INTERNAL MEDICINE

□ CASE REPORT □

# Delayed Polyneuropathy Induced by Organophosphate Poisoning

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## Abstract

An 89-year-old man attempted suicide by ingesting a pesticide (trichlorfon). After surviving the initial critical period in the intensive care unit, he developed rapidly progressive distal weakness and sensory disturbance. Electrophysiological examinations revealed sensory motor axonal polyneuropathy. Delayed polyneuropathy is a rare manifestation of organophosphate poisoning. Nerve conduction studies play an important role in the diagnosis of this rare clinical condition.

**Key words:** insecticide, poisoning, neuropathy, cholinergic syndrome, nerve conduction study, neurotoxicology

**(Intern Med 56: 1903-1905, 2017)**
**(DOI: 10.2169/internalmedicine.56.7921)**

## Introduction

Organophosphate poisoning shows clinical symptoms in three phases. It first manifests as a cholinergic syndrome; the symptoms include miosis, nausea, vomiting, diarrhea, dyspnea, and bradycardia. Seizure, coma, and respiratory failure may also occur. Intermediate syndrome, which typically occurs at 24-96 hours after an intensive cholinergic crisis, is characterized by acute ventilatory insufficiency due to the paralysis of the respiratory muscles. Intermediate syndrome is thought to result from a dysfunction of the neuromuscular junction, which occurs in association with the prolonged overstimulation of the cholinergic receptors (1). Finally, on rare occasions, delayed neuropathy develops at several weeks after exposure (2). Organophosphate-induced delayed neuropathy (OPIDN) is an axonal polyneuropathy that is characterized by distal weakness and sensory loss, which may be progressive and severe (3).

The earliest epidemics of OPIDN, which were known as Ginger Jake paralysis, were caused by consuming alcohol contaminated with triortho-cresyl phosphate in the United States during the prohibition era (4). Although the incidence of Ginger Jake paralysis subsided after the 1950s, similar incidents have been reported after acute and chronic poisoning due to pesticide exposure in agriculture, industry and suicide attempts. We herein report a case of severe OPIDN that occurred due to the ingestion of organophosphate.

## Case Report

An 89-year-old male farmer attempted suicide by ingesting pesticide (Diptelex). The patient appeared to have ingested 200 mL of a 50% Diptelex solution. He had no particular medical history and no history of sensorimotor symptoms. His respiration became weak during ambulance transportation and assisted ventilation was started. On arrival at the emergency room, he was in deep coma with a blood pressure of 141/90 mmHg and a pulse rate of 50 beats/min. He had pinpoint pupils and diminished tendon reflexes. His plasma cholinesterase level was <1 U/L and his serum potassium level was 2.6 mEq/L. His complete blood counts were normal. His serum urine nitrogen and creatinine levels were 13 mg/dL and 0.82 mg/dL, respectively. He was intubated and treated with gastric lavage and intravenous atropine. Pralidoxime (2-PAM) infusion was started at 2 hours after the ingestion of the pesticide and was continued for 5 days (total 8.5 g). At 10 days after admission, his plasma cholinesterase level recovered to 112 U/L. His consciousness

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Received for publication August 4, 2016; Accepted for publication November 20, 2016
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**Table.** **The Results of Nerve Conduction Study.**

| Motor nerve conduction studies | CMAP amplitude (mV) | Distal latency (ms) | Conduction velocity (m/s) |
|---|---|---|---|
| lt. median | 0.8* | 5.3* | 48.8* |
| lt. ulnar | 3.8 | 3.1 | 43.3* |
| lt. tibial | 0.055* | 7.1* | 34.0* |
| Sensory nerve conduction studies | SNAP amplitude (μV) | Distal latency (ms) | Conduction velocity (m/s) |
| lt. median | 5.7* | 3.4 | 41.4* |
| lt. ulnar | 2.1* | 3.1 | 45.2 |
| lt. sural | | NE* | |
| F-wave study | F-wave latency (ms) | F-wave occurrence (%) | |
| lt. median | | NE* | |
| lt. ulnar | 24.1 | 50%* | |

Asterisks (*) indicate abnormal values in our institute standard values. CMAP: compound muscle action potential, SNAP: sensory nerve action potential, NE: not evoked

