CASE REPORT

A case of percutaneous absorption of an organophosphate pesticide

Toru Hifumi, Hayato Yoshioka, Kazunori Imai, Toshihiro Tawara, Takashi Kanemura, Eiju Hasegawa, Hiroshi Kato, Yuichi Koido

Abstract: The cases of intake of organophosphate pesticides reported in Japan are mainly due to oral ingestion associated with attempted suicides. We report a case of organophosphate pesticide poisoning in which percutaneous absorption was suspected to be the cause. A 61-year-old woman was brought to our hospital because of consciousness disturbance. She was found lethargic, lying in the bathroom, by her husband. She had a significant medical history of hypertension. On admission, her Glasgow coma scale (GCS) score was 14/15. Her vital signs were as follows: body temperature, 35.3°C; blood pressure, 185/102 mmHg; heart rate, 106 /min; and respiratory rate, 23 /min. Her oxygen saturation was 100%. Her pupils were 2 mm in diameter, equal in size, round, and reactive. The rest of the examination was unremarkable. Chest X-ray, head CT, and head MRI were performed, but failed to identify the cause of the consciousness disturbance. Three hours after arrival, her oxygen saturation level had fallen and diaphoresis, miosis, and lacrimation had developed, while she was intubated under sedation. Prior to tracheal intubation, we asked her whether she had taken any organophosphate agent, which she denied. No organophosphate smell was detected from the endotracheal tube. Nine hours after arrival, her cholinesterase level was reported to be 11 IU/l, and we could finally confirm the diagnosis. Pralidoxime and atropine therapy was accordingly started. Seventeen hours after arrival, her family brought bottles of pesticide (smithion®) to the hospital. It transpired that she had handled this organophosphate pesticide without wearing gloves, and that earlier she had received abrasions to her hands. Therefore, it was assumed that the organophosphate was easily absorbed through her skin. Critical care physicians should bear in mind that whenever they see patients with consciousness disturbance, percutaneously absorbed organophosphate poisoning could be one of the causes.

Key words: ① organophosphate poisoning, ② percutaneous absorption, ③ pesticide

Introduction

Cases of organophosphate pesticide oral ingestion are commonly reported in Japan; however, other processes by which toxicants pass across body membranes and enter the bloodstream, such as percutaneous absorption, are thought to be rare.

The diagnosis of organophosphate poisoning can be complicated if we make the assumption that oral ingestion is the only absorption route. This is particularly applicable when a patient denies taking any organophosphate pesticide. In cases of organophosphate poisoning, any delay in starting treatment is critical.

Here, we report a rare case of percutaneous absorption of an organophosphate pesticide.

Case report

Patient: A 61-year-old woman.
Medical/family history: She had a significant history of hypertension, although the medical history of her family was unremarkable.
Clinical history: She was brought to our hospital due to consciousness disturbance. She had been found lethargic, lying in the bathroom, by her husband early in the morning, and he called an ambulance. She had appeared normal until she developed consciousness disturbance.

On admission, her Glasgow coma scale (GCS) score...
was 14/15. Her vital signs were as follows: body temperature was 35.3°C, blood pressure was 185/102 mmHg, heart rate was 106 bpm, and respiratory rate was 23 /min. Her oxygen saturation was 100% while breathing 10 l/min of oxygen via a non-rebreather mask. Although lethargic, she responded appropriately to questions. Her pupils were 2 mm in diameter, equal in size, round, and reactive. The rest of the examination was unremarkable.

The laboratory data showed the increase in WBC counts (Table 1). A urine toxicology screening test (Triage®DOA, Sysmex) was negative for all toxic agents. Chest X-ray, head CT, and head MRI were performed, but failed to identify the cause of consciousness disturbance. Lumbar puncture was also performed, which was negative for meningitis. She was admitted to the ICU for further evaluation. We took on this patient from the emergency physicians with a diagnosis of consciousness disturbance of unknown cause.

Three hours after arrival, her oxygen saturation had fallen, and diaphoresis, miosis, and lacrimation had developed while she was intubated under sedation. At this point, we considered organophosphate poisoning as a possible diagnosis. We therefore examined the level of serum cholinesterase. Although, prior to tracheal intubation, we asked her whether she had taken any organophosphate agent, she strongly denied it. Furthermore, no smell of organophosphate was detected from the endotracheal tube.

