



A Case Report of Toxic Brain Syndrome Caused by Methyl Bromide

Metil Bromid İnhalasyonunun Neden Olduğu Toksik Beyin Sendromu

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Methyl bromide (CH₃Br) is a halogenated aliphatic hydrocarbon that may cause acute and chronic toxicities. We describe a case of a 44-year-old male patient who developed toxic brain syndrome (TBS) and central nervous system (CNS) toxicity after exposure to CH₃Br by inhalation. Toxicity began with progressive nervousness, dysarthria and coordination disorder. The complaints on admission to the hospital were speech defect, balance disorder, consciousness disorder and involuntary movements. The patient was treated symptomatically in the intensive care unit (ICU), and organic reasons were excluded. Findings in the magnetic resonance imaging were considered secondary demyelination related to systemic intoxication. Because of the CH₃Br, alkylates the crucial sulfhydryl-containing enzymes, N-acetylcysteine was used as a source of sulfhydryl groups for the treatment of the patient. He was hospitalised for nearly 1.5 months in the ICU.

Keywords: Methyl bromide, poisoning, central nervous system toxicity

Metil bromid (CH₃Br), akut ve kronik toksiteye neden olabilen halojenli alifatik hidrokarbondur. İnhalasyon yolu ile CH₃Br maruziyeti olan 44 yaşında bir erkek hastada toksik beyin sendromu gelişimi sunulmuştur. Toksikite, ilerleyen sinirlilik, dizartri ve koordinasyon bozukluğu ile başlamıştır. Hastanın hastaneye başvuru sırasındaki şikayetleri; konuşma defekti, denge ve bilinç bozukluğu ve istemsiz hareketlerdir. Hasta yoğun bakım ünitesinde (YBÜ) semptomatik olarak tedavi edilmiş ve organik sebepler dışlanmıştır. Manyetik Rezonans görüntülemesindeki bulguları, sistemik intoksikasyona sekonder demiyelinizasyon olarak değerlendirilmiştir. CH₃Br, sülfidril içeren enzimleri alkilediğinden, hastanın tedavisinde N-asetilsistein kullanılmıştır. Hasta yaklaşık olarak bir buçuk ay YBÜ’nde takip edilmiştir.

Anahtar Kelimeler: Metil bromid, zehirlenme, santral sinir sistemi toksisitesi

Introduction

Methyl bromide (CH₃Br) is a halogenated aliphatic hydrocarbon that is used as a biocide fumigant (1). Colourless and nearly odourless, CH₃Br is a highly volatile liquid that exists in a gaseous state at ambient temperature. The route of entry is generally through inhalation and less commonly from skin exposure (1).

Signs and symptoms of acute toxicity are associated with the central nervous system (CNS), as well as with the cardiovascular and respiratory systems. In nonfatal cases, complete recovery may take several months. Neuropsychiatric signs may persist indefinitely (1). Treatment of CH₃Br poisoning has largely been supportive. Haemodialysis lowers serum bromide levels, but there is no evidence that dialysis affects patient outcomes (1). Some studies have found that haemodialysis is effective in the early period (2, 3).

Acute toxicity has been documented well, but little information is available about the effects of chronic toxicity. We described a case of chronic unintentional exposure to CH₃Br by inhalation that resulted in toxic brain damage (TBD) and CNS toxicity.

Case Presentation

A 44-year-old man was admitted to the emergency service with speech defect, involuntary movements and balance and consciousness disorder. The patient complained about progressive nervousness, dysarthria and coordination disorder while using the computer in the last 2 weeks.

