

Case Report

Organophosphorus agent induced delayed neuropathy: a case report

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Received: 10 January 2016

Revised: 24 January 2016

Accepted: 28 January 2016

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ABSTRACT

A 40-year old male, was presented with complaint of difficulty in walking with inability to flex foot and toes in bilateral feet ("foot drop"), which was acute at the onset and gradually progressive since the past 7 days. The patient's wife and their 2 children had similar complaint with the same period of onset. At home, his family used cottonseed oil as cooking oil with wheat grain mixed with castor oil. On neurological examination, he was found to have lower motor neuron weakness with spasticity. After ruling out other common causes of polyneuropathy and lower motor weakness; due to high suspicion of poisoning by food adulterant, RBC acetyl cholinesterase (AChE) and plasma cholinesterase (BuChE) were tested at National Institute of Occupational Health (NIOH), which came low and confirmed diagnosis of Organophosphorus (OP) poisoning. Nerve conduction study was done; which showed decreased amplitude of conduction in bilateral peroneal and right tibial nerve along with decreased mean nerve conduction velocity of bilateral median nerve. Thus patient was diagnosed with organophosphorus agent induced delayed axonal type of polyneuropathy and physiotherapy was started as treatment. OP compounds are a diverse group of chemicals which are principally used as insecticides in agriculture. Following organophosphate poisoning (OPP), 3 well-defined neurological syndromes are recognised: cholinergic crisis, intermediate syndrome and delayed polyneuropathy. Some organophosphates, particularly triorthocresyl phosphate (TOCP) and tricresyl phosphate (TCP), produce delayed neuropathy. On ingestion, they do not produce significant cholinergic crisis, but 7 to 20 days later it leads to a pure motor axonal neuropathy with wrist and foot drop. The mechanism may involve inhibition of neuropathy target esterase (NTE), which is found in the brain, peripheral nerves, and lymphocytes. This form of toxicity has been seen occasionally in small epidemics in India due to adulteration of cooking oil with TOCP.

Keywords: Organophosphorus poisoning, Neuropathy

INTRODUCTION

Organophosphorus (OP) compounds are a diverse group of chemicals comprising of esters, amides or thiol derivatives of phosphoric acid; which are principally used as insecticides in agriculture. They are potent cholinesterase inhibitors capable of causing severe cholinergic toxicity following cutaneous exposure, inhalation, or ingestion.

Following organophosphate poisoning (OPP), 3 well-defined neurological syndromes are recognized. These are cholinergic crisis, intermediate syndrome and delayed polyneuropathy. Some organophosphates, particularly triorthocresyl phosphate (TOCP) and tricresyl phosphate (TCP), produce what is called delayed neuropathy. Organophosphorus agent induced delayed neuropathy (OPIDN) typically occurs one to three weeks after

ingestion of one of a small number of specific organophosphorus agents, including chlorpyrifos.¹

This form of toxicity has been seen occasionally in small epidemics in India due to adulteration of cooking oil with TOCP. However, it is uncommon with presently used organophosphates such as chlorpyrifos. Most cases of mild delayed neurotoxicity improve with time, but permanent disability-an upper motor neuron syndrome with spasticity of the lower extremities-usually follows in severe cases.²

CASE HISTORY

A 40-year old male, working as a worker at a machine factory, ex-chronic alcoholic, was presented with complaint of difficulty in walking with inability to flex foot and toes in bilateral feet ("foot drop"), which was acute at the onset and gradually progressive since the past 7 days.

The patient had no history of upper respiratory or gastrointestinal infection for the past one month; neither did he have any past history of fever, trauma to leg or back, exposure to pesticide or alcohol ingestion (last intake of country liquor was 8 months ago).

He also had no past history of hypertension or diabetes. He was given injectable vitamin B₁₂ supplementation at Civil Hospital, Sola, Ahmedabad; before 1 week, for the same complaint.

He was on a vegetarian diet. At home, his family used cottonseed oil as cooking oil with wheat grain mixed with castor oil. His sleep, bowel and bladder habits were unaltered. The patient's wife and their 2 children had similar complaint with the same period of onset.

On general examination, the patient was conscious, and oriented to time, place and person. He was slim built and fairly nourished. There were no signs of icterus, pallor, cyanosis, edema or lymphadenopathy.

On systemic examination, respiratory, cardiovascular and gastrointestinal systems were unremarkable.

Vitals

- *Temperature:* normal
- *Pulse:* 84/minute with regular rhythm and good volume in right radial artery.
- *Blood Pressure:* 106/70 mmHg

Nervous system examination

- Conscious and fully oriented
- *Pupil:* normal in size, both eye reactive to light
- *Power:* 5/5/5/5
- *Plantar:* absent/absent
- *Tone:* hypertonia in both lower limbs

- *Deep tendon reflexes:* ankle, knee, supinator, biceps and triceps were exaggerated
- No cerebellar signs or nystagmus present
- No sensory involvement
- Joint position unaltered
- *Foot drop:* present

Thus, impression of lower motor neuron weakness with spasticity emerged.

Investigations

Complete blood count, renal and liver function tests of the patient were unremarkable. The patient was HIV and HBsAg non-reactive. Electrocardiogram and chest X-ray were also normal. He had normal serum vitamin B₁₂ (929 pg/ml) and Serum Creatinine Phosphokinase (146) level.

Due to suspicion of OP poisoning, RBC acetyl cholinesterase (AChE) and plasma/pseudo/butyl cholinesterase (BuChE) were tested at National Institute of Occupational Health (NIOH); which came low [RBC AChE – 636 (1900-3400), BuChE – 1728 (2900-5800)].

Nerve conduction study was done; which showed,

- Decreased amplitude of conduction in bilateral peroneal and right tibial nerve.
- Decreased MNCV (mean nerve conduction velocity) of bilateral median nerve.
- Normal MNCV of bilateral tibial and peroneal nerve.

Impression

Thus patient was diagnosed with organophosphorus agent induced delayed axonal type of polyneuropathy; and food samples were sent for testing at the forensic science laboratory to identify the culprit poison. The Result of which is awaited at present (Figure 1).



Figure 1: Foot drop.

Treatment

Physiotherapy was started and regular follow-up was advised.

DISCUSSION

On ingestion, organophosphorus agent do not produce significant cholinergic crisis, but 7 to 20 days later it leads to a pure motor axonal neuropathy with wrist and foot drop. Carbamates are only rarely associated with the development of OPIDN.^{3,4}

The mechanism may involve inhibition of neuropathy target esterase (NTE), rather than alterations in RBC acetylcholinesterase function.⁵ This enzyme, which is found in the brain, peripheral nerves, and lymphocytes, is responsible for the metabolism of various esters within the cell.

Affected patients present with transient, painful "stocking-glove" paresthesias followed by a symmetrical motor polyneuropathy characterized by flaccid weakness of the lower extremities, which ascends to involve the upper extremities. Sensory disturbances are usually mild. Delayed neurotoxicity primarily affects distal muscle groups, but in severe neurotoxicity, proximal muscles groups may also be affected.⁶

Electromyograms and nerve conduction studies of affected patients reveal decreased firing of motor conduction units.⁷

Histopathologic sections of peripheral nerves reveal Wallerian (or "dying-back") degeneration of large distal axons.⁸

The risk of developing OPIDN is independent of the severity of acute cholinergic toxicity. Some organophosphorus agents, such as parathion, are potent cholinergic agents but are not associated with OPIDN. Others, such as triorthocresyl phosphate in OPIDN.^{9,10}

Most cases of mild delayed neurotoxicity improve with time; in severe cases, an upper motor neuron syndrome with spasticity of the lower extremities usually causes permanent disability.

Agents associated with organophosphorus induced delayed neuropathy:

- Chlorpyrifos
- Leptophos
- Malathion
- Mipafos

- Merphos
- Trichlorfon
- Triorthocresylphosphate (TOCP)
- Tricresylphosphate (TCP)

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Acharya H, Kelaiya A, Singel V, Kapadia R. Organophosphorus agent induced delayed neuropathy: a case report. *Int J Res Med Sci* 2016;4:674-6.