

# MRI brain in monohalomethane toxic encephalopathy: A case report

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## Abstract

Monohalomethanes are alkylating agents that have been used as methylating agents, laboratory reagents, refrigerants, aerosol propellants, pesticides, fumigants, fire-extinguishing agents, anesthetics, degreasers, blowing agents for plastic foams, and chemical intermediates. Compounds in this group are methyl chloride, methyl bromide, methyl iodide (MI), and methyl fluoride. MI is a colorless volatile liquid used as a methylating agent to manufacture a few pharmaceuticals and is also used as a fumigative insecticide. It is a rare intoxicant. Neurotoxicity is known with both acute and chronic exposure to MI. We present the characteristic magnetic resonance imaging (MRI) brain findings in a patient who developed neuropsychiatric symptoms weeks after occupational exposure to excessive doses of MI.

**Key words:** Methyl iodide; MRI brain; toxic encephalopathy

## Introduction

Methyl iodide (MI) is a monohalothane used as an organic chemical agent/methylating agent in the synthesis of various pharmaceutical drugs. It is also used as a fumigative pesticide commonly in greenhouses and strawberry farming. The main route of exposure is via inhalation and less commonly via skin and the digestive tract.<sup>[1]</sup> Neurological symptoms are usually apparent weeks to months later. Patients can present with a wide range of symptoms. Both acute and chronic neurotoxicity is known. Acute toxicity can be mild or severe. Mild toxicity is characterized by headache, dizziness, nausea, and visual disturbances. Severe neurotoxicity can cause acute cerebellar dysfunction, Parkinsonism like symptoms, seizures, brain hemorrhage, and coma. Stroke-like presentation has also been described.<sup>[2]</sup> Chronic exposure

can cause cranial neuropathy, pyramidal and cerebellar dysfunction, polyneuropathies, and behavioral changes.

Few case reports have been described, however.<sup>[1-5]</sup> As far as we know, none of them mention abnormal magnetic resonance imaging (MRI) findings except one.<sup>[1]</sup>

Therefore, we present a case of acute-on-chronic toxicity of MI with the characteristic MRI brain findings.

## Case Report

A 29-year-old female, working in a pharmaceutical company, presented with sudden-onset diplopia, slurred speech, imbalance while walking, and behavioral changes which had developed over a period of 2-3 days. She reported to have headache for 2 weeks. On examination, she had cerebellar signs, bilateral extensor plantar reflexes, and bilateral VI nerve palsy. After ruling out other possibilities clinically, the clinician raised the possibility of probable toxic encephalopathy. A detailed personal and occupational history was obtained. Occupational history revealed that the pharmaceutical company used MI as a chemical intermediate. There was increase in its production in last 2 months probably leading her to sudden exposure of excessive amounts of MI before she presented. In view of the rapid onset of neuropsychiatric symptoms, acute

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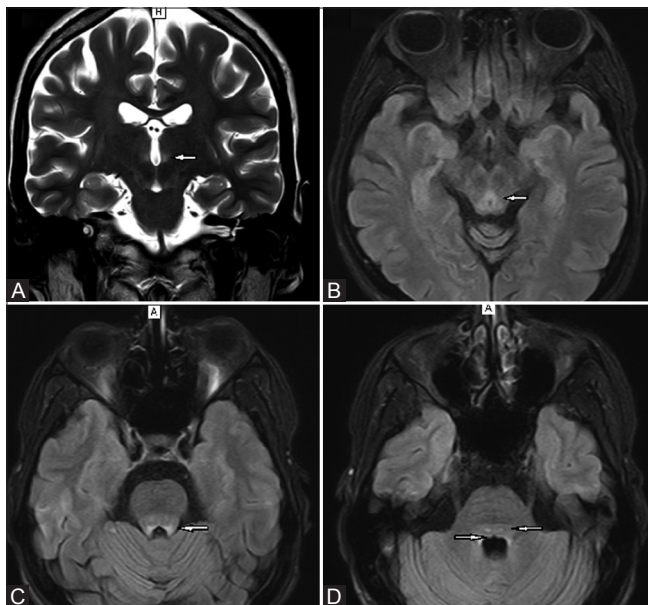
MI toxic encephalopathy was suspected and MRI brain was advised.