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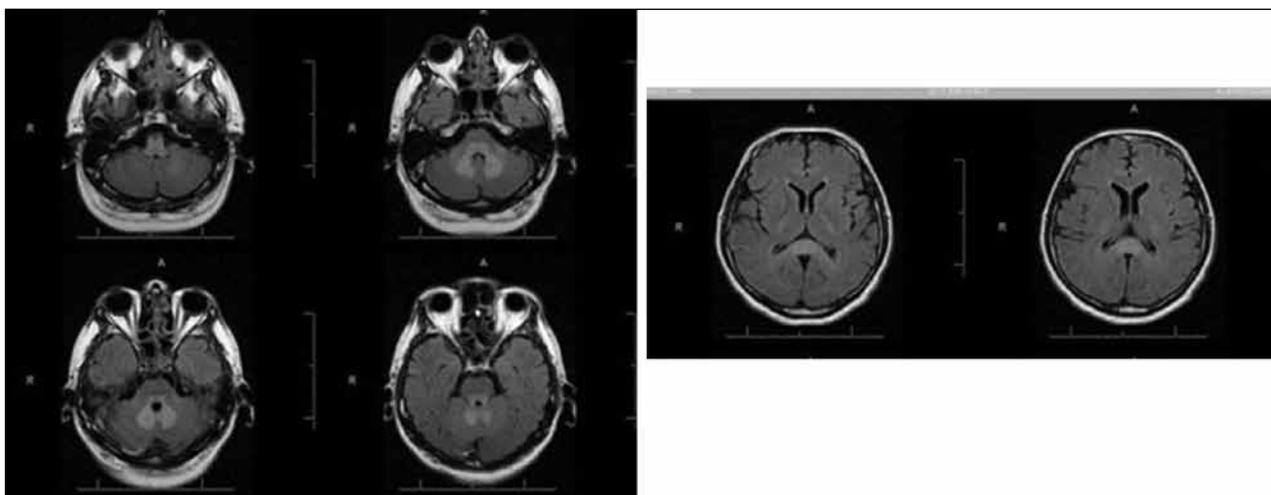


Figure 1. Axial fluid-attenuated inversion recovery (FLAIR) images show increased signal intensity in the regions of the medulla oblongata, posterior pons and posterior mesencephalon, bilateral dentate nuclei of cerebellum and splenium of the corpus callosum

Laboratory examinations revealed the following: glucose 89 mg dL⁻¹, blood urea nitrogen (BUN) 13.4 mg dL⁻¹, creatinine 0.9 mg dL⁻¹, sodium 144 mEq L⁻¹, calcium 10.1 mEq L⁻¹, chloride 112 mEq L⁻¹, haemoglobin (Hb) 14.9 mg dL⁻¹, haematocrit (Hct) 43.5%, white blood cell (WBC) 11.8 10³ µL⁻¹, platelet (Plt) 245.10³ µL⁻¹, aspartate aminotransferase (AST) 21 UL⁻¹, alanine aminotransferase (ALT) 31 UL⁻¹, gamma-glutamyltransferase (GGT) 48 UL⁻¹, lactate dehydrogenase (LDH) 20.8 UL⁻¹, amylase 72 UL⁻¹, activated partial thromboplastin time (APTT) 35.3 sec, prothrombin time (PT) 14.8 sec, fibrinogen 345 mg dL⁻¹, international normalised ratio (INR) 1.15 and pseudocholinesterase level 7920 I UL⁻¹.

Vital signs were as follows: body temperature 36.5°C, arterial blood pressure (ABP) 128/88 mmHg, pulse 87 beats/min, respiratory rate 21/min and oxygen saturation 97%. The electrocardiogram was normal. He was admitted to the intensive care unit (ICU) with a preliminary diagnosis of cerebrovascular disease. Computerised tomography (CT) and magnetic resonance (MR) imaging were normal. He was confused, uncooperative, disoriented and agitated. Meningeal irritation findings and bilateral Babinski signs were positive. His Glasgow Coma Scale (GCS) was E4M4V3. The pupils were isocoric, and bilateral pupillary light reflexes were positive. His Hb, WBC, Plt, coagulation test and kidney and liver function tests were within the normal ranges. His neurologic status worsened, and his agitation increased. He started to have visual hallucinations. Midazolam and haloperidol were used as a method of producing sedation.

