CASE REPORT

Subcutaneous injection of organophosphate (Fenitrothion)— Management of preventing the appearance of toxic symptoms: A case report

Hitomi Nakamura | Ichiro Hirayama ២ | Takahiro Hiruma | Kent Doi

Department of Emergency and Critical Care Medicine, The University of Tokyo, Tokyo, Japan

Correspondence

Ichiro Hirayama, Department of Emergency and Critical Care Medicine, The University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan.

Email: ichirohirayama1983@gmail.com

Abstract

There is a risk of unnecessary extensive incision because of swelling after the subcutaneous injection; however, removing completely the injected organophosphate by making a skin incision before the appearance of toxic symptoms could reduce sequelae.

KEYWORDS

acetylcholinesterase, organophosphate, poisoning, subcutaneous injection

1 | INTRODUCTION

The time to onset of organophosphate poisoning symptoms varies widely. When administering subcutaneous injection, attention must be paid to systemic and local symptoms. Before the appearance of toxic symptoms, skin incision, and washing may prevent the spread of inflammation to the subcutaneous tissue and may reduce sequelae.

Organophosphate poisoning is an important problem in rural regions of the world. The number of organophosphate poisoning cases is estimated to be approximately 3 000 000 per year. Medical management is difficult, and the mortality rate is more than 15%.^{1,2} Organophosphate poisoning by subcutaneous injection is rare. Compared to oral exposures of organophosphate, dermal absorption of organophosphate is slow but continuous from the site of injection.³ In cases of parenteral injection of organophosphate, attention must be paid to the possibility of a late onset of poisoning. Patients need to be admitted to the hospital because of the potential for organophosphate poisoning, and they must be monitored because the time to onset of symptoms is varied. However, the duration of monitoring is unknown. An early skin incision and the removal of the residual organophosphate could prevent the occurrence of organophosphate poisoning.

Here, we report the case of a 54-year-old man who was admitted to our hospital with a chief complaint of pain in the left forearm that was self-injected with fenitrothion.

2 | CASE REPORT

A 54-year-old Japanese man complained of redness and pain in his left forearm. Before 24 hours, he injected himself with 5 ml of 50% fenitrothion to commit suicide. His vital signs on arrival were as follows: blood pressure, 127/77 mm Hg; pulse, 105 beats per minute; body temperature, 37.5°C; respiratory rate, 18 breaths per minute; SpO₂, 100% without oxygenation; Glasgow Coma Scale, E4V5M6. He had a past history of depression. However, he had not been prescribed drugs for depression. His pupil size was 3/3 mm, and the light reflex was rapid on both sides. There was no excessive sweating or salivation. The cholinesterase level was 244 U/L (normal range: 240-486 U/L). There were no findings of organophosphate poisoning, but he was admitted to the hospital, because the poisoning symptoms could be delayed. His left forearm had redness and swelling (Figure 1A), and he had hypoesthesia at the part of the distal skin from the wound.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes. © 2021 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

WILEY_Clinical Case Reports

2.1 | Wound management on admission

On admission to the hospital, his wound was cooled. However, swelling of the wound had spread, and his body temperature increased to 38.7°C on day 4 (Figure 1B). He was diagnosed with cellulitis, and cefazolin administration was initiated. His wound had redness and swelling, which gradually localized. On day 17, fluid retention was suspected by palpation of the localized part. The puncture was performed, and 10 mL of yellow serous exudate was aspirated. Despite the puncture, fluid retention was observed under the skin; therefore, a dermatologist performed skin incision, washing, and necrotic tissue debridement on day 20 (Figure 1C). The odor of fenitrothion originated from the wound. The adipose tissue was necrotic, and the nerves were exposed. No necrosis was found in the muscles. The wound culture was negative, and there were no signs of infection. Wound cleaning was performed every day, and silver sulfadiazine cream was applied to the wound. On day 45, the odor of fenitrothion disappeared. For promoting the granulation of the wound, trafermin was sprayed, and a prostaglandin-containing ointment was applied. In addition, negative-pressure wound therapy was performed from day 52 to day 81. On day 83, he was discharged (Figure 1D).

