Case Study

A Case of Acute Organotin Poisoning

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Alkyl compounds of tin chlorides are widely used for the production of plastics in the chemical industry. They inhibit the dissociation of hydrochloric acid from polyvinyl chloride (PVC) and in combination with PVC they are not toxic. However, as free molecules, organic tin compounds are highly toxic in contrast to inorganic tin compounds1). The toxic components are dimethyltin chloride and trimethyltin chloride. Previous studies have reported that dimethyltin chloride is toxic to the liver and kidneys, whereas trimethyltin chloride damages the central nervous system2–4). The neurotoxicity of dialkyltin or trialkyltin compounds has been recognized in animal studies, but only a few descriptions of their human toxicity have been reported1, 5–14). Especially, reports of human dimethyltin intoxication are very rare15). We report here a case with neurological manifestations similar to trialkyltin encephalopathy from the exposure to dimethyltin compounds.

Case Presentation

A 43-yr-old male with disorientation and behavioral change was admitted to our hospital. He had been working as a tank cleaner for several different companies in the previous 8 yr, and a week before admission he had cleaned a tank which had contained dimethyltin (DMT) for 4 d. A day after finishing the job, he suffered from dizziness, disorientation, hallucination, irritability and decreased memory. The behavioral changes did not improve and mental deterioration progressed. Brain magnetic resonance image (MRI) taken at another clinic did not explain his condition, and he was transferred to the emergency room of Ulsan University Hospital on the 4th day after the cessation of 4 days’ exposure to DMT.

Clinical Features and Laboratory Findings

The patient showed blood pressure of 110/70 mmHg, pulse rate of 85 per min, respiratory rate of 19 per min, and body temperature of 36.3°C with drowsy consciousness in the emergency room. The pupils were symmetric with a pupil size of approximately 3 mm. The light reflex, corneal reflex, and muscle power were within the normal range. The past medical history and family history were non-contributable. Posterior anterior chest X-rays showed normal findings. All the clinical procedures were performed with the patient’s/patient’s family’s informed consent. The serum level of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were 81 and 46 IU/l, respectively. The result of spinal tapping was negative on the 4th day of admission. On the fourth day of hospital admission, the patient deteriorated into a state of coma, and he was placed on mechanical ventilation. He also showed metabolic acidosis in arterial blood gas analysis (ABGA) (pH 7.178, pO2 71.5 mmHg, pCO2 25.1 mmHg, HCO3 9.1 mmol/l, SaO2 93.2%) along with severe hypokalemia (K+ 4.2 mmol/l), and difficulty in respiration. Electrocardiogram showed ST depression and T-wave flattening due to hypokalemia. The patient showed signs of acute renal failure (from BUN 58.3 mg/dl and Cr 1.32 mg/dl, to BUN 67.6 mg/dl and Cr 2.35 mg/dl) the next day.

On day 7, the patient’s blood test showed WBC count of 9,360 per mm3, hemoglobin of 11.2 g/dl, platelet count of 185,000 per mm3, AST of 351 IU/l, ALT of 119 IU/l, BUN of 78.3 mg/dl, Cr of 3.07 mg/dl, LDH of 1,030 IU/l, CPK of 9,686 IU/l, CK-MB of 38.29 IU/l, compatible with acute renal failure and rhabdomyolysis. From hospital day 7, British-anti-Lewisite (BAL) was injected intramuscularly at a dose of 2.5 mg/kg four times daily for two days, and twice a day for the two next days, and then once a day for four consecutive days. On day 9, liver function improved, and hypokalemia was corrected (K+ 4.2 mmol/l) with the conservative treatment, however, metabolic acidosis persisted.

The fluid-attenuated inversion recovery (FLAIR) brain MR imaging taken on day 12, showed extensive, symmetric high signal lesions of white matter in the subcortical and deep white matter of bilateral cerebral hemispheres, posterior rim of the internal capsule, corpus callosum, cerebral peduncle, corticospinal track, and middle cerebellar peduncle (Fig. 1A–D). Therapeutically, dexamethasone was administered in attempt to treat the cerebral edema. Metabolic acidosis was corrected on day 14. An electroencephalogram test suggested a moderate diffuse cerebral dysfunction. From day 20, the patient’s consciousness gradually improved and he responded to verbal commands. However, he continued to show disorientation, retrograde amnesia, and severe
motor ataxia. MRI on day 90 (Fig. 1E–H) showed no parenchymal lesion on FLAIR imaging. Nerve conduction velocity test showed that the sensory potentials of both superficial peroneal nerves and the compound muscle action potential (CAMP) of the deep peroneal nerve were not evoked. The test suggested both peroneal neuropathy of axonal type. The patient was discharged on the day 163 from the hospital, still showing moderate motor ataxia, memory loss, disorientation, and speech difficulty (Table 1).