The follow-up vital signs were: body temperature 37°C, ABP 166/83 mm Hg, pulse 98 beats min⁻¹, respiratory rate 34 min⁻¹ and oxygen saturation 100%. The physicians suspected toxic substance exposure. A perforated and empty CH₃Br tin box (Metabrom® 98% CH₃Br, 2% chloropicrin) for bedbugs was found his bedroom. The patient's findings were evaluated to be compatible with CH₃Br poisoning. Twenty hours

of N-acetylcysteine (NAC) treatment was administered with the recommendation of the Poison Information Centre. On the second day of observation, the patient was referred to a nearby university hospital's emergency service. Within 5 hours of observation, the patient was intubated to control his agitations and was admitted to the intensive care unit. A nephrologist evaluated the patient for haemodialysis, but there was no need in this case. His lumbar puncture was negative, and the brain CT was normal. In the MR imaging, increased signal intensity in the regions of the medulla oblongata, posterior pons, posterior mesencephalon, bilateral dentate nuclei of the cerebellum and splenium of the corpus callosum was seen (Figure 1). The MR was found to be compatible with the TBD while evaluated with the clinical findings. Due to the long-term endotracheal intubation, tracheostomy was performed on the 13th day. After 17 days, axial FLAIR images showed normal signal intensity in the medulla oblongata, pons, mesencephalon and dentate nuclei but increased signal intensity in the cerebral peduncles. Increased signal intensity in the splenium of the corpus callosum continued, which was compatible with systemic intoxication-related secondary demyelination (Figure 2). With the ameliorating neurological findings, the patient was transferred to the Nazilli State Hospital ICU on the 18th day. He had a lung infection and was immobile. He was treated for the infection. The tracheostomy was closed. Supportive treatment was applied. The physical therapy programme included passive range of motion (ROM) exercises, active assisted ROM exercises and progressive mobilisation with a physical therapist in the ICU every day. On the 48th day, the patient was transferred to the Physical Therapy and Rehabilitation Service (PTRS) with a speech disorder, bilateral positive Babinski signs and 3/5 paraparesis. He was standing with a walker. He had acceptable leg and trunk strength against gravity. He improved orthostatic tolerance. The focus of the physical therapy programme was to start walking re-education and functional training. The patient was discharged on the 16th day of hospitalisation in the

