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Toxic Leukoencephalopathy and Hypokalemia Due to Exposure to Trimethyltin

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Dear Editor,

Trimethyltin (TMT) is a by-product of organotin compounds, which are widely used as heat stabilizers. Unfortunately, TMT is a toxicant affecting several organs, including the brain.[1] Herein we describe a case of TMT intoxication characterized by symmetrical leukoencephalopathy and severe hypokalemia.

A previously healthy 22-year-old man presented with subacute headache, amnesia, and weakness. He worked in a rubber manufactory where plastic scraps were melted by heating them to 250°C. The other worker involved in the same work process had similar symptoms, while those working in other rooms were symptom-free. A neurologic examination disclosed retrograde amnesia, limb tremor, cerebellar ataxia, and generalized decreases in muscular tone and deep tendon reflexes. The findings of serum hematologic and biochemical tests were normal except for severe hypokalemia (2.1 mmol/L). Brain T2- and diffusion-weighted magnetic resonance imaging (MRI) performed on day 4 of hospitalization revealed symmetrical hyperintensities in the brain stem, cerebellum, corpus callosum, internal capsule, and subcortical spaces (Fig. 1A-D). The cerebrospinal fluid was normal except for an opening pressure of 220 mmH_2O. The electroencephalograph indicated excessive slow-wave activity. Blood and urine samples were obtained on day 7 of hospitalization for toxicology analyses by the Institute of Forensic Science, Ministry of Justice, PRC. A combination of inductively coupled plasma-mass spectrometry and high-performance liquid chromatography revealed elevated concentrations of TMT in both the blood (78.92 ng/mL, normal range=0.11–1.75 ng/mL) and urine (349 ng/mL, normal range=5.72–48.7 ng/mL). The levels of triethyltin (20.45 ng/mL) and lead (0.57 ng/mL) in the urine were within the normal limits (13.4–65.0 and 0.55–4.69 ng/mL, respectively). A diagnosis of acute TMT encephalopathy was made, and the patient was treated with intravenous methylprednisolone, potassium chloride, mannitol, and neuroprotectives. His clinical condition improved gradually, with hypokalemia being corrected 2 weeks later. Follow-up MRI performed 3 months later showed complete resolution of the lesions (Fig. 1E-H), which was accompanied by a complete clinical recovery.

Intoxication caused by TMT was first reported in 1978,[1] since when the incident rate has been increasing. Most cases of accidental TMT poisoning are work-related.[2] With a latency of 3–6 days, TMT encephalopathy is clinically characterized by limbic-cerebellum syndrome, including delirium, confusion, amnesia, ataxia, tremor, and seizure.[3] Hypokalemia as well as cardiac and hepatic dysfunctions are also common findings. Typical neuroimaging findings of TMT encephalopathy involve widespread abnormal signal intensities in the basal ganglia, corpus callosum, subcortical white matter, brain stem, and cerebellum, all of which disappear after several months.[4,5]

Pathologic studies of TMT poisoning in humans have found neuronal necrosis in the hippocampus, cerebral cortex, basal ganglia, Purkinje cell layer of the cerebellum, and spinal cord. Electron microscopy has demonstrated abundant lysosomal dense bodies and disor-

