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Case Report

Severe Fenitrothion Poisoning Complicated by Rhabdomyolysis in Psychiatric Patient

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Non-traumatic rhabdomyolysis associated with organophosphate intoxication has not been generally reported. We report here in a severe case of fenitrothion poisoning complicated by rhabdomyolysis. A 43-year-old woman ingested approximately 100 ml of fenitrothion emulsion (50%) in an attempt to commit suicide. On day 3 after admission, her creatine phosphokinase (CPK) peaked at 47,762 IU/L. She received supportive treatment included sodium bicarbonate and fluid resuscitation. However, muscarinic symptoms including excessive miosis and salivation developed on day 5 when her CPK levels decreased. The delay in cholinergic symptoms might have been due to the trihexyphenidyl she took with the antipsychotic drugs. Fortunately, the present patient recovered from the acute cholinergic crisis, and acute renal failure was prevented by early diagnosis. This is a case of organophosphate poisoning complicated by rhabdomyolysis in a psychiatric patient. The masking of acute cholinergic symptoms should be taken into consideration in such patients.

Key words: fenitrothion, organophosphate poisoning, rhabdomyolysis, psychiatric patient

Non-traumatic rhabdomyolysis associated with drug overdose or chronic drug intake has been reported [1]. However, there have been a few reports of organophosphate-induced rhabdomyolysis [2-4], despite its nicotinic effects caused by the inactivation of acetylcholinesterase. We report here in a case of severe fenitrothion (sumithion) poisoning complicated by rhabdomyolysis.

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Case Report

A 43-year-old woman was admitted to the Emergency Ward of St. Mary's Hospital following suicidal ingestion of an approximately 100 ml fenitrothion emulsion (50%). She had been treated with various medications including bromperidol, propericiazine, trihexyphenidyl HCl, diazepam, and nitrazepam for a medical history of schizophrenia. The patient's blood pressure was 110/70 mmHg, and her pulse was 126 beats/min. On arrival, she exhibited vomiting, loss of sensation in the arms and legs, and muscle fasciculation (clonic seizures) requiring intravenous diazepam. Both eyes were deviated upwards. Laboratory data included: hemoglobin 14.6 g/dL, white blood cells 19,900/mm^3, platelet 250,000/mm^3, GOT 46 IU/L,

GPT 19 IU/L, blood glucose 265 mg/dL, blood urea nitrogen (BUN) 14.2 mg/dL, serum creatinine 0.66 mg/dL, potassium 5.87 mEq/L (normal: 3.5-4.8 mEq/L), calcium 8.8 mg/dL, sodium 145.1 mEq/L, chloride 103.1 mEq/L, serum creatine phosphokinase (CPK) 319 IU/L (normal: 14-158 IU/L), lactate dehydrogenase (LDH) 1,315 IU/L (normal: 200-400 IU/L), amylase 492 IU/L, (normal: 105-440 IU/L) PaO_2 125.0 mmHg, $PaCO_2$ 39.4 mmHg, pH 6.91, HCO_3 7.5 and base excess -26.5 mmol/L. The erythrocyte and plasma cholinesterase activities (EChE and PChE) were 6,541 IU/L (normal: 10,000-14,000 IU/L) and 656 IU/L (normal: 1,900-3,900 IU/L), respectively, and the plasma concentration of fenitrothion was 18.8 μg/ml. Gastrointestinal lavage followed by activated charcoal treatment was performed immediately. Ventilation was immediately supported via a nasal endotracheal tube due to inadequate respiration. Sodium bicarbonate was intravenously administered to correct the acidosis. PAM (2.0 g) was intravenously infused, but atropine sulfate was not given because her pupils were almost normal and no excessive salivation was observed.

On day 3 (52 h after ingestion), her CPK peaked at 47,762 IU/L (6.9% of the MB isoenzyme). GOT and LDH were elevated similarly to CPK and peaked at 238 IU/L and 2,760 IU/L, respectively (Fig. 1). Serum myoglobin and aldolase on day 4 were 5,500 ng/ml (normal under 35 ng/ml) and 363.0 IU/L (normal: 1.7-5.7 IU/L/37°C), respectively. These results suggested complications of rhabdomyolysis. The patient was therefore treated with sodium bicarbonate and hydration to protect her kidney function from acidosis and precipitation of myoglobin in the tubules.

The plasma levels of fenitrothion decreased gradually from a high initial level on admission, but it continued to be detected until 25 days after ingestion (Fig. 2). Since excessive miosis, salivation, and fasciculation developed on day 5, atropine sulfate was administered to keep the pupillary enlargement within a mild range. The intravenous infusion of PAM at 0.25 g/h for 6 days was restarted 10 days after administration was initially stopped because of persisting severe cholinergic symptoms.