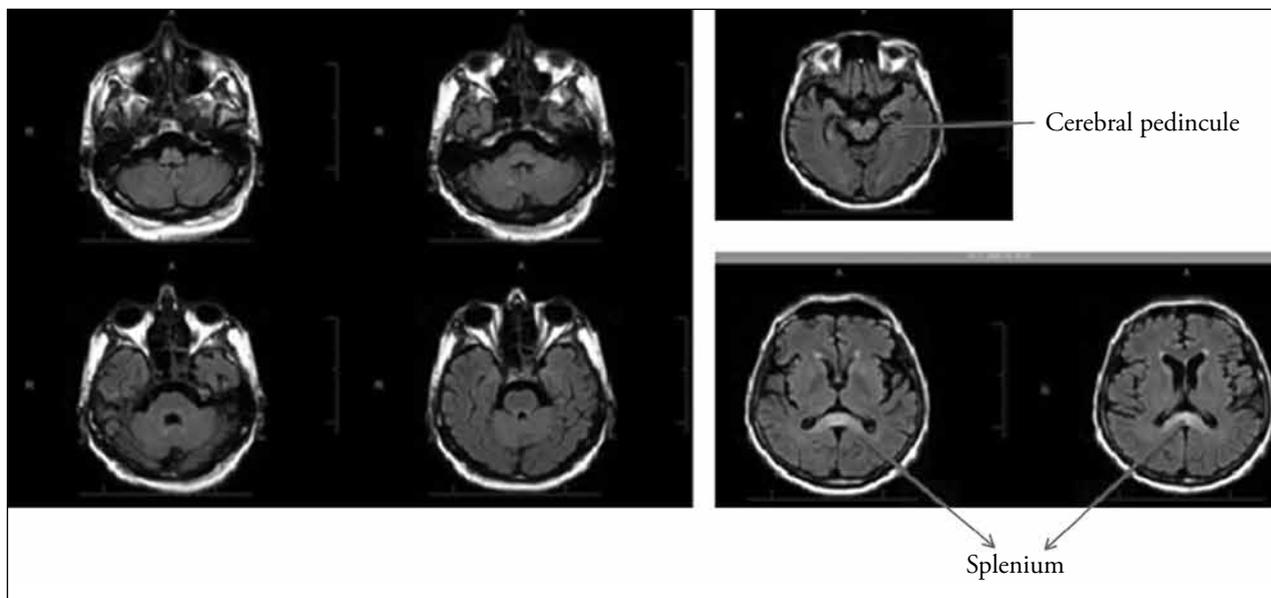


Figure 2. After 17 days, axial fluid-attenuated inversion recovery (FLAIR) images show normal signal intensity in the medulla oblongata, pons, mesencephalon and dentate nuclei but increased signal intensity in the cerebral peduncles. Increased signal intensity in the splenium of the corpus callosum is continued

PTRS. The patient is still being followed by the DEU Neurology Service and Nazilli State Hospital PTRS. The patient had a speech disorder (he jabbered but had understandable speech) and spasticity of the right quadriceps muscle. He can walk independently. He returned to his pre-event work.

Discussion

We describe a case of CNS toxicity of chronic unintentional exposure to CH_3Br through inhalation (1). After acute and chronic exposure to CH_3Br , a variety of neurobehavioral manifestations, including depression, irritability, confusion and personality changes, have been reported. In the acute phase, neurologic symptoms include lethargy, tremors, twitches, seizures, ataxia, headaches and paraesthesia. Persistent neurologic symptoms may occur after severe acute exposure (1).

Although the majority of poisonings are related acute exposures, in chronic exposure cases, neurologic findings, such as paraesthesia, cerebellovestibular and pyramidal deficits paraesthesia of legs, paroxysmal vertigo, decreased pain and vibratory sensation on the feet, impaired cerebellar signs and hyperactive reflexes, visual disturbance, dysarthria, decreased muscle strength and gait disturbances, were reported (4).

Our patient had been exposed to CH_3Br for 2 years; the clinical signs, such as speech defect, coordination disorder and involuntary movements, had started within the last 2 weeks. Prolonged low-level exposure to CH_3Br has produced protracted impairment of basal ganglion function and is characterised by incoordination of movement of all extremities (1). During the hospitalisation period, the neurological findings of our patient progressed and were accepted as toxic brain

injury. In some reports, MR imaging findings after CH_3Br intoxication described symmetric T2 signal abnormalities in the posterior putamen, subthalamic nuclei, restiform bodies, vestibular nuclei, inferior colliculi and periaqueductal grey matter (5, 6).

Methyl bromide poisoning is difficult to confirm, because routine laboratory testing has not been reliable. Bromide is not thought to be responsible for the clinical toxicity of CH_3Br . Measurable levels of the parent compound are not feasible due to its rapid reduction, a result of a direct tissue chemical reaction (7). Serum inorganic bromide levels may be useful in confirming exposure if intake of inorganic bromide can be excluded. If measured late in the course of poisoning, bromide levels are often normal and thus only variably helpful (7). Minor ($<117 \text{ mmol L}^{-1}$) or marked hyperchloraemia ($>124 \text{ mmol/L}$) was reported in chronic bromism. Although we could not measure the blood bromide levels, high chloride levels may support CH_3Br exposure. An elevated serum bromide concentration may cause a false elevation in serum chloride concentrations. In this case report, the diagnosis was based on history and clinical signs. But, a high level of chloride may support the diagnosis (8).

Conclusion

Although we could not measure CH_3Br levels in the blood or any body fluid, the findings, such as speech defect, coordination disorder and involuntary movements in a 2-week period and confusion, orientation deficit, agitation and visual hallucination in the hospitalisation period, were not related to a neurodegenerative disease; all of them were compatible with toxic brain injury.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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