

A Rare Case of Podophyllin Poisoning: Early Intervention is Lifesaving

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ABSTRACT

Accidental poisoning in children is very common, making up 10.9% of all unintentional injuries worldwide. Africa has the highest incidence of fatal poisonings worldwide, at 4 per 100,000. Poisoning with podophyllin is rare, with most cases documented around the 1970s to 1980s. Podophyllin is a resin mixture obtained from the dried Rhizome and roots of *Podophyllin peltatum* (North America) and *Podopyllin emodi* (India). Podophyllotoxin is the most toxic chemical present in the podophyllin, which is lipid soluble; so crosses the cell membrane easily and inhibits mitotic spindle formation. Both topical application and oral consumption can cause podophyllin poisoning. Neurotoxicity is the most serious effect along with bone marrow depression, gastrointestinal irritation, and hepatic and renal dysfunction. Management of podophyllin toxicity is mainly symptomatic, and no specific antidote exists. We report a case of a 2-year-old-year girl with accidental podophyllin poisoning, who presented with neurotoxicity followed by multiorgan dysfunction and then succumbed. Education of parents and healthcare workers on home safety still remains the mainstay of prevention.

Keywords: Accidental poisoning, Multiorgan dysfunction, Neurotoxicity, Podophyllin.

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INTRODUCTION

Accidental poisoning in children is a common occurrence, making up to 10.9% of all unintentional injuries worldwide. 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 to 1980s. The last known reported case in India was a pediatric patient in 2002 and a 3-year-old child in South Africa in 2015.

CASE DESCRIPTION

A 2-year-old girl was admitted after accidental ingestion of 5 mL of podophyllin containing topical solution (Podowart 20%), originally prescribed for an adult for warts. Mother had given podophyllin by mistake in place of albendazole syrup prescribed for worm infestation. She had presented to hospital 6 hours, post-ingestion with vomiting and altered sensorium. On examination, she was comatose (GCS—E2V2M4), febrile 102 F, tachycardia heart rate—140/minute with feeble peripheral pulses, a systolic blood pressure of 60 mm Hg, RR—50/minute, and a saturation of 85% in room air. She was managed conservatively with gastric lavage with charcoal, fluid bolus, oxygen, and inotropes. But after 1 hour, she developed right focal seizures with secondary generalization, for which she was loaded with fosphenytoin and then levitiracetam. As the general condition of the child deteriorated, she was referred to our hospital.

On arrival at emergency, she was comatose with GCS—6/15 (E1V1M4), heart rate—140/minute with cold and calmy extremities with feeble pulses, blood pressure was not recordable, and saturation was 57% on room air. She was resuscitated with rapid fluid boluses, adrenaline infusion then intubated, and ventilated in pediatric intensive care unit. At the time of admission, baby already developed multiorgan dysfunction, i.e., renal (anuria for 4 hours), hepatic (transaminitis), central nervous system (CNS) (altered sensorium, coma), cardiovascular (shock and severe metabolic acidosis) (PH—6.95, PCO₂—59, PaO₂—15, bicarbonate—12 and BE—19),

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and respiratory (severe hypoxia). Central line and arterial line were placed and inotropes (adrenaline, noradrenaline, and vasopressin) are optimized. Peritoneal dialysis was started as there is anuria and severe metabolic acidosis (Tables 1 and 2).

Her initial laboratory investigations revealed Hb—6.8 g/dL, TLC—3,100 (N—26, L 71%), TPC—50,000, Na—151, potassium—2.8, calcium—3.9, urea—29, creatinine—0.5, SGOT—646, SGPT—206, and prothombin time—46 second with an INR of 4.7. She had received one unit of PRBC. Child also received one unit of FFP and one unit of RDP along with vitamin K as there is oozing from central and arterial line site and through the endotracheal tube. Within next 48 hours, her general condition further deteriorated and she was succumbed. We lost this child because of delayed referral, delay in intubation at referral center, and probably aspiration during transport leads to severe hypoxia.

DISCUSSION

Podophyllin is a resin mixture obtained from the dried rhizome and roots of *Podophyllin peltatum* (North America) and *Podopyllin emodi* (India).² This resin contains at least 16 chemicals including podophyllotoxin, alpha and beta peltatin, desoxypodophyllotoxin, and quercetin. Of these, the toxic agent is thought to be

Table 1: Serial arterial blood gas

Parameter	Day 1 referral center	Day 2 admission	Day 2	Day 3	Day 4
PH	7.23	6.95	6.903	7.372	7.164
PCO ₂	43	59	52	29.	50
PaO ₂	221	15	22.4	72	39
HCO ₃ ⁻	17.8	12.5	7.7	18	15
BE	-8	-19	-20	-9	-10
Na/K/Cl ⁻	145/2.7/110	157/3/119	150/2.5/120	161/3.3/129	153/5.8/123
Anion gap	20	29.56	25	14	20
Lactate		12	12.2	6.2	5.4