Paralleling the recovery of EChE and PChE activities, the clinical findings of organophosphate intoxication gradually disappeared. Serum creatinine maintained a normal level during the therapeutic period. A mild BUN elevation of 28.4 mg/dL (normal 10-20 mg/dL) was recognized from day 6. CPK became temporarily elevated again on day 18 following a lack of muscle fasciculation control, but the patient exhibited an almost complete recovery by day 38.

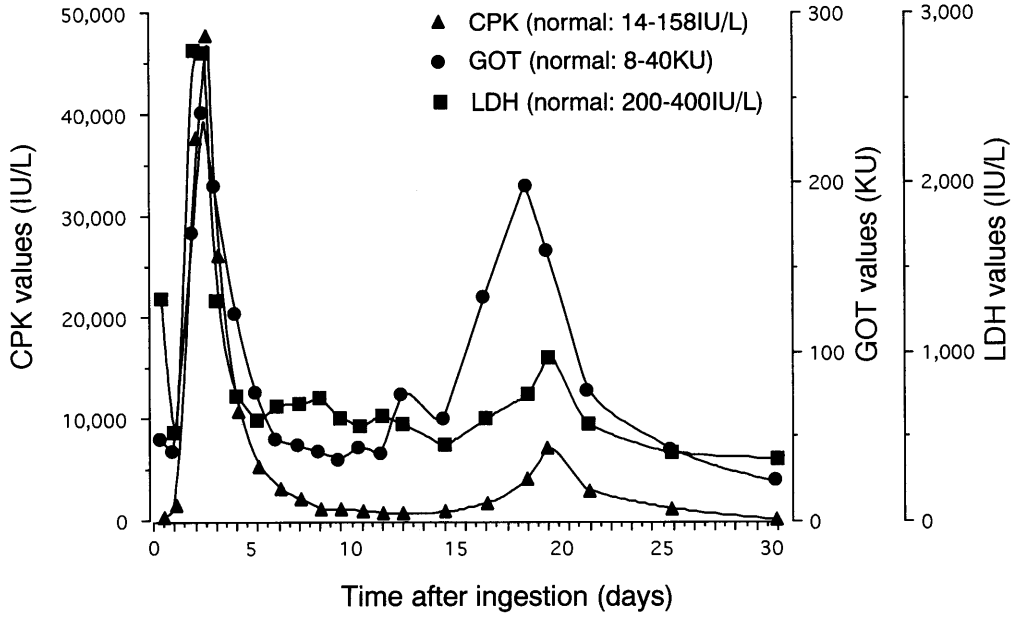

Fig. 1 Time course of creatine phosphokinase values in a patient with acute fenitrothion poisoning.

Measurement

Fenitrothion was extracted from the plasma (0.25 ml) with ethyl acetate (4 ml) and was analyzed by gas chromatography with an instrument equipped with an alkali flame thermionic detector sensitive to phosphorus [5]. The glass column (1.5 m × 3.4 mm I.D.) was packed with 10% Apiezon Grease L on Chromosorb W AW DMCS (60–80 mesh). The temperature at the injection and detection parts was set at 250°C, and the column temperature was 210°C. Helium, at a flow rate of 66 ml/min was used as the carrier gas. The EChE and PChE activities were determined by the method of modified Ellman's acetylthiocholine/DTNB [6].

Discussion

Fenitrothion is used around the world as an organophosphate insecticide because of its relatively low human toxicity [7]. However, suicidal or accidental ingestion of fenitrothion has been reported [8, 9]. Fenitrothion is readily absorbed after ingestion and is converted by oxidative desulfuration to a toxic metabolite, fenitrooxon, in the liver. In the present case, we observed a manifestation of fenitrothion poisoning by a time course of plasma fenitrothion concentrations as well as EChE and PChE activities. The plasma level of fenitrothion on admission (1.5 h after ingestion) was almost the same as that in the case reported by Yoshida *et al.* [9], in which the patient died of respiratory failure 6 days after ingestion. Therefore, the present case seemed to be one of severe fenitrothion poisoning.

This case is an example of non-traumatic rhabdomyolysis complicated by organophosphate poisoning as confirmed by extremely high CPK levels. Rhabdomyolysis is a clinical syndrome characterized pathologically by skeletal muscle injury and causing the movement of intracellular contents into the plasma. Since CPK exists primarily in the cytosol of striated and cardiac muscle, it is the most sensitive laboratory marker for rhabdomyolysis. The patient exhibited elevated LDH and GOT levels as well as CPK levels (Fig. 1), which may have been due to the presence of these enzymes in cardiac and striated muscle tissue in high concentrations.