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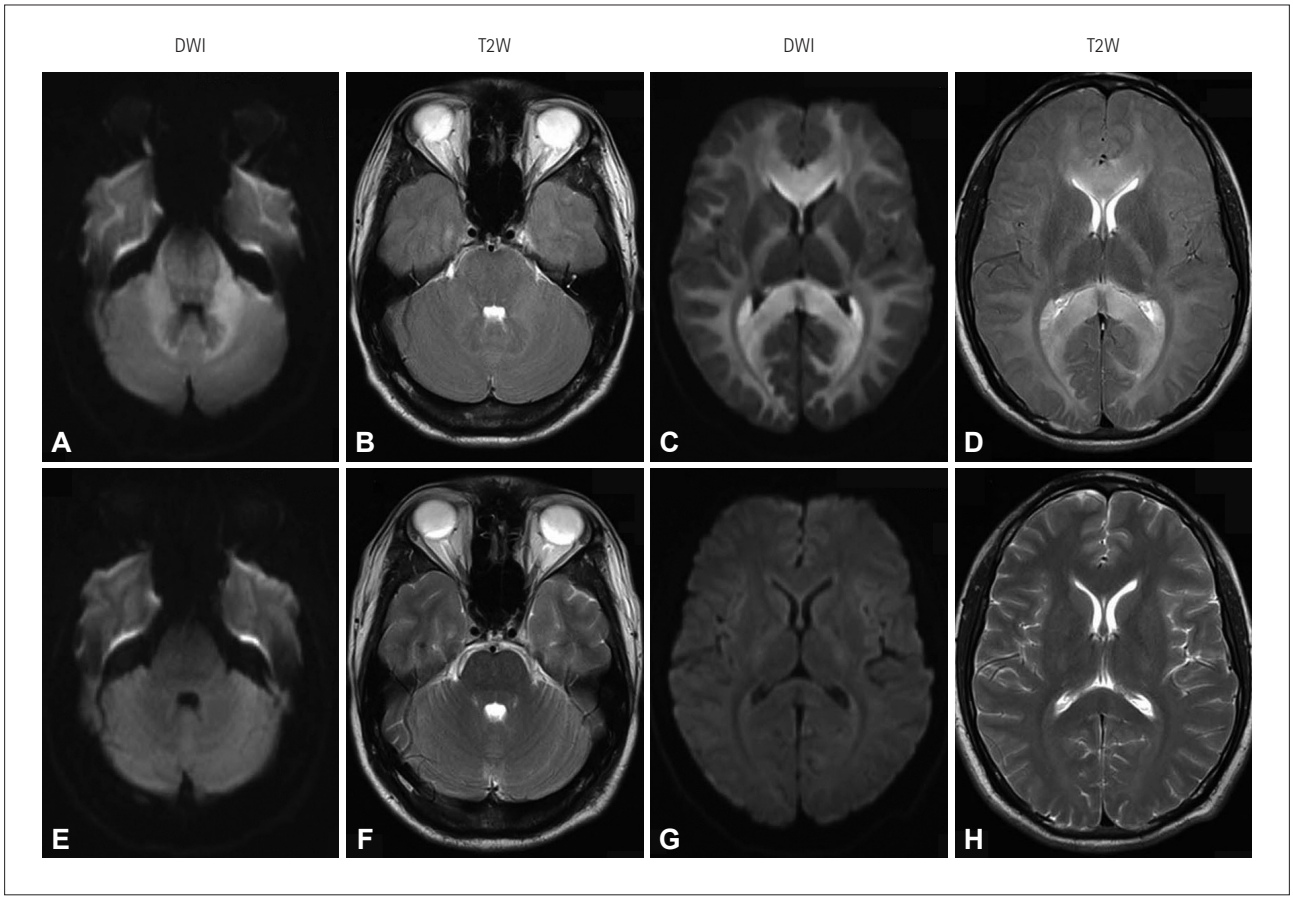

Fig.1. Neuroimage findings of this patient. A-D: Initial brain MRI showed symmetrical hyperintensities in the brain stem, cerebellum, corpus callosum, internal capsule, and subcortical spaces. E-H: Follow-up brain MRI performed 3 months later revealed complete resolution of these lesions. DWI: diffusion-weighted imaging, T2W: T2-weighted.

ganization of the endoplasmic reticulum in neurons.[6] The mechanisms underlying the neurotoxicity of TMT remain unclear, but the release of endogenous excitatory toxins, hyperammonemia, decreased γ-aminobutyric acid concentration, and inhibition of Ca^{2+}-ATPase have been proposed.[7] Regarding hypokalemia, Tang et al.[2] demonstrated that TMT could directly inhibit the activity of H^+/K^+-ATPase in renal intercalated cells, resulting in reduced reabsorption of potassium.

No specific treatments are available for TMT encephalopathy. Symptomatic therapies include hypertonic dehydrants, potassium supplementation, and antiepileptic drugs. Glucocorticoids have been used empirically to attenuate brain edema. Hemodialysis and plasmapheresis can be attempted in cases with a heavy TMT load. While most patients improve gradually after removing the exposure and receiving symptomatic treatments, death from TMT intoxication has been reported.[3] Workers should be warned of the risks and dangers of working with organotin compounds, and appropriate protective measures should be taken to avoid adverse effects.

Conflicts of Interest

The authors have no financial conflicts of interest.

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