**Fig. 1.** Axial fluid-attenuated inversion recovery brain MRI at the hospital on day 12 of hospitalization showed extensive, symmetric high signal lesions in the subcortical and deep white matter of bilateral cerebral hemispheres (A), posterior rim of the internal capsule and corpus callosum (B), cerebral peduncle (C), middle cerebellar peduncle (D). MRI on day 90 (E through H) showed no parenchymal lesion.

**Table 1.** Clinical course and laboratory findings

<table>
<thead>
<tr>
<th>HD</th>
<th>Clinical course</th>
<th>Treatment</th>
<th>Laboratory findings</th>
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<tbody>
<tr>
<td></td>
<td></td>
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<td>K+ (mmol/l)</td>
</tr>
<tr>
<td>1</td>
<td>Drowsy</td>
<td>Conservative Tx</td>
<td>3.5</td>
</tr>
<tr>
<td>4</td>
<td>Comatous, intubation</td>
<td>Conservative Tx</td>
<td>1.6</td>
</tr>
<tr>
<td>7</td>
<td>Ventilator care</td>
<td>Chelation started</td>
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</tr>
<tr>
<td>9</td>
<td>Fever, ventilator care</td>
<td>Chelation</td>
<td>4.2</td>
</tr>
<tr>
<td>12</td>
<td>Ventilator care</td>
<td>Chelation</td>
<td>3.7</td>
</tr>
<tr>
<td>14</td>
<td>Ventilator weaning</td>
<td>Chelation stopped</td>
<td>4.8</td>
</tr>
<tr>
<td>20</td>
<td>Drowsy</td>
<td>Conservative Tx</td>
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<tr>
<td>23</td>
<td>Alert</td>
<td>Conservative Tx</td>
<td>3.7</td>
</tr>
<tr>
<td>163</td>
<td></td>
<td>Discharged</td>
<td>3.9</td>
</tr>
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</table>


**Occupational History**

The patient’s had been an office worker at an insurance company until 8 yr ago. He had then worked as a tank cleaner for several different companies in the previous 8 yr, and also performed the same cleaning job for 8 d last
year without any problem. One week before admission, he had cleaned a tank used in the manufacture of dimethyltin dichloride (DMTC) for 4 d. The size of the tank was $2.25 \times 2.25 \times 3.4$ m. The DMTC was made from inorganic tin and methyl chloride under 4.5 atmospheric pressure at 170°C. An engineer at the company said that less than 0.3% of trimethyltin chloride (TMTC) was produced as a by-product in the reaction. The patient had worked inside the tank, while three other workers assisted him outside the tank. Before the tank was opened, it was washed with methanol and water several times for several weeks. He had to remove the remainder of the inorganic tin accumulated at the bottom of the tank with an air drill. He wore personal protective clothes and an air supplied mask.

**DMT and TMT in Blood and Urine**

Speciation analysis of alkyltin in urine and blood were performed using a combination of high performance liquid chromatography (HPLC, Model HP-1100, Agilent, USA) and inductively coupled plasma-mass spectrometry (ICP-MS, Model HP4500, Agilent, USA).

Urine was diluted 5 times with ultra-pure water, tap water purified through Milli-Q-ICP-MS (Millipore Japan, Tokyo, Japan). Blood was diluted 10 times with ultra-pure water and filtrated through Microcon (YM-10, Millipore, MA, USA). Fifty microliters of the sample were injected into the HPLC. Inorganic tin (In-Sn), MMT, DMT, and TMT were separated by HPLC using a cation-exchange column (RSpak NN-614, Shodex, Japan), and the mobile phase (5.0 mM HNO$_3$, 6.0 mM NH$_4$NO$_3$, 1.5 mM pyridine dicarboxylic acid) at a flow rate of 1 ml/min. ICP-MS was used for the determination of tin and 1 mg/l of germanium solution was used as the internal standard. The ICP-MS detection mass was set to $m/z$ 118 ($^{118}\text{Tin}^+$) and $m/z$ 72 ($^{72}\text{Ge}^+$). Detection limits for In-Sn, MMT, DMT and TMT were 0.1, 0.1, 0.05, and 0.5 µg Sn/l, respectively. The chromatograms of tin compounds in standard solution, urine and blood of the patient are shown in Fig. 2.

DMT and TMT concentrations in blood and urine collected during hospitalization are shown in Table 2. TMT concentrations were higher than DMT concentrations in all blood samples. The highest DMT concentration in blood was found on the 3rd day of BAL treatment, but TMT was highest at the first sampling on the 3rd day of hospitalization. The highest urinary concentrations of DMT and TMT were found on the 3rd and 5th day of hospitalization, respectively. During chelation therapy, urinary DMT and TMT concentrations were elevated. A trace amount of urinary DMT was detected on the 27th day after discharge, but TMT was not detected in the urine.