MRI brain was done at our center. T2-weighted and fluid-attenuated inversion recovery (FLAIR) images revealed bilateral symmetrical hyperintense signal in peri-third ventricular thalami [Figure 1A], peri-aqueductal region [Figure 1B], dorsal pons in the region of superior colliculus [Figure 1C], medial lemniscus and abducens nuclei [Figure 1D], and dorsal medulla and inferior olivary nuclei [Figure 2A]. Bilateral symmetrical hyperintense signal was also noted in dentate nuclei [Figure 2B]. Dentate nuclei lesions had target appearance; they were extremely bright in the center on T2-weighted images and were surrounded by a rim of ill-defined mild hyperintensity.

All these lesions were hypointense on T1-weighted images [Figure 2C]. No restriction of diffusion was noted on diffusion-weighted images (DWI) [Figure 2D]. Mild cortical and cerebellar atrophy was evident. However, the basal ganglia appeared normal. No evidence of altered signal was noted in the corpus callosum. No contrast was administered and MR spectroscopy was not performed.

Based on the clinical profile, possibility of MI toxic encephalopathy was considered and other differentials with similar MRI features were excluded. Patient was advised follow-up MRI after avoiding exposure to MI.

Repeat MRI brain was done after 4 months which showed complete resolution of the above-mentioned findings [Figure 3], confirming the diagnosis.



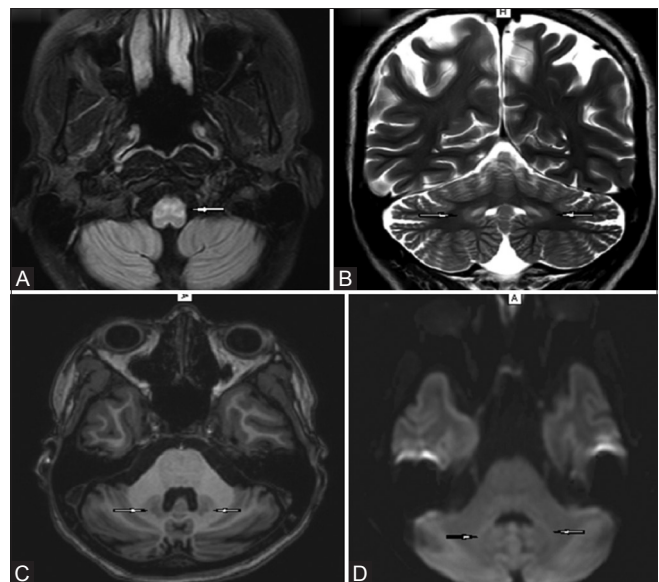
**Figure 1 (A-D):** T2W coronal image shows hyperintense signal in peri-third ventricular thalami (A), Flair axial image shows hyperintense signal in periaqueductal gray matter (B), in the superior colliculus (C), abducens nuclei and median lemniscus in the region of dorsal pons (D)

## Discussion

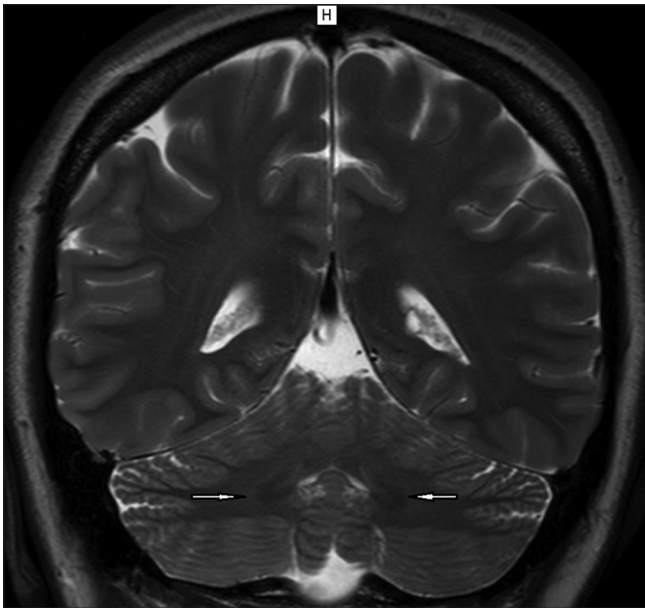
MI is a rare intoxicant, and hence the exact incidence of its poisoning is not known. Though a few case reports exist, as per our knowledge, only one report had described abnormal MRI findings mentioning abnormal signal in the splenium of corpus callosum.<sup>[1]</sup>