2.2 | Cholinesterase and acetylcholinesterase levels

After admission to the hospital, the cholinesterase level gradually decreased from the day after admission (Figure 2). Although there were no symptoms of organophosphate poisoning, the level fell below 8 U/L on day 11. A skin incision

was made on his left forearm on day 20. The acetylcholinesterase level was 1124 U/L immediately before the skin incision. The cholinesterase and acetylcholinesterase levels gradually recovered (Figure 2). The acetylcholinesterase level was 5573 U/L 1 month later, and the cholinesterase level at the time of discharge was 312 U/L.

2.3 | Follow-up of the patient

After discharge, he followed up with the dermatology and psychiatry outpatient departments.

Nine months later, muscle weakness was not observed, and he resumed his activities of daily life, although hypoesthesia was remained as if a piece of paper was on from the back of the left hand to the fingertips. For depression, medications were prescribed with regular follow-ups with his local doctor.

3 | **DISCUSSION**

Time to the onset of symptoms of organophosphate poisoning when injected subcutaneously varies widely. In subcutaneous organophosphate poisoning, acetylcholinesterase levels, which reflect the severity of organophosphate poisoning, may help the clinician in decision-making regarding treatment. Compared to oral intake, subcutaneous organophosphate poisoning involves local complications. Early skin incision (before the appearance of symptoms of organophosphate poisoning), washing, and necrotic tissue debridement may prevent the spread of inflammation to the subcutaneous tissue and may help to reduce sequelae.



FIGURE 1 Clinical course of the wound. A, His left forearm had redness and swelling on admission. B, Redness and swelling had spread on day 4. C, A skin incision was made on day 20. Fenitrothion has remained and continues dissolving the fat. D, Granulation of the wound had been promoted on discharge

FIGURE 2 Time course of cholinesterase (ChE) and acetylcholinesterase (AChE) levels with wound management. He was diagnosed with cellulitis on day 4, and cefazolin (CEZ) administration was started. For promoting the granulation of wound, negative-pressure wound therapy (NPWT) was performed from day 52 to day 81. ChE levels were measured by biochemical tests in our hospital. Contrarily, AChE levels were determined at another facility wherein measurement was possible



There have been several reports of organophosphate poisoning caused by subcutaneous injection and the time to onset of these symptoms varied (3-60 hours).³ Symptoms of organophosphate poisoning are classified into three categories according to their mode of action: (A) muscarinic actions, (B) nicotinic actions, and (C) central nervous system-stimulating effect. Treatment with a muscarinic antagonist (atropine) or an acetylcholinesterase reactivator (oximes) should be performed.¹ In our case, symptoms of organophosphate poisoning did not appear. On day 20, a skin incision was made. At that time, fenitrothion remained in the wound. The reason for the delayed fenitrothion absorption might be its chemical structure. Fenitrothion has high lipid solubility and a sulfur moiety. High lipid solubility might result in a prolonged cholinergic phase, and the bioactivation process of the sulfur moiety might delay the onset of the toxic symptoms.⁴

During subcutaneous injection of organophosphate, it is important to pay attention to local complications. Swelling, necrosis, and infection around the injection site are usually observed, and abscess, nerve damage, and muscle damage are caused by the spread of inflammation to the subcutaneous tissue. In severe cases, wherein compartment syndrome or chronic cholinergic crisis occurs, there may be a need for amputations.⁵ Early skin incision, washing, and necrotic tissue debridement may prevent the spread of inflammation and may help reduce sequelae. Immediately after the injection, the incision range cannot be determined due to swelling of the skin, and there is a possibility that an unnecessary incision will be made. As reported in published studies, the toxic symptoms had already appeared by the time a skin incision was made. Therefore, a skin incision has been recommended to completely remove organophosphate from the subcutaneous tissue to prevent local and systemic symptoms. In our patient, fenitrothion was observed to remain when a skin

incision was made on day 20. At that time, the patient had no toxic symptoms of organophosphate poisoning yet. Our findings suggest that an incision should be made before the appearance of toxic symptoms.

