

Management of thallium poisoning

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A case of acute thallium poisoning in a 67-year-old Chinese woman is described. She presented with acute pain in the chest, abdomen, and lower limbs. The diagnosis was not made, however, until alopecia developed. Detoxification treatment, which included Prussian blue (potassium ferric hexacyanoferrate) was given, but further neurological damage occurred. The patient's motor function recovered after 1 year, but residual sensory neuropathy remained. This case illustrates that tissue-bound thallium may cause prolonged neurological damage if detoxification therapy is not commenced within 72 hours of the onset of acute poisoning. Acute abdominal pain and painful neuropathy in the lower extremities are important early diagnostic clues for timely therapy. However, by the time alopecia develops—typically around 2 weeks after the onset of symptoms—detoxification therapy may not be able to prevent the development of prolonged neurological damage.

HKMJ 2000;6:316-8

Key words: Ferrocyanides/therapeutic use; Poisoning/drug therapy; Thallium/poisoning; Time factors

Introduction

Thallium is a heavy metal that is used in the manufacture of electronics, alloys, and glass. In clinical practice, thallium 201 is used as a radioactive tracer in heart scintigraphy to detect myocardial ischaemia. Thallium and its salts are highly toxic, however, and industrial safety guidelines exist in the workplace. Accidental poisoning has become rare in the domestic setting since the 1970s, when thallium-based rodenticides were banned in many countries. The majority of reported cases of thallium poisoning in the past two decades have been caused by deliberate poisoning.¹⁻⁵

Case report

A 67-year-old Chinese woman was admitted to a county hospital in San Jose, California, United States, in September 1997 because of acute pain in the chest, abdomen, and lower limbs. The pain in the lower limbs was described as burning and severe. There was no vomiting or diarrhoea. The patient was discharged after 3 days, but the cause of her illness was undetermined.

The patient presented to the author's private clinic 1 week later because of persistent symptoms. Physical

examination of the patient showed mild tenderness over the abdomen, and electrocardiography showed non-specific T-wave inversion in the anterior leads. Routine urinalysis gave normal results, and laboratory tests showed normal blood cell counts, blood glucose level, and kidney and liver function. The patient was treated symptomatically with analgesics. She was soon readmitted to hospital, however, because of prostration and fainting spells, as well as persistent symptoms. The patient suspected that she was being poisoned. Paranoid psychosis and trichotillomania were diagnosed, and she was admitted under restraint to the psychiatric department for observation.

After being discharged home, at week 5, she returned to the author's private clinic. According to the patient, the pain had become less severe. Physical examination showed diffuse alopecia, which had started 2 weeks after the onset of the initial symptoms. Thallium poisoning was suspected. A urine sample was taken to measure its thallium content by graphite-furnace atomic absorption spectroscopy. The urine level of thallium was 8.56 µmol/L (normal level, <0.003 µmol/L; a level of >0.98 µmol/L is toxic). The case was reported to the police; the prime suspect was the patient's 73-year-old cohabitant.

A dose of activated charcoal was given in the emergency department of a nearby district hospital, and the patient was discharged home with a 2-week supply of succimer (2,3-dimercaptosuccinic acid). At

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follow-up at week 6, however, it was found that the pain in her chest, abdomen, and lower limbs had subsided, but symptoms of peripheral neuropathy had emerged—namely, bilateral numbness and loss of exteroceptive and proprioceptive sensations in the toes. She had mild weakness in the proximal muscles of the lower limbs, as indicated by the patient's difficulty in rising from the squatting position. She also complained of right-sided headache and tachycardia. She was immediately admitted to the Stanford University Medical Center for treatment with oral Prussian blue (potassium ferric hexacyanoferrate, $\text{KFe}_{(III)}[\text{Fe}_{(III)}(\text{CN})_6]$) 4 g every 8 hours.

The blood thallium level at the time of hospitalisation was 0.15 $\mu\text{mol/L}$ (normal level, $>0.07 \mu\text{mol/L}$; $>0.49 \mu\text{mol/L}$ is toxic). No other heavy metals were present. The patient tolerated Prussian blue very well, but hypoesthesia developed over the medial aspect of her left calf on the second day of treatment. She was discharged home 1 week later, when the urine level of thallium was 0.14 $\mu\text{mol/L}$.

In week 9, the patient experienced neurological deterioration, impairment of short-term memory, double incontinence, tremor, ataxia, and falls. Physical examination showed hypoesthesia of the right trigeminal nerve, general weakness of the extremities (grade 4/5), cerebellar ataxia, tremor, and dyskinesia. Plantar reflexes were normal, and the urine thallium level was 0.33 $\mu\text{mol/L}$. By week 14, the right facial numbness fully recovered. By week 20, there was recovery of sphincter control and regrowth of hair. Urine thallium was undetectable 2 weeks later. The weakness in the lower limbs, unsteady gait, falls, and bruises persisted until August 1998, when her condition noticeably improved, although residual weakness remained.

Discussion

Thallium salts are colourless, tasteless, and odourless. They are readily absorbed, and thallium becomes distributed throughout the intravascular compartment within 4 hours. Redistribution between the extracellular and intracellular compartments is complete within 24 hours. Forty percent of the absorbed poison is excreted by the kidneys; 60% is excreted in the faeces, but its presence in the body is prolonged by the enterohepatic circulation. The elimination half-life can be as long as 30 days. A dose of 10 to 15 mg/kg is lethal.⁵

Within the cells, thallium displaces potassium in the Na-K ATPase channel, which is responsible for

generating ionic gradients in nerve, heart, and muscle cells. Thallium also binds to sulphhydryl groups, which act against free radicals, and with riboflavin, which mediates hydrogen transfer in tissue respiratory systems and provides energy to maintain axon integrity. The clinical manifestations of thallium poisoning depend on the dosage, chronicity, body weight, individual susceptibility, and the onset of treatment. Early aggressive therapy with Prussian blue, forced diuresis, and haemodialysis may not only be life-saving, but also reduce the duration and extent of neurological damage if they are given within 72 hours, as has been illustrated in five reported cases.^{1,2} Despite the fact that the peak serum level of thallium exceeded 24 $\mu\text{mol/L}$ in one case, neurological recovery was complete within 1 month in all five cases.

In contrast, in a case in which treatment was delayed for 5 days after the onset of symptoms, the neurological damage lasted for more than 9 months.³ Other case reports have shown that more prolonged and possibly permanent neurological complications can occur when treatment is delayed until after the onset of alopecia.^{4,5} An extended electrophysiological study of a case of thallium poisoning has shown that distal axonopathies of the lower extremities may take more than 2 years to recover.⁶ Neurological deficit lasting more than 30 years has also been reported.⁷ In this case, treatment with Prussian blue in the 7th week of illness did not prevent the progression of neurological damage, although the thallium level had decreased to a non-toxic level after treatment.

A high index of suspicion is required to diagnose thallium poisoning at an early stage. Important clues are acute abdominal symptoms and painful neuropathy in the extremities occurring within 72 hours of the onset of initial symptoms. Differential diagnoses include botulism, ciguatera poisoning, porphyria, Guillaine-Barré syndrome, and poisoning with other heavy metals.

Thallium may be detected in the urine 1 hour after thallium ingestion, but most clinical laboratories may not have the available facilities to quantitatively analyse the thallium content. A rapid quantitative urine test can be done by mixing urine with 0.4% sodium bismuth in 20% nitric acid and 10% sodium iodide. A red precipitate indicates thallium is present.⁸

References

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