The complication of rhabdomyolysis was diagnosed based on a marked increase in CPK levels after admission. Although only a few cases of organophosphate poisoning complicated by rhabdomyolysis have been

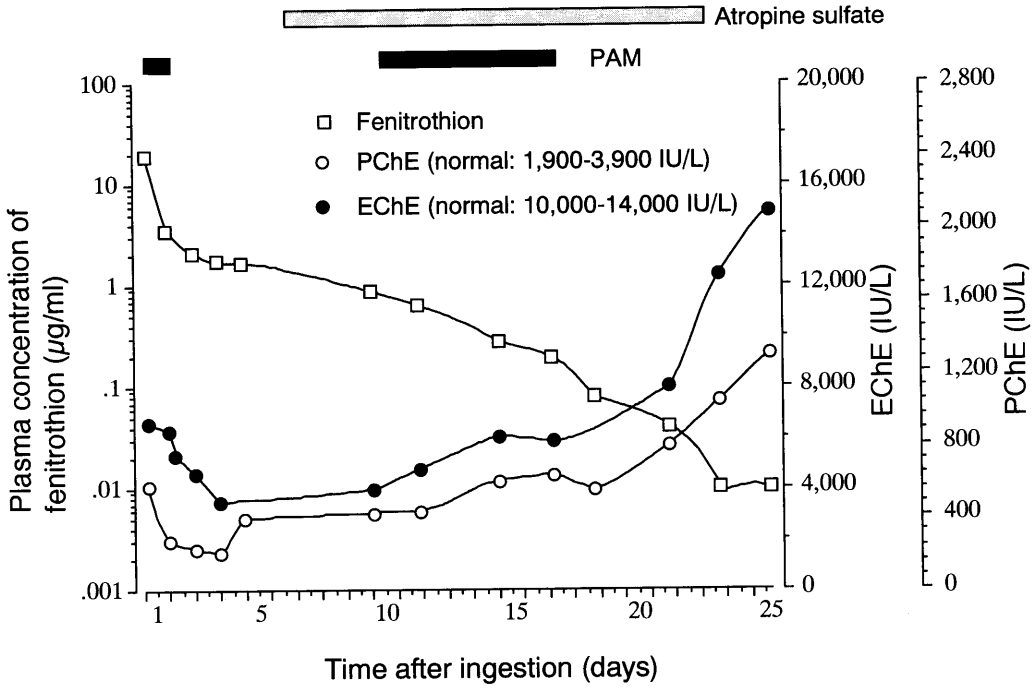

Fig. 2 Time course of EChE and PChE activity *vs.* plasma fenitrothion concentrations.

reported [3], rhabdomyonecrosis lesions in the diaphragm have been observed in rats poisoned with a relatively low dose of organophosphate [10]. It has also been reported that a Rhesus monkey with acute organophosphate poisoning exhibited significant increases in CPK, LDH, GOT, GPT, and potassium ion levels, associate with damage to striated muscle and metabolic acidosis [11].

The present patient exhibited both psychiatric disease and acidosis, both of which are described as predisposing factors for the manifestation of rhabdomyolysis [2]. She was in a coma and had clonic seizures on arrival at the hospital, and her CPK levels temporarily re-elevated on day 18 following a lack of muscle fasciculation control. Her psychiatric condition, muscle compression induced by the coma, and seizures may have contributed to the rhabdomyolysis.

Atropine sulfate treatment was not necessary until 5 days after admission despite high serum fenitrothion concentrations and severe ChE inhibition (Fig. 2). The lack of need for this treatment may have been due to the anticholinergic effects of trihexyphenidyl, which the patient had taken along with her antipsychotic drugs. Drug overdose in psychiatric patients is relatively common [12]. It has also been reported that acute cholinergic symptoms are not often recognized on admission in organophosphate poisoning in depressed patients, even if ChE levels are markedly inhibited [13]. Therefore, the measurement of serum organophosphate levels is as important as that of ChE activity. Early treatment with PAM is significant to the recovery of EChE and PChE activities.

Psychiatric patients sometimes exhibit rhabdomyolysis related to their medicine [12]. Thus, the prescribed antipsychotic drugs of the present patient may also have contributed to the development of rhabdomyolysis. Fortunately, the present patient recovered from the acute cholinergic crisis and was protected against acute renal failure by early diagnosis. In conclusion, we should consider the possible occurrence of rhabdomyolysis and the masking of acute cholinergic symptoms of organophosphate poisoning in psychiatric patients.

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