Nine hours after arrival, her cholinesterase level was 11 IU/l (normal range: 100–240 IU/l). At this point, we could finally confirm the diagnosis of organophosphate poisoning, for which pralidoxime (PAM) and atropine therapy was started. The initial dose of PAM was 0.5 g in 100 ml of normal saline, followed by 0.5 g/hr of continuous infusion. One milligram of atropine was administered initially, followed by continuous infusion maintained within the range 0.3 to 0.5 mg/hr, which was titrated due to the persistence of bronchorrhea.

Seventeen hours after arrival, her family brought a bottle of pesticide (smithion®) to the hospital, and it transpired that she had handled this organophosphate pesticide without wearing gloves 12 hours before arrival. Fig. 1 shows her left hand on the day of admission, indicating that there were rhagades and scabs. Atropine was gradually tapered off, and discontinued on the 16th day.

Table 1  Laboratory data on admission

<table>
<thead>
<tr>
<th>Blood cell count</th>
<th>Cl</th>
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<tbody>
<tr>
<td>WBC</td>
<td>22,300 /μl</td>
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<tr>
<td>RBC</td>
<td>511 × 10⁴ /μl</td>
</tr>
<tr>
<td>Hb</td>
<td>14.6 g/dl</td>
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<tr>
<td>Ht</td>
<td>41.9 %</td>
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<tr>
<td>Plt</td>
<td>44.6 × 10⁴ /μl</td>
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<table>
<thead>
<tr>
<th>Biochemistry</th>
<th>Coagulation system</th>
<th>Biochemistry</th>
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<tbody>
<tr>
<td>TP</td>
<td>Cl</td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td>Ca</td>
<td></td>
</tr>
<tr>
<td>UN</td>
<td>CRP</td>
<td></td>
</tr>
<tr>
<td>Cr</td>
<td>GLU</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>APTT</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>PT</td>
<td></td>
</tr>
<tr>
<td>LDH</td>
<td>BGA (10 l/min non-rebreather mask)</td>
<td></td>
</tr>
<tr>
<td>AMY</td>
<td>pH</td>
<td></td>
</tr>
<tr>
<td>CK</td>
<td>PCO₂</td>
<td></td>
</tr>
<tr>
<td>Na</td>
<td>PO₂</td>
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<tr>
<td>K</td>
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<td>BE</td>
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AMY, amylase; APTT, activated partial thromboplastin time; BGA, blood gas analysis; Ca, calcium; Cl, chloride; Cr, creatinine; GLU, glucose; K, potassium; Na, sodium; Plt, platelet; PT, prothrombin time; TB, total bilirubin; TP, total protein; UN, urea nitrogen.

Fig. 1 The photograph of patient’s left hand taken on the day of admission
There were rhagades and scabs on the patient’s left hand.
On the 8th day, tracheostomy was performed, and she was weaned off the ventilator on the 15th day. The serum cholinesterase level gradually increased and had reached the lower limit of the normal range by the 28th day (Fig. 2). She was transferred to an internal ward on the 10th day and discharged on the 80th day.

**Discussion**

Organophosphate compounds are easily absorbed through the skin, lungs, and gastrointestinal tract. They bind to acetylcholinesterase, also known as RBC acetylcholinesterase or neural acetylcholinesterase, and render this enzyme non-functional. Acetylcholinesterase is the enzyme responsible for the hydrolysis of acetylcholine to choline and acetic acid, and its inhibition leads to an overabundance of acetylcholine in the synapse. The onset and duration of acetylcholinesterase inhibition by organophosphate compounds varies depending on the rate of inhibition, the route of absorption, the enzymatic conversion to active metabolites, and the lipophilicity of the organophosphate agent. In the present case, there were two major factors that made it difficult for us to confirm the diagnosis of organophosphate poisoning. The first factor was that she had developed only consciousness disturbance at the time of hospital arrival. Other specific symptoms of organophosphate poisoning, such as diaphoresis, miosis, and lacrimation, developed 3 hours after arrival in the ICU. At this point, we finally considered organophosphate poisoning as a possible diagnosis, and accordingly examined the level of serum cholinesterase. In the emergency room, organophosphate poisoning was not considered as a differential diagnosis, since only consciousness disturbance was apparent at that time.

The cholinergic toxidrome of organophosphate poisoning comprises overstimulation of muscarinic and nicotinic receptors. Muscarinic manifestations include excessive salivation, miosis, diarrhea, and bradycardia, whereas nicotinic manifestations include muscle fasciculation and tachycardia. Organophosphate poisoning can also influence the central nervous system (CNS) and result in seizures and altered consciousness.

In acute intoxication, early coma, distinguished from intermediate syndrome by the fact that the symptoms develop acutely within a few hours, is multi-factorial and related to neurogenic, cardiac, and respiratory effects. Organophosphate administration evokes excitatory electroencephalogram (EEG) changes that results in focal seizures in animal models. According to our patient’s history, she may have experienced seizure, and a post-ictal state is suspected as a cause of her consciousness disturbance.

For most agents, oral or respiratory exposure generally results in signs or symptoms within 3 hours, whereas the symptoms of toxicity from dermal absorption may be delayed by up to 12 hours. The patient described here had handled organophosphate pesticides 12 hours before arrival, which is consistent with the presumption of dermal absorption delay.

Since this patient’s symptoms developed in the ICU,
critical care physicians should be aware that whenever they see patients with consciousness disturbance, organophosphate poisoning could be one of the causes.

The second confounding factor was that this patient strongly denied the possibility of organophosphate pesticides ingestion. In the absence of a known ingestion or exposure, the clinical features of cholinergic excess should indicate the possibility of organophosphate poisoning. For moderate to severe intoxication, the clinician should act on a patient’s clinical impression and on the history of exposure, rather than wait for laboratory confirmation 10).

In the case of mild poisoning where the differential diagnosis may be puzzling, the results of the cholinesterase test may be necessary to establish a definite diagnosis 10). Although an assay for serum cholinesterase activity is easily performed, the results do not correlate well with the severity of poisoning 11). Serum cholinesterase level varies by a hereditary deficiency of this enzyme, liver dysfunction, malnutrition, iron deficiency anemia, and drugs. This makes the enzyme a less-than-perfect biomarker for organophosphate poisoning for the baseline levels in an individual are unknown 12). No medical history related to the lower baseline of serum cholinesterase was found for this patient, and we confirmed the diagnosis with a serum cholinesterase level of 11 IU/l (normal range: 100–240 IU/l) instead of examining RBC acetylcholinesterase level.

Many organophosphate agents have a characteristic petroleum or garlic-like odor, which may be helpful in hands. Therefore, the organophosphate was presumed to the respiratory route was thought to be less likely, have been easily absorbed through the skin. In contrast, transdermal absorption was not strongly suspected, since we paid more attention to the ingestion route.

Several reports have mentioned the cases of transdermal absorption of organophosphate pesticides 3-4), and the dermal route is generally regarded as being particularly important in many cases of accidental intoxication 13-15). In the present case, the patient had handled an organophosphate pesticide without wearing gloves, and, in addition, had earlier received abrasions to her hands. Therefore, the organophosphate was presumed to have been easily absorbed through the skin. In contrast, the respiratory route was thought to be less likely, considering that the activity had been performed in a well-ventilated environment.

Fenitrothion is considerably less toxic than parathion, although the range of insecticidal activity is very similar 16). Removal of parathion from the skin is difficult, even with 30 sec scrub with soap and water, followed by an alcohol wash 17). Absorption of fenitrothion varies according to the part of the body exposed. For example, the forehead of monkeys has been shown to be 2.3 times more permeable to fenitrothion than the forearm 18).

Conclusions

Critical care physicians should bear in mind that whenever they see patients with consciousness disturbance, percutaneously absorbed organophosphate poisoning could be one of the causes.

Part of this case was presented at the 37th Annual Meeting of the Japanese Society of Intensive Care Medicine, Hiroshima, 2010.

References

3) Clifford NJ, Nies AS. Organophosphate poisoning from wearing a laundered uniform previously contaminated with parathion. JAMA 1989;262:3035-6.