvement and gained consciousness with spontaneous respiration and 5 mm size of pupils showing both direct and consensual pupillary reactions bilaterally with weaning from ventilation. However, the child was emotionally labile and showed signs of fear. The power remained decreased in all upper and lower limbs, for which oral supplementation of methylcobalamin, zinc, and physiotherapy was started for rehabilitation.

DISCUSSION

Opiate refers to products found in opium, the natural opiates are being derived from resin of opium poppy, *Papaver somniferum*. Opiates include natural plant alkaloids such as morphine, codeine, and many semi-synthetic derivatives. An opioid has same functional and pharmacological properties of an opiate, regardless of its structure. Unfortunately, non-medical prolonged misuse without medical supervision can lead to opioid dependence and other health problems. Their pharmacological effects can lead to breathing difficulties, miosis, confusion, delirium, delusions, hallucination, seizure, and even death can occur.[2]

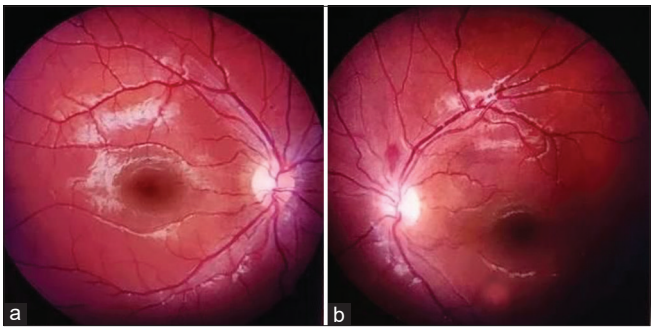

Figure 1: (a and b) Early papilledema both eyes with flame-shaped hemorrhage superior to the disc in the left eye.

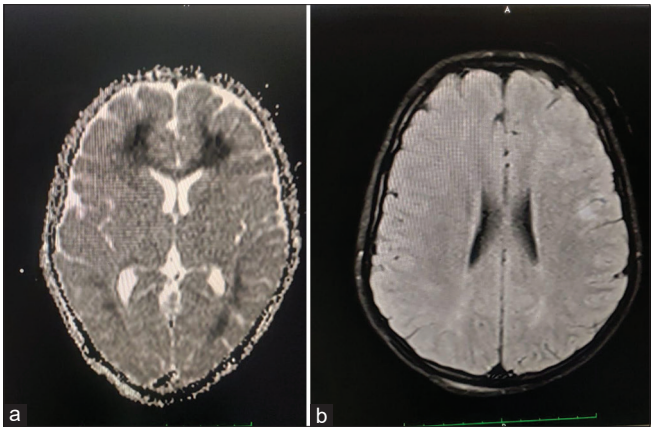

Figure 2: (a and b) Symmetrical areas of altered signal intensity showing diffusion restriction of DW/ADC diffusely involving the subcortical white matter in bilateral cerebral hemispheres.

Opioid use among children both by accidental and intentional ingestions is rising frequently.[1,4] Significant opioid exposure remains rare in pediatric age group and unfortunately if it occurs, it can result in neurological effects and complications.[4] In children with opioid overdose, neuroimaging reveals the significant white matter changes, on T2-weighed MR images, in both the cerebrum and cerebellum. The symmetric white matter changes in both cerebrum and cerebellum are the classic hallmark on radiology.[4] The anterior limb of internal capsule and proximate subcortical and periventricular white matter is usually spared.[5] Moreover, the degree of involvement depends on case to case.[6-8] However, in this case, the MRI revealed involvement of bilateral cerebral hemispheres (involving perirolandic subcortical white matter, frontal, parietal, occipital, and temporal subcortical white matter). Periventricular white matter, corpus callosum, basal ganglia, and brain stem were spared. Morphine carries high affinity to bind to μ receptors with weak binding tendency for delta and kappa receptors. Cerebellar and limbic systems have been found to have greatest intensity of these receptors. The stimulation of these receptors has been postulated to produce

a state of cellular energy depletion and this effect may be enhanced by hypoxia/acidosis.[9] In a study by Ammon-Treiber *et al*., the neurotoxic effects of morphine have been demonstrated to get aggravated by hypoxia/hypoglycemia.[10] Naloxone, a pure competitive opioid specific antagonist, has affinity for reversing actions of opioid agonists such as morphine, methadone, and fentanyl. Naloxone has short duration of action compared to methadone, extended-release morphine, buprenorphine, extended-release oxycodone, and fentanyl. Thus, the effect of naloxone may wane before the respiratory depression caused by these opioids, thus necessitated by repeat doses or continue naloxone infusion.

CONCLUSION

An increased awareness of such a condition is of paramount importance, depicting the rising prevalence of opioid intoxications among pediatric populations. Opioid toxicity in children affects toddlers (due to accidental ingestion) and adolescents due to deliberate ingestion.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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