

Delayed myelopathy after organophosphate intoxication: A case report

SAGE Open Medical Case Reports
Volume 10: 1–4
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DOI: 10.1177/2050313X221104309
journals.sagepub.com/home/sco



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Abstract

Organophosphate-induced delayed neuropathy, a central-distal axonopathy, passes through latent, progressive, static and improvement phases. During the improvement phase, the peripheral nerves regenerate unmasking the spinal cord lesion with myelopathic features. We report a case of a 16-year-old male who developed myelopathy 6 weeks following chlorpyrifos poisoning. He had a motor weakness of 4/5 in bilateral hips and 3/5 in bilateral knees and ankles. Spasticity and exaggerated reflexes with ankle clonus were present in the lower limbs. Sensory and the upper limb motor examinations were all normal. Pertinent blood, cerebrospinal fluid and nerve conduction tests were normal. Magnetic resonance imaging of the spine showed features of cord atrophy. Three months following physiotherapy, his power improved to 5/5 in bilateral knee and hip joints and 4/5 in bilateral ankles with spasticity. Organophosphate-induced delayed neuropathy can present as earlier as 6 weeks with myelopathy. Previous history of organophosphorous exposure is important in myelopathy or peripheral neuropathy.

Keywords

Organophosphate, organophosphate poisoning, chlorpyrifos, myelopathy

Date received: 27 February 2022; accepted: 6 May 2022

Introduction

Accidental or intentional ingestion of organophosphate (OP) is common in Nepal.¹ It can present as acute cholinergic crisis, intermediate syndrome and organophosphate-induced delayed neuropathy (OPIDN). Acute cholinergic crisis, as a result of inhibition of acetylcholinesterase, can manifest either with the involvement of muscarinic (lacrimation, salivation, miosis, bradycardia, emesis, diarrhea, etc.) or nicotinic receptors (muscle weakness, fasciculation, cramps, twitching). After about 24–96 h, intermediate syndrome, presenting as weakness of the proximal limb muscles, flexors of neck and respiratory muscles can occur.² OPIDN is a central-peripheral distal axonopathy: peripheral distal axonopathy can predominantly present as a motor polyneuropathy, and central axonopathy can present with myelopathic features.^{3,4} These usually develop 7–20 days after exposure to an OP agent.⁵ Here, we present a case of a 16-year-old male who presented with the features of organophosphate-induced delayed myelopathy following the ingestion of chlorpyrifos and cypermethrin.

Case presentation

A 16-year-old male presented to our center with altered sensorium, hypersalivation, hyperlacrimation, bradycardia and miosis approximately 1 h after consuming 100 mL of organophosphate poison (50% chlorpyrifos and 5% cypermethrin) with suicidal intention. Emergency management was done with gastric lavage, atropine infusion and pralidoxime. After 48 h, the patient developed difficulty in holding his head up from the pillow. During the course, he also developed aspiration pneumonia of the right lower lobe, which was treated

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Table 1. Blood and CSF investigations.

Blood investigations			
Components	Finding	Unit	Reference value
Renal function test			
Urea	6	mmol/L	1.6–7
Creatinine	73	μmol/L	60–115
Sodium	138	mEq/L	135–146
Potassium	3.9	mEq/L	3.5–5.2
Liver function test			
Total bilirubin	16	μmol/L	3–21
Direct bilirubin	4	μmol/L	0–5
Aspartate aminotransferase	10	U/L	37
Alanine aminotransferase	18	U/L	42
Alkaline phosphatase	128	U/L	<306
Prothrombin time	12	seconds	10–12
Vitamins level			
Vitamin B12	282	pg/mL	239–931
Folic acid	5.2	ng/mL	2.76–20
Total and differential counts			
WBC	6400	Cells/mm ³	4000–11,000
RBC	4.8	Cells/mm ³	4.5–5.5
Hemoglobin	16	gram%	12–18
PCV	46.3	%	36–54
MCV	95	f/l	82–92
MCH	33	pg	27–32
MCHC	34	%	32–36
Platelets	262,000	Cells/mm ³	150,000–400,000
Serology (HIV, Hepatitis B and C)	Negative		
CSF findings			
Sugar	70	mg/dL	50–76
Protein	51.7	mg/dL	15–50
RBC	Absent		0–10
WBC	<5 (100% lymphocytes)	Cells/mm ³	0–5

CSF: cerebrospinal fluid; RBC: red blood cells; WBC: white blood cells; PCV: packed cell volume; MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration.

with antibiotics. The patient gradually improved and was discharged after 20 days of hospital stay.

After 6 weeks of organophosphate ingestion, he again presented in our emergency department with gradual onset of bilateral lower limb weakness for 7 days. Patient initially noticed a dragging of his feet while walking. His symptoms progressed over a period of 7 days to the extent that he needed support both on standing from sitting position and walking on leveled ground. His bladder and bowel habits were normal. At presentation, the patient was afebrile, oriented to time, place and person. Higher mental functions, cranial nerve and sensory examinations were normal. There was no muscle atrophy, but spasticity was present in both the lower limbs with a power of Medical Research Council (MRC)⁶ 4/5 in bilateral hips and 3/5 in bilateral knees and ankles. Lower limb reflexes were brisk with an ankle clonus and bilateral extensor plantar response. Tone, power and reflexes were normal in both the upper limbs.

Routine blood investigations were normal (Table 1). Cerebrospinal fluid (CSF) examination showed normal sugar, protein and cells (Table 1). There was absence of oligoclonal bands. CSF cytology was negative for malignancy and IgG index was normal. Serum aquaporin-4 or myelin oligodendrocyte globulin antibodies were absent. Nerve conduction study of the upper and lower limbs showed normal motor and sensory amplitudes, latencies and conduction velocities. Magnetic resonance imaging (MRI) of the spine showed mildly roomy CSF space around the dorsal cord without any signal changes in the cord suggestive of cord atrophy (Figure 1) with no abnormal findings in MRI of the brain.

The patient was treated with a 5-day course of 1 g/day of intravenous methylprednisolone, calcium and vitamin B1 supplements, and regular extensive physiotherapy of the lower limbs. The progressive symptoms of the patient were static during the hospital stay. He was discharged with an

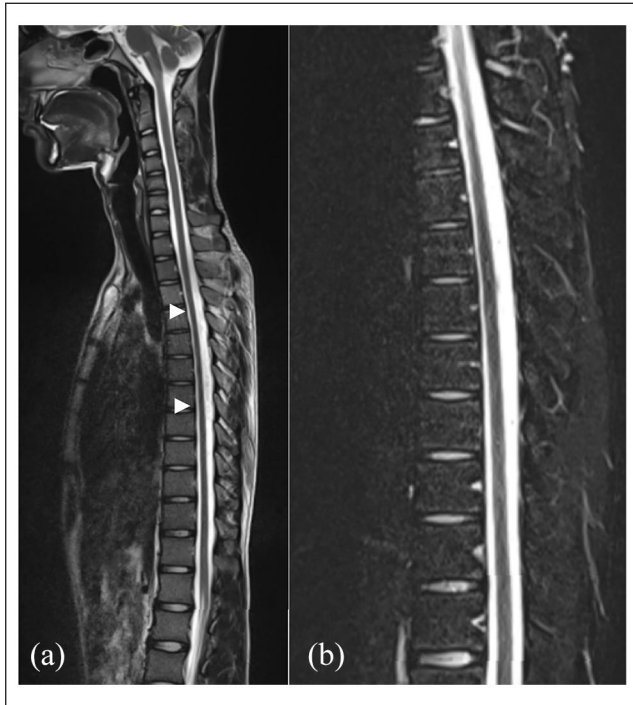


Figure 1. (a) T2-weighted sagittal whole spine with white arrowhead and (b) STIR sagittal dorsal spine showing mildly roomy CSF space around the dorsal cord suggesting mild cord atrophy. No signal changes were seen in the cord.

oral dose of 50 mg of prednisolone for 10 days along with physiotherapy. On 3-month follow-up, the patient improved with a power of 4/5 in ankles and 5/5 in knee and hip joints bilaterally. The patient was able to walk without support on a plain surface but had a spastic gait. There was mild difficulty while standing from supine and sitting position, and needed support on walking upstairs and downstairs.

Discussion

Neurological manifestations in OP poisoning can be classified into three types: type 1 paralysis or cholinergic crisis, type 2 paralysis or intermediate syndrome and type 3 paralysis or OPIDN.⁷ Type 1 paralysis occurs within 24 h while Type 2 paralysis occurs 24 h following the poisoning. The clinical features of type 2 paralysis can occur as a distinct entity or may overlap with acute cholinergic crisis.^{2,8} In our case, the patient presented with cholinergic crisis after 1 h of ingestion for which atropinization was done. After 48 h, he developed weakness of neck muscles as a part of type 2 paralysis. Type 3 paralysis occurred after 6 weeks of ingestion.

OPIDN, either clinical or subclinical, was observed in about 35% from a 6-month follow-up study. However, only 13% were clinically symptomatic.⁹ The mechanism of OPIDN has been linked to neuropathy target esterase (NTE), now known as patatin-like phospholipase domain containing protein 6 (PNPLA6).¹⁰ This is a serine hydrolase with

phospholipase activity and is encoded by PNPLA6 gene located on human chromosome 19p13.2. It likely plays a role in membrane lipid homeostasis. Mutations in this gene have been shown to cause neurodegenerative conditions.¹⁰ OPIDN occurs with certain inducing agents like chlorpyrifos, dichlorvos, isophenos and methamidophos. These agents lead to more potent inhibition of NTE than acetylcholinesterase (AChE) with subsequent aging of NTE.¹¹ Inhibition of NTE results from phosphorylation and aging occurs when the lateral side chain leaves the phosphorylated NTE.¹² Seventy to ninety percent of NTE should be inhibited for the neuropathic effects to appear. Chlorpyrifos poisoning, as in our case, produces an active metabolite that has a ratio of anti-AChE to anti-NTE equal to 0.07 and is known to cause OPIDN.¹³ Moreover, a recent study has shown a newer mechanism involving the agonism of transient receptor potential cation channel, member A1 (TRPA1) by organophosphates. TRPA1, a channel that is permeable to calcium ions (Ca^{2+}), causes an influx of Ca^{2+} and plays a role in myelin damage as in ischemia.¹⁴

OPIDN can be classified into four stages: Latent, Progressive, Stationary and Improvement stages.⁴ Latent period is characterized by a delay of 10 days to 3 weeks in developing neurological symptoms. In the progressive phase, signs and symptoms advance rapidly to present with motor-sensory polyneuropathy. Sensory symptoms can include both positive and negative symptoms like cramping, tingling, burning pain in the calves, and glove and stocking type of sensory loss. Motor signs comprise foot drop and may progress to involve all four limbs with flaccid paralysis. During the stationary phase, neurological symptoms persist. As the patient enters the improvement phase, the sensory symptoms resolve prior to motor symptoms. The peripheral nervous system regenerates during this phase and hence spasticity with exaggerated reflexes occurs as a sign of unmasking of the lesion in the spinal cord.⁴

Our patient presented after a latent phase of 34 days with signs of corticospinal tract involvement in the form of bilateral lower limb spastic weakness, ankle clonus and extensor plantar reflex. However, he had no sensory or lower motor neuron symptoms. These manifestations occurred over a period of 1 week and were static throughout his hospital stay of 10 days. This could represent an overlap between the progressive and the improvement phase. This also suggests a rapid peripheral nerve regeneration or greater effect of the organophosphate on central compared to peripheral nervous system in the patient. A greater propensity for central nervous system impairment was apparent with organophosphate in a study by Agapejev et al.¹⁵ Such effects, manifesting as pyramidal tract signs, were seen more toward the latter part of the illness.¹⁶

Myelopathic cases reported in the literature have delayed onset spastic quadriparesis with bladder involvement,³ spastic quadriparesis with sensory motor neuropathy,¹⁷ and pure motor spastic paraparesis.¹⁸ These presentations were after 18 months of exposure to the organophosphate.^{17,18} Our case also had a pure motor spastic paraparesis. These features

presented quite early (6 weeks) in our case. A similar early presentation with dorsal cord atrophy at 2 months post-exposure had been reported.³

Rehabilitative therapy along with proper nursing care has shown to improve the condition from a long-term follow-up study.¹⁹ Corticosteroids have also been used as a neuroprotective drug in OPIDN.²⁰ In our case, the patient was treated with intravenous methylprednisolone and extensive physiotherapy of the lower limbs. Since the patient presented with progressive disabling symptoms and reports of demyelinating disorders such as multiple sclerosis or neuromyelitis optica usually take around 7–10 days in our settings, steroids were started. Although the patient did not show instant improvement, he gradually improved and was independent in most of his activities on 3-month follow-up.

Conclusion

OPIDN can present with myelopathic features as early as 6 weeks after ingestion of agents like chlorpyrifos. History of previous OP exposure should be sought in cases of myelopathy or peripheral neuropathy. Patients may require prolonged and extensive rehabilitation.

Data availability

The data supporting the findings of the case are available upon request to the corresponding author.

Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

Ethical approval


Our institution does not require ethical approval for reporting individual cases or case series.

Informed consent

Written informed consent was obtained from the patient and legally authorized representative of the subject for anonymized patient information to be published in this article.

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References

1. Utyasheva L, Sharma D, Ghimire R, et al. Suicide by pesticide ingestion in Nepal and the impact of pesticide regulation. *BMC Public Health* 2021; 21: 1136.
2. Senanayake N and Karalliedde L. Neurotoxic effects of organophosphorus insecticides. An intermediate syndrome. *N Engl J Med* 1987; 316: 761–763.
3. Thivakaran T, Gamage R, Gunarathne KS, et al. Chlorpyrifos-induced delayed myelopathy and pure motor neuropathy: a case report. *Neurologist* 2012; 18(4): 226–228.
4. Abou-Donia MB. Organophosphorus ester-induced chronic neurotoxicity. *Arch Environ Health* 2003; 58(8): 484–497.
5. Nayak P, Mallick AK, Mishra S, et al. Organophosphorus-induced toxic myeloneuropathy: series of three adolescent patients with short review. *J Pediatr Neurosci* 2019; 14(1): 42–45.
6. Medical Research Council. *Aids to the examination of the peripheral nervous system*. London: Her Majesty's Stationery Office, 1976.
7. Wadia RS, Sadagopan C, Amin RB, et al. Neurological manifestations of organophosphorus insecticide poisoning. *J Neurol Neurosurg Psychiatry* 1974; 37(7): 841–847.
8. Eddleston M, Mohamed F, Davies JO, et al. Respiratory failure in acute organophosphorus pesticide self-poisoning. *QJM* 2006; 99(8): 513–522.
9. Pannu AK, Bhalla A, Vishnu RI, et al. Organophosphate induced delayed neuropathy after an acute cholinergic crisis in self-poisoning. *Clin Toxicol* 2021; 59(6): 488–492.
10. Richardson RJ, Fink JK, Glynn P, et al. Neuropathy target esterase (NTE/PNPLA6) and organophosphorus compound-induced delayed neurotoxicity (OPIDN). *Adv Neurotoxicol* 2020; 4: 1–78.
11. Mangas I, Vilanova E, Estévez J, et al. Neurotoxic effects associated with current uses of organophosphorus compounds. *J Braz Chem Soc* 2016; 27: 809–825.
12. Lotti M and Moretto A. Organophosphate-induced delayed polyneuropathy. *Toxicol Rev* 2005; 24: 37–49.
13. Moretto A and Lotti M. Poisoning by organophosphorus insecticides and sensory neuropathy. *J Neurol Neurosurg Psychiatry* 1998; 64(4): 463–468.
14. Ding Q, Fang S, Chen X, et al. TRPA1 channel mediates organophosphate-induced delayed neuropathy. *Cell Discov* 2017; 3: 17024.
15. Agapejev S, Vassiliev I and Lima MM. Neurologic manifestations in 93 patients with exogenous poisoning caused by non-therapeutic chemical substances. *Arq Neuropsiquiatr* 1986; 44(3): 232–242.
16. Senanayake N. Tri-cresyl phosphate neuropathy in Sri Lanka: a clinical and neurophysiological study with a three year follow up. *J Neurol Neurosurg Psychiatry* 1981; 44(9): 775–780.
17. Chuang CC, Lin TS and Tsai MC. Delayed neuropathy and myelopathy after organophosphate intoxication. *N Engl J Med* 2002; 347: 1119–1121.
18. Agarwal A, Garg D, Goyal V, et al. Acute encephalopathy followed by delayed myelopathy: a rare presentation of organophosphate poisoning. *Trop Doct* 2020; 50(2): 162–164.
19. Sahoo P, Mohamed F, Sahu M, et al. Rehabilitation of organophosphate induced delayed polyneuropathy. *Int J Phys Med Rehabil* 2018; 6: 1000481.
20. Balali-Mood M and Saber H. Recent advances in the treatment of organophosphorus poisonings. *Iran