

MRI Brain Features in Nitrobenzene Toxic Encephalopathy

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A 22-year-old man was brought to the hospital with a history of alleged consumption of about 100 ml of herbicide two hours prior to admission. He was drowsy and cyanotic with an oxygen saturation of 70%. However arterial blood gas (ABG) analysis showed normal partial pressure of oxygen (PaO₂). Methemoglobin level in the ABG analyzer was greater than 40%. The content of the herbicide was found to be nitrobenzene which causes methemoglobinemia. Gastric lavage was done and patient was treated with intravenous methylene blue. He was asymptomatic for five days after which he developed multiple organ dysfunction syndrome (MODS)—hepatitis, pancreatitis, rhabdomyolysis, and acute kidney injury—due to probable delayed nitrobenzene release from storage organs. The patient required mechanical ventilation and was given supportive treatment. He was noticed to have titubation with bilateral horizontal nystagmus, and rigidity of the limbs over the next two to three days. Magnetic resonance imaging (MRI) of the brain was done on day 9, which showed a characteristic pattern of symmetrical fluid-attenuated inversion recovery (FLAIR) hyperintensities in the splenium of the corpus callosum and bilateral dentate nuclei. Patchy FLAIR hyperintensities were seen in the substantia nigra bilaterally [Figure 1]. Diffusion-weighted imaging (DWI) showed hyperintensities in the corpus callosum and dentate nuclei with high apparent diffusion coefficient (ADC) values suggesting a T2 shine-through effect [Figure 2]. There was no enhancement in post-contrast T1-weighted images (T1WI) or blooming in the gradient sequences [Figure 3]. A diagnosis of toxic encephalopathy due to nitrobenzene

poisoning was made and he was given supportive treatment. Patient gradually recovered from MODS and was weaned off the ventilator. However, he had persisting bradykinesia with tremors of the head, dysarthria and truncal ataxia. Over the next few months, the patient made partial recovery and was able to ambulate without support.

DISCUSSION

Nitrobenzene once ingested can rapidly result in methemoglobinemia, which causes tissue hypoxemia and can lead to multiple organ failure and death.^[1] However, animal studies and a few clinical case reports have identified an independent direct neurotoxicity of nitrobenzene resulting in toxic encephalopathy. Boukobza M, *et al.*^[2] in 2015, first described the characteristic MRI features of nitrobenzene poisoning. The patient after consuming nitrobenzene had developed extrapyramidal features with ataxia and brain MRI showed T2 hyperintensities of the dorsal medulla, dorsal pons, periaqueductal grey matter, red nuclei, cerebellar dentate nuclei, internal capsule, corpus callosum, and in the centrum semiovale. A similar case was reported in India in a 17-year-old girl with nitrobenzene poisoning. After methylene blue treatment, she showed initial transient improvement with deterioration in sensorium six days later. Brain MRI showed FLAIR hyperintensities in the splenium of corpus callosum and dentate nuclei as well as corticospinal tracts.^[3] Our patient had similar findings on MRI consistent with toxic encephalopathy due to nitrobenzene. Interestingly our patient also showed involvement of substantia nigra, which has not been described in previous literature. It is

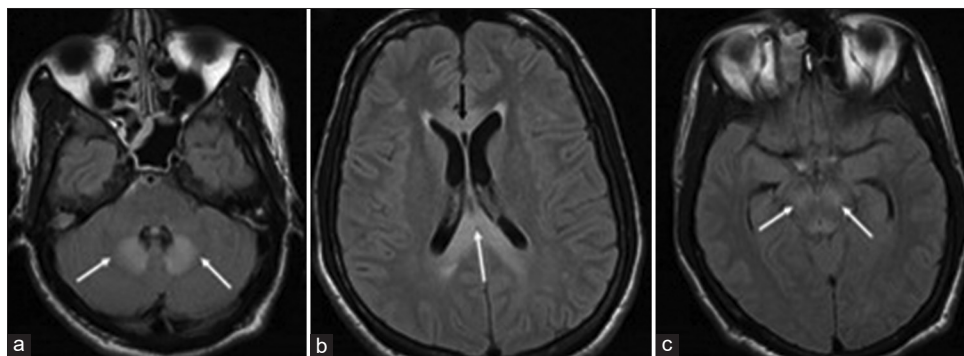


Figure 1: Shows bilateral symmetrical areas of hyperintensity involving dentate nuclei (a), corpus callosum (b) and substantia nigra (c) on Fluid-Attenuated Inversion Recovery (FLAIR) sequence

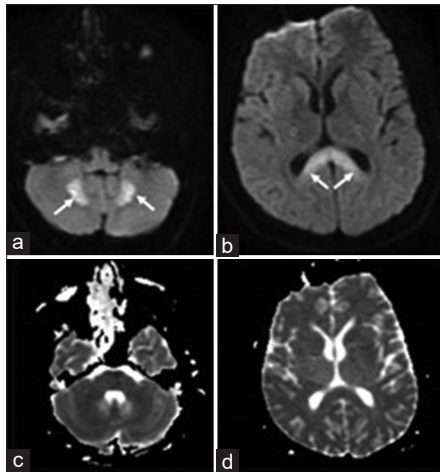


Figure 2: Diffusion-weighted images (DWI) show bilateral symmetrical hyperintensities involving dentate nuclei (a) and splenium of corpus callosum (b) with corresponding high apparent diffusion coefficient (ADC) values (c, d)

possible that areas of the basal ganglia are also vulnerable to nitrobenzene toxicity.

The predilection to cerebellar deep nuclei basal ganglia and corpus callosum has been well described in several drug and toxic encephalopathies. The specific involvement of certain areas in the brain is attributed to variable vulnerability to different toxins or metabolic derangements. Methyl bromide poisoning, metronidazole and isoniazid toxicity have a predilection for cerebellar dentate nuclei.^[4] These are thought to be “energy deprivation syndromes” which interfere with metabolic pathways in adenosine triphosphate (ATP) production.^[5] Nitrobenzene similarly causes energy deprivation in the brain by utilization of Nicotinamide adenine dinucleotide phosphate (NADPH) for its metabolism. Secondly the metabolic product is a free anion which reacts with oxygen and results in free radical injury. Several animal studies have shown that there are spongiform and hemorrhagic lesions in the brainstem and cerebellar nuclei following nitrobenzene poisoning.^[1] The neuroimaging findings further confirm the vulnerable areas of the brain to nitrobenzene toxicity.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

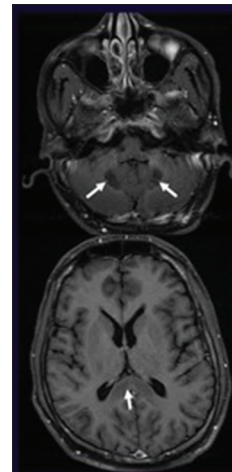


Figure 3: Post contrast T1WI, shows no enhancement in the corresponding areas

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Nil.

Conflicts of interest

There are no conflicts of interest.

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