In our case, there was bilateral symmetrical hyperintense signal on T2-weighted and FLAIR images in peri-third ventricular thalami, peri-aqueductal region, dorsal pons, median lemniscus, abducens nuclei, dorsal medulla, inferior olivary nuclei, and dentate nuclei.

However, similar findings have been described in methyl bromide poisoning, a more common intoxicant.<sup>[6-8]</sup> Clinical manifestations of MI poisoning are also similar to those of methyl bromide intoxication. This is likely to be due to similar mechanisms of action as both of them belong to the same monohalothane group.<sup>[4]</sup> Experiments of methyl bromide on rat brain have shown that methyl bromide causes methylation of sulfhydryl groups of creatine kinase and inactivates it, leading to irreversible interference in microsomal metabolism.<sup>[9]</sup> Thus, generation of energy is affected due to inactivation of the enzymes involved in glycolysis and pyruvate oxidation.<sup>[10-12]</sup> Periventricular gray matter, brainstem, and cerebellar nuclei are the areas vulnerable to this metabolic derailment, which explains the characteristic anatomical distribution of signal abnormalities in these poisonings. This is why these MRI findings also simulate those seen in a number of syndromes associated with



**Figure 2 (A-D):** FLAIR axial image shows bilateral symmetrical hyperintense signal in inferior olivary nuclei (arrow) (A), T2W coronal image shows bilateral symmetrical signal in cerebellar dentate nuclei (arrows) (B), T1W axial image shows bilateral nearly symmetrical hypointense signal in dentate nuclei (arrows) (C), DWI shows no restricted diffusion in dentate nuclei (arrows) (D)



**Figure 3:** T2W coronal image shows absence of altered signal in the dentate nuclei in follow-up MRI

tissue energy deprivation, i.e., “energy deprivation syndromes.”<sup>[12]</sup>

Therefore, the list of differential diagnoses for MRI brain findings in MI poisoning is wide and includes other energy deprivation syndromes such as non-alcoholic Wernicke’s encephalopathy, drug-induced toxic encephalopathy, enteroviral encephalitis, etc. Some of them are described below.

In non-alcoholic Wernicke’s encephalopathy, increased T2-weighted and FLAIR signal intensities in the regions of the peri-aqueduct, periventricle, and medial thalami are the main features.<sup>[13]</sup> Signal intensity alterations in cerebellum, cerebellar vermis, cranial nerve nuclei, red nuclei, dentate nuclei, caudate nuclei, splenium, and cerebral cortex represent atypical MRI findings.

In drug-induced toxic encephalopathy (e.g., metronidazole), dentate nuclei are most commonly involved followed by tectum, red nucleus, peri-aqueductal gray matter, and dorsal pons. The dorsal medulla and the corpus callosum are less often affected. When corpus callosum is involved, splenium is affected in all cases.<sup>[14]</sup>

Enteroviral (EV71) encephalitis is another condition that shows bilateral symmetrical signal in dorsal brainstem and cerebellar dentate nuclei.<sup>[15]</sup>

In the pediatric age group, similar findings can be seen in Leigh’s disease in which abnormal high signal intensity on T2-weighted images is noted in basal ganglia, particularly

the putamen, periventricular white matter, corpus callosum, peri-aqueductal gray matter, and brainstem.

To conclude, bilateral symmetrical distribution of abnormal signal in dorsal brainstem and cerebellar dentate nuclei points out to disorders causing toxic metabolic turbulence. A detailed clinical history including drug and occupational history can narrow down the list of differentials and clinch the diagnosis.

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