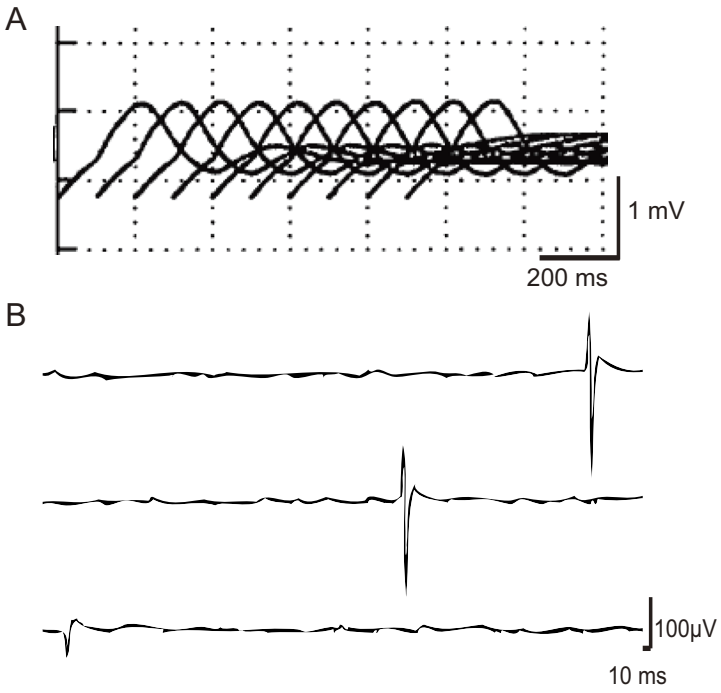


**Figure.** **The electrophysiological test recordings. A: Harvey-Masland test at 3 Hz. The compound muscle action potential showed no waning after low-frequency ulnar nerve stimulation. B: Needle electromyography (EMG) of the biceps brachii in a resting condition. Abundant denervation potentials were detected.**

also fully recovered and he was able to walk using a walker. His hand movement was dexterous. After one month of general recovery, he showed rapidly progressive limb weakness and could no longer hold objects with his hands or stand unassisted. The muscle strength, as quantified by the Medical Research Council (MRC) scale, of his proximal upper extremity muscles was 2-3, while that in the intrinsic hand muscles was 0. Fasciculation was prominent in the biceps brachii muscle. With the exception of the relatively spared iliopsoas (3, 3) and quadriceps (1, 1) muscles, the strength of all of his leg muscles was 0. Neither facial weakness nor dysarthria were observed. He had total analgesia below both knees. The joint and vibration sensations of the lower extremities also showed severe symmetric disturbance. The deep tendon reflexes of the upper limbs were diminished, and the patellar and Achilles tendon reflexes were absent. The patient's planter responses were bilaterally indifferent. The results of screening for serum anti-ganglioside antibodies (anti-GM1, GM2, GM3, GD1a, GD1b, GD3, GT1b, GQ1b, and Gal-C for both IgM and IgG classes) were all negative. His serum levels of vitamin $B_1$ (43 ng/mL), folate (11.2 ng/mL), and copper (144 μg/dL) were normal. The patient's cerebrospinal fluid showed no pleocytosis; however, the protein level was elevated (86 mg/dL). The results of a

nerve conduction study, which are summarized in Table, suggested severe sensory motor axonal polyneuropathy. A Harvey-Masland test showed no waning with low frequency (3 Hz) or high frequency (30 Hz) stimulation of the ulnar nerve (Figure A). A needle electromyography (EMG) examination detected denervation potentials in the anterior tibialis, quadriceps femoris and biceps brachii (Figure B).

## Discussion

Our patient developed acute cholinergic syndrome after ingesting organophosphate pesticide and suffered from delayed neuropathy. A nerve conduction study revealed distal-dominant sensory motor axonal polyneuropathy. The characteristic clinical and electrophysiological features supported the diagnosis of OPIDN.

Unlike acute cholinergic syndrome and the intermediate syndrome, OPIDN is not directly related to cholinergic overstimulation. The lack of the waning phenomenon in the Harvey-Masland test in our patient suggests that the neuromuscular transmission failure did not persist after the initial stage of cholinergic crisis. Previously, OPIDN has sometimes been reported as Guillain-Barré syndrome because of its rapid progression after a latent period and systemic involvement. However, the current consensus is that OPIDN is distinct from Guillain-Barré syndrome and is caused by the neurotoxicity of organophosphorus compounds. The absence of anti-ganglioside antibodies in our patient supports this notion. Electrophysiological examinations are important in the diagnosis of OPIDN for distinguishing it from the initial cholinergic crisis and intermediate symptom.

It has been proposed that OPIDN is caused by the covalent inhibition of neuropathy target esterase (NTE) (5). For instance, the administration of potent NTE inhibitors in animals causes neuropathy (6), and mutations of the NTE gene are associated with slowly developing motor neuron disorders similar to OPIDN. The inhibition of the NTE activity by organophosphate may perturb the metabolism of important membrane phospholipids, potentially leading to axonopathy. Whereas the initial cholinergic syndrome and intermediate syndrome can be treated by pralidoxime and anticholinergic treatments, there is no known treatment for OPIDN. The long-term functional sequelae of OPIDN are often severe and the development of an effective treatment is awaited.

**The authors state that they have no Conflict of Interest (COI).**

**Acknowledgement**

The authors thank Dr. Susumu Kusunoki at Kinki University for performing the measurement of the anti-ganglioside antibodies and Ms. Yumiko Tanji for providing valuable technical assistance.

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