Podophyllin Toxicity with Systemic Manifestations in a Young Male

Manish Jha¹, Shivanshu Raj Goyal², Subhash Chander Sharma³

Abstract
Podophyllin poisoning is a rare but a fatal poisoning with a long term systemic and neurological sequelae. There has been no case report reported in an adult in India. We present a 28-year-old young male with podophyllin poisoning. This report confirms the transient central neurotoxicity of podophyllin and persistent peripheral neurotoxicity of podophyllin.

Case Report
A 28-year-old gentleman presented to the ED (Emergency Department) with a 2 days history of deteriorating sensorium. Two days ago he was found unconscious alongside road with a leaflet of PODOWART PAINT (Podophyllin resin paint 20% + Benzoin + Aloes and Salicylic acid solution) inside his pocket. With this background he underwent gastric lavage at a nearby hospital and was referred to our center. There was no history of previous psychiatric disorder, head trauma, drug or alcohol abuse, or other toxin exposure. He is a known case of hypothyroidism on tablet Eltroxin 25 mcg once a day with no other co-morbidities.

On examination, his blood pressure was 110/70 mm of Hg, temperature 38.0 degree Celsius, heart rate 100 BPM and regular, respiratory rate of 18 BPM with SpO₂ of 94% on room air at rest. His GCS (Glasgow Coma Scale) being with EEG and ECG was performed which revealed subtle area of hyper intensity in left frontal white matter and moderate to severe cerebral dysfunction respectively. CSF analysis and all cultures were noncontributory. Hence, a diagnosis of acute Podophyllin toxicity secondary to PODOWART PAINT ingestion was made, on the basis of history and examination. Further, upper GI endoscopy, performed to rule out any evidence of corrosive injury, was normal.

He was managed in intensive care unit (on symptomatic lines by way of intra venous fluids, anti-convulsants, anti-edema measures and anti pyretics). He was tracheotomised on day 4 and all cultures were noncontributory. Brain MRI and EEG were performed which revealed subtle area of hyper intensity in left frontal white matter and moderate to severe cerebral dysfunction respectively. CSF analysis and all cultures were noncontributory. Hence, a diagnosis of acute Podophyllin toxicity secondary to PODOWART PAINT ingestion was made, on the basis of history and examination. Further, upper GI endoscopy, performed to rule out any evidence of corrosive injury, was normal.

He was weaned off the ventilator by day 8 with GCS of E4VTM3. At this stage, his Nerve Conduction Velocity (NCV) study was performed which pointed towards a distal symmetrical large fibre sensorimotor axonal polyneuropathy involving both lower and upper limbs. Subsequently a percutaneous endoscopic gastrostomy (PEG) was performed upon him to aid in long term feeding and he was shifted to floor once he was able to maintain himself on room air.

Discussion
Podophyllin, used for topical treatment of external genital warts caused by human papillomavirus (HPV), and other warts, is a resin mixture obtained from the dried Rhizome and roots of Podophyllin peltatum (North America) and Podophyllum emodi (India).¹ 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 Podophyllotoxin, a lipid soluble compound that crosses cell membranes with ease,² fatal dose of podophyllin resin for humans has been estimated to be 0.3g to 0.6g, or as little as one half teaspoon of 25% podophyllin resin in benzoin tincture.³

Systemic toxicity may result from either topical exposure or ingestion of this alkaloid.⁴ According to the CDC, podophyllin is no longer recommended as a treatment of external genital warts because of safer alternative options.⁷ Podophyllotoxin and its derivatives bind to the enzyme topoisomerase II

Table 1: Day-wise investigations for differential diagnosis

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Day 3</th>
<th>Day 5</th>
<th>Day 6</th>
<th>Day 8</th>
<th>Day 10</th>
<th>Day 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>14</td>
<td>13.3</td>
<td>13.9</td>
<td>13</td>
<td>11</td>
<td>11.5</td>
</tr>
<tr>
<td>TLC</td>
<td>19.6</td>
<td>6.7</td>
<td>9.2</td>
<td>9.0</td>
<td>13.7</td>
<td>15.5</td>
</tr>
<tr>
<td>Platelets</td>
<td>75000</td>
<td>29000</td>
<td>58000</td>
<td>108000</td>
<td>283000</td>
<td>448000</td>
</tr>
<tr>
<td>BUN</td>
<td>13.06</td>
<td>14.50</td>
<td>17.21</td>
<td>15.03</td>
<td>13.98</td>
<td>13.3</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.37</td>
<td>0.80</td>
<td>0.97</td>
<td>0.95</td>
<td>0.79</td>
<td>0.73</td>
</tr>
<tr>
<td>T. bil</td>
<td>1.07</td>
<td>7.11</td>
<td>3.69</td>
<td>2.05</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGOT</td>
<td>196</td>
<td>64</td>
<td>111</td>
<td>86</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SGPT</td>
<td>92</td>
<td>40</td>
<td>122</td>
<td>143</td>
<td></td>
<td></td>
</tr>
<tr>
<td>INR</td>
<td>1.52</td>
<td>1.28</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GCS</td>
<td>EIV1M2</td>
<td>EIV1M3</td>
<td>EIV1M3</td>
<td>E3V1M3</td>
<td></td>
<td></td>
</tr>
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</table>
Management of podophylline toxicity is mainly supportive, no specific antidote exists. Activated charcoal is recommended for gastrointestinal decontamination. If topical contact occurs, wash with soap and water. Intensive management of ventilation and circulation, accompanied by monitoring for above-mentioned complications is required. Haemoperfusion should be used for severe systemic poisoning since it has been shown to be effective in reducing the plasma fraction of podophyllotoxin 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 2015.9,12,13 A fatal case relating to topical application was reported in 1954.14

The initial manifestations exhibited by our patient, headache, nausea, diarrhea, and altered sensorium with hepatic impairment are among those previously described.15 Peripheral destruction of platelets has not been described earlier. Later in the course, our patient showed features of paralytic ileus and peripheral neuropathy, all known complications of the toxicity.

Ethical approval. Informed consent for the publication of this case report was obtained from the father of the patient.

References