**Discussion**

We diagnosed the present case as alkyltin intoxication for the following reasons. First, the clinical features in the present case are compatible with those of trialkyltin encephalopathy\textsuperscript{6, 10, 16, 17}. Second, the worker was exposed to alkyltin for 4 d, and high DMT and TMT concentrations...
in urine and blood were detected. Third, other cerebral diseases such as brain tumor, cerebrovascular disease, and encephalitis were ruled out by clinical features, brain MRI and spinal tapping. Fourth, the extensive, symmetric high signal lesions throughout the white matter of the brain in MRI support the diagnosis of alkyltin encephalopathy.

The first symptoms occurred on the day following 4 days’ exposure in the present case. The latent period in the present case is compatible with that (1–3 d) reported in another study.1) The present case had neurologic sequelae such as motor ataxia, memory loss, disorientation, and speech difficulty even after the urinary alkyltin level returned to the normal range. Previous studies have also reported various neurologic sequelae.9, 10, 17) Our case showed severe hypokalemia. This finding was previously reported several times.1, 10, 18, 19) Tang et al.13) induced hypokalemia in Sprague-Dawley rats by exposure to TMT. They suggested TMT could induce acute renal leakage of potassium.

In the present study, the first MRI taken before admission showed normal findings, and the second FLAIR MR imaging taken on day 12 of hospitalization, showed the extensive, symmetric high signal lesions throughout the white matter of the brain (Fig. 1). MRI on day 90 of hospitalization showed no parenchymal lesion on FLAIR imaging (Fig. 1). Edema confined to the white matter caused by trialkyl tin has been reported in human and animal studies. An experiment on rats and dogs showed that triethyl tins produced edema confined to the white matter, but no vascular damage was found. More than 100 deaths and over 200 cases of illness occurred in France in 1954 due to the ingestion of a preparation containing diethyltin diiodide and triethyltin monoiodide. A pronounced edema of the white matter of the brain was seen in the fatal cases.16) Triethyltin-treated rats showed edema of the white matter in the central nervous system without neuronal damage.8) Our case is the first to show leukoencephalopathy induced by alkyltin using MRI.

In the present case, BAL treatment was performed and the patient recovered from coma. Rey et al.1) reported that the excretion rate of total tin in the urine correlated with the severity of the intoxication by DMTC and TMTC and a patient with more than 1 mg/l of tin excretion showed severe neurological defect. The highest urinary level of total tin in the present patient was 860 µg/g Cr and this level was consistent with his severe condition, coma. It was reported that plasma separation or D-penicillamine therapy had no effect on urinary excretion or clinical condition, but BAL treatment was effective, as in the present case.

TMT is a by-product of DMTC manufacture. A previous report showed that 8% of TMT was produced as a by-product of DMTC.10) Although many cases of

<table>
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<th>HD</th>
<th>MMT-U (µg/g Cr)</th>
<th>DMT-U (µg/g Cr)</th>
<th>TMT-U (µg/g Cr)</th>
<th>DMT-B* (µg/l)</th>
<th>TMT-B** (µg/l)</th>
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<td>3</td>
<td>–</td>
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<td>39.6</td>
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<tr>
<td>17</td>
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<td>611.1</td>
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<tr>
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</table>

27th day after discharge: 0.2(µg/l)
alkyltin-induced encephalopathy have been caused by exposures to mixtures of DMT and TMT1, 6, 9, 10, 16), those reports suggested that TMT was responsible for the encephalopathy, because previous studies have shown that trimethyltins are more neurotoxic than dimethyltin compounds21–23), and because organotin compounds are said to undergo biotransformation by dealkylation in in vitro and in vivo experimental studies24, 25). However, species analysis of organotin was not performed in those studies, so they could not identify the type of organotin. More than 1,000 people were poisoned by misusing organotin contaminated industrial lard as cooking oil in southeast China in 199915, 18). The contaminated lards mostly contained DMT compounds, but the contents of trimethyltin in urine and blood were much higher than that in the lards, thus, Jiang et al.15) suggested that DMT was absorbed and could be methylated to TMT in vivo. Jenkins et al.14) also pointed out the need to investigate DMT neurotoxicity in humans. In the present study, a worker who was exposed to DMT compounds showed neurologic manifestations similar to those of trialkyltin encephalopathy along with high levels of both DMT and TMT in the urine and blood. Whether TMT compounds detected in the urine and blood are due to exposure to TMT as a by-product of DMT production or from methylation of DMT in vivo remains to be solved.

The patient wore personal protective clothes and an air-supplied mask. However, the severe clinical features suggest that he might have been exposed to rather high concentrations of alkyltins. We assume that the personal protective devices were inappropriate, and significant exposure might have occurred via inhalation and skin absorption. The present case shows the importance of workplace risk assessment of organotin compounds and strict observance of preventive measures against acute poisoning, especially, when working in a confined space.

The present study has the following limitations. We were not able to simulate the cleaning process that had taken place inside the tank, so we could not determine how much DMT or TMT was produced in the working environment, and what the exact exposure route was during the cleaning job.

In conclusion, the patient appeared to have been intoxicated from acute exposure to a high level of organotin while cleaning a tank.

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**Reference**


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