Table 2: Serial laboratory investigations

Investigations	Normal value	Day1 (at referral center)	Day 2 (admission)	Day 3	Day 4
Hemoglobin	11–14 g/dL	11.2	6.8	13.1	10.7
TLC	5,000–15,000/ μ L	11,900	3,100	2,700	1,900
DC	N—40–60, L—35–65	N—18, L—71	N—26, L—71	N—35, L—56	N—71, L—20
TPC	1.5–4.5 L	1.9 L	50,000	30,000	20,000
CRP (Q)	6 mg/L		18.4	150	
Electrolytes (Na/K/Ca)		153/3/4	151/2.0/3.9	159/2.5/6.4	152/5.8/7
Urea	12–42 mg/dL	19	29	61	84
Creatinine	0.5–1.0 mg/dL	0.5	0.5	1.3	2.5
S. bilirubin	0.2–1.2 mg/dL	23	0.1	0.55	1.48
SGOT	0–40 U/L	258	646	1,013	750
SGPT	5–50 U/L	88	204	270	256
ALP	<then 390 U/L	239	117	203	131
Albumin	3.5–5 g/dL	2.5	1	2.3	2
PT/INR	10–15/seconds	20/1.3	46/4.7	35/3.5	32.4/3.24
GCS		E3V4M5	E2VTM3	E1 VT M 1	E1VTM1

podophyllotoxin, a lipid soluble compound that crosses cell membranes with ease. This substance and its derivatives have a colchicine-like effect, arresting the mitotic spindle.³ Neurotoxicity may be related to its *in vitro* ability to bind microtubular protein and to inhibit axoplasmic flow.³ Podophyllin has been used for external application in treatment of anogenital warts, condyloma accuminatum, and malignancy basal cell epitheliomas, wet and exudative types of eczema, and molluscum contagiosum.² According to the CDC, podophyllin is no longer recommended as a treatment of external genital warts because of safer alternative options.⁴ Podophyllin poisoning following both topical application and oral consumption has been reported in adults.^{2,5} Fatal dose of podophyllin resin for humans has been estimated to be 0.3 g to 0.6 g, or as little as one-half teaspoon of 25% podophyllin resin in benzoin tincture.⁶ There is a case report of podophyllin toxicity in a child aged 2 years in western literature.³ There is only one case reported in child in the Indian literature in 2002; hence, we report this case of accidental consumption of podophyllin in a 2-year-old girl.

Podophyllotoxin and its derivatives bind to the enzyme topoisomerase II during the late S and early G2 stage and arrests mitosis to produce its cytotoxic effects. Neurotoxicity, in addition, may be due to direct nonspecific effects on the neurons and glial cells.⁷ Multiorgan dysfunction after podophyllin ingestion manifests as bone marrow suppression (thrombocytopenia and leucopenia; early features), gastrointestinal irritation (in the form of nausea, vomiting, abdominal pain, and diarrhea), and renal and

hepatic failure (electrolyte disturbances, including hypokalemia and hypoglycemia).

Neurotoxicity is the most severe effect of podophyllin poisoning. Central nervous system presentation varies from altered sensorium, confusion, hallucinations, stupor, seizures to coma, and ultimately death. Peripheral neuropathies usually appear late in the course of illness but can appear early with motor (hypotonia and hyporeflexia), sensory (paresthesia, glove and stocking loss of light touch, and proprioception), and autonomic deficits (paralytic ileus, hypotension, tachycardia, urinary retention and apnea).⁸ The CNS toxicity is usually transient and reversible over a period of up to ten days, but deep coma leading to a fatal outcome or severe encephalopathy characterized by irreversible cognitive dysfunction, which may also occur. The course of the neuropathy is chronic and the recovery is delayed⁹ sometimes improvement being minimal.¹⁰

Management of podophyllin toxicity is mainly symptomatic, and no specific antidote exists. Activated charcoal is recommended for gastric lavage after recent ingestion.¹¹ If topical contact occurs, wash with soap and water. Intensive management of ventilation and circulation, accompanied by monitoring for above-mentioned complications is required. Hemoperfusion should be used for severe systemic poisoning since it has been shown to be effective in reducing the plasma fraction of podophyllin toxin and other active metabolites.



The first fatal case after oral administration was reported in 1890. The last known reported case in India was a pediatric patient in India in 2002 and a 3-year-old child in South Africa in 2015.^{11,12} A fatal case relating to topical application was reported in 1954.¹³ Education of parents and healthcare workers on home safety still remains the mainstay of prevention. Most poisoning cases require supportive management, and poison control centers should be contacted early for management guidelines. Ideally, these types of toxic drugs should not be available over the counter without prescriptions.

CONCLUSION

Though a rare entity and scarcely reported; physicians should be aware about podophyllin toxicity. Neurotoxicity is the most dangerous complication but it can present with multiorgan dysfunction also. Treatment is mainly symptomatic. It can be fatal if not treated early. Parental awareness is very important to avoid this type of accidental toxicity. One should not forget to take help of poison control centres for management of this type of rare toxicity.

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