Accidental podophyllin poisoning in a 3-year-old child

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Accidental poisoning in children remains a common presentation in healthcare centres worldwide, with the highest rates of fatal poisonings occurring in Africa. Podophyllin, commonly used for genital warts, is a rare agent in poisoning cases. A few cases have been reported in the international literature, with serious systemic and neurological side-effects. We report a case of accidental podophyllin poisoning in a 3-year-old boy, which was complicated with organ dysfunction. The case highlights the severe neurological side-effects of podophyllin poisoning and the importance of accident prevention in our communities.

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A 3-year-old male was admitted after accidentally ingesting an unknown amount of a podophyllin-containing topical solution, originally prescribed for an adult member of the family. Prior to his hospital admission, milk was given as a home remedy, consequently followed by massive emesis and diarrhoea. He presented to hospital 5 hours post ingestion with an altered sensorium. Activated charcoal was administered via nasogastric tube. He had no known medical conditions or previous admissions to hospital. His growth and development were normal for his age. After initial stabilisation, he was transferred to a tertiary hospital for further intensive care. In the paediatric intensive care unit, the child was assessed to have a Glasgow Coma Scale (GCS) of 5/15 (E = Eyes, 1; V = Verbal, 1; M = Motor, 4). He did not require any airway support or mechanical ventilation, but was placed on nasal prong oxygen. Initially, the peripheral neurological and general examination was normal. Laboratory investigations revealed renal and hepatic impairment, as well as bone marrow suppression (Table 1).

Twenty-four hours post podophyllin ingestion, the child's GCS remained 5/15; however, he had now developed abnormal neurological signs, including hypotonia, areflexia with no clonus and reduced power in all limbs, but with no evidence of a pseudobulbar palsy. He had no signs of autonomic dysfunction; however, he did show deficits in sensation examination with loss of pain and touch. Proprioception and temperature examination were not conclusive owing to the age of the patient and his reduced GCS. He was assessed as having a possible sensory-motor peripheral neuropathy. He was monitored closely and managed supportively. Feeding was initiated via a nasogastric tube. The child's GCS improved to 9/15 (E4, V2, M3) 72 hours after ingesting the podophyllin, but he then exhibited signs of a pseudobulbar palsy.

After 6 days in high care, the child developed a paralytic ileus, requiring nasojejunal tube placement, bowel rest and antibiotics. During this time, his renal and liver impairment and blood counts steadily improved.

Further investigations revealed a normal computed tomography scan of the brain; however, a magnetic resonance image of the brain revealed cortical atrophy that was not in keeping with his age. An electroencephalogram showed a background of slowing and of low-amplitude (4 Hz) wave activity, but no focal or epileptiform activity. Nerve conduction studies confirmed a sensory-motor neuropathy. A videofluoroscopic study (modified barium swallow), done to assess the extent of his pseudobulbar palsy, revealed a delay in the triggering of the swallowing reflex.

He has regained minimal motor and sensory function, and receives regular physio- and occupational therapy as part of his continued rehabilitation. He awaits a percutaneous gastrotomy to assist with appropriate feeding.

Discussion

Accidental poisoning in children is a common occurrence, making up 10.9% of all

Table 1. Trends of blood results

Investigation	Reference range*	Admission	Day 1	Day 3	Day 7
Full blood count					
Haemoglobin	10.5 - 14.5 g/dL	11.3	7.4	9.0	8.1
White cell count	5.5 - 15.5 × 10^3 cells/μL	10.9	11.5	4.4	16.8
Platelets	170 - 380 × 10^3 μL	200	79	67	575
Urea and electrolytes					
Urea	2.5 - 6.5 mg/dL	16.3	20.6	2.5	1.2
Creatinine	<46 μmol/L	90	125	26	21
Liver function tests					
ALP	60 - 320 IU/L	454	288	165	131
ALT	<45 IU/L	69	80	52	16
AST	16 - 69 IU/L	Not done	230	93	62
GGT	<45 IU/L	87	60	35	25
Coagulation tests					
INR	0.8 - 1.2	1.43	2.29	0.96	1.06

ALP = alkaline phosphatase; ALT = alanine aminotransferase; AST = aspartate transaminase; GGT = gamma glutamyl transpeptidase; INR = international normalised ratio.

*National Health Laboratory Services age and gender specific laboratory reference ranges.

unintentional injuries worldwide.[1] Africa has the highest incidence of fatal poisonings worldwide, at 4 per 100 000.[1] Poisoning with podophyllin is rare, with most cases documented around the 1970s - 1980s. The drug is widely used for the treatment of genital warts. The last known reported case was a paediatric patient in India in 2001.[2] There are very few reports on the toxic effects of this compound, and therefore the serious systemic and neurological effects of podophyllin are not fully appreciated.

Podophyllin use began in the 1800s, variously as an emetic and cathartic agent to an antivenom and suicidal agent.[3] Later, its use was extended as a local agent for skin lesions.[3] The widespread use of podophyllin for condyloma acuminatum only began in 1942.[3] The first documented side-effects were reported around 1835, when a woman developed abdominal cramps and pain after ingestion,[3] and the first fatal case after oral administration was reported in 1890. A fatal case relating to topical application was reported in 1954.[3] The active constituent of the drug is podophyllotoxin, a lipid-soluble compound extracted from the resin of *Podophyllin* plant roots, which readily crosses cell membranes.[2,3] Podophyllotoxin is a cytotoxic agent that inhibits DNA synthesis as well as cell mitosis in metaphase.

Podophyllin has both local and systemic effects associated with topical and oral use. It is a severe irritant to mucous membranes, with local effects including erythematous, oedematous and ulcerative skin lesions, burns and conjunctivitis.[4,5] Systemic toxicity causes multiorgan dysfunction. Gastrointestinal irritation in the form of nausea, vomiting, abdominal pain and diarrhoea, and bone marrow suppression with thrombocytopenia and leucopenia, manifest early in the presentation. Renal and hepatic failure with electrolyte disturbances, including hypokalaemia and hypoglycaemia, have been noted in several cases.[2,5]

Neurotoxicity is the most severe effect of podophyllin poisoning.[2,5] Initially, the presentation includes altered sensorium ranging from confusion to coma, but may include hallucinations, stupor, seizures and ultimately death.[2,5,6] Peripheral neuropathies can appear early, but mostly present some days later with motor (hypotonia, hyporeflexia) and sensory (paraesthesia, glove and stocking loss of light touch and proprioception) deficits.[2,5] Autonomic neuropathies can also be present, manifesting as paralytic ileus, hypotension, tachycardia, urinary retention and apnoea.[2,5] Our patient had complications of bone marrow suppression, renal and hepatic impairment, as well as peripheral and autonomic neuropathies.

The management of podophyllin ingestion and subsequent toxicity is mainly supportive, as no specific antidote exists. Activated charcoal is recommended for use after a recent ingestion.[2,5] Adequate management of ventilation and circulation is required, accompanied by monitoring for the abovementioned complications. Haemoperfusion to reduce plasma levels of podophyllin has been reported in the literature; however, its use has only been reported in adults and its effect on outcomes remains unclear.[5]

In South Africa, Malangu *et al.*[7] reported that 17% of total paediatric ward admissions are due to acute poisoning, with the majority being unintentional poisonings and with children <10 years of age comprising 80% of all poisoning victims. Podophyllin is still a widely used treatment, especially as a topical application. Despite podophyllin poisoning being rare, with few reported cases, the toxic side-effects (especially the neurotoxicity) must be highlighted because of the associated morbidity and mortality.[8]

Accidental poisoning in children, as in this case, is a preventable injury. Education of parents and healthcare workers on home safety still remains the mainstay of prevention. Most poisoning cases require supportive management, and poison control centres should be contacted early for management guidelines.

Ethical approval

Informed consent for the publication of this case report was obtained from the mother of the child.

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