3.1 | Acetylcholinesterase level in subcutaneous injection of organophosphate

Acetylcholinesterase is considered a good marker of the severity of organophosphate poisoning.¹ However, in general, the delay in obtaining the results of acetylcholinesterase activity prevents its use during clinical decision-making. In our case, the level just before the skin incision was approximately 20% of the normal levels. The timing of a skin incision was made suggests that the patient might have been at the point just before the symptoms of organophosphate poisoning would have appeared. Monitoring acetylcholinesterase levels may be useful on the cases, the time to onset of toxic symptoms is unpredictable such as subcutaneous injection. Fenitrothion remained in the wound when a skin incision was performed. If it had completely absorbed, it may have caused organophosphate poisoning.

4 | CONCLUSIONS

The time to onset of organophosphate poisoning caused by subcutaneous injection varies widely. In subcutaneous administration of organophosphate, care should be taken to monitor the patient for both systemic signs and local complications. Before the appearance of symptoms of organophosphate poisoning, making a skin incision, washing, and necrotic tissue debridement may prevent the spread of inflammation to the subcutaneous tissue and may help to reduce sequelae.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient for publication of this case report and its accompanying image.

ACKNOWLEDGMENTS

We are grateful to Etsuko Hamada and Prof. Masato Maekawa (Hamamatsu University Hospital) to measure acetylcholinesterase. We would like to thank Editage (http:// www.editage.com) for English language editing. Published with written consent of the patient.

CONFLICT OF INTEREST

None declared.

AUTHOR CONTRIBUTIONS

HN, IH, TH, and KD contributed to the management of the patient. HN drafted an initial manuscript. IH, TH, and KD critically reviewed the manuscript. All the authors contributed to writing the manuscript and have provided written consent for publication.

ETHICAL APPROVAL

Published with the written consent of the patient.

DATA AVAILABILITY STATEMENT

Data sharing was not applicable to this article as no datasets were generated or analyzed during the current study.

ORCID

Ichiro Hirayama D https://orcid.org/0000-0002-8811-4752

REFERENCES

- Eddleston M, Buckley NA, Eyer P, Dawson AH. Management of acute organophosphorus pesticide poisoning. *Lancet.* 2008; 371(9612):597-607.
- Karunarathne A, Gunnell D, Konradsen F, Eddleston M. How many premature deaths from pesticide suicide have occurred since the agricultural Green Revolution? *Clin Toxicol (Phila)*. 2020; 58(4):227-232.
- Saito T, Uenotsuchi T, Uchi H, Moroi Y, Furue M. Delayed systemic toxicity and extensive cutaneous necrosis due to suicidal injection of organophosphate pesticide. *J Dermatol.* 2012;39(5):499-500.
- Bala I, Pratap M, Nakra D, Ramprabhu T. Prolonged cholinergic crisis and compartment syndrome following subcutaneous injection of an organophosphate compound for suicide attempt. *J Forensic Leg Med.* 2008;15(4):256-258.
- Tao Y, Liu T, Han J, Jian X, Kan B. Clinical characteristics and treatment of mixed-pesticide poisoning in a patient: reflections on a particular case. *J Int Med Res.* 2020;48(12):300060520977392.

How to cite this article: Nakamura H, Hirayama I, Hiruma T, Doi K. Subcutaneous injection of organophosphate (Fenitrothion)—Management of preventing the appearance of toxic symptoms: A case report. *Clin Case Rep.* 2021;9:e04424. <u>https://doi.</u> org/10.1002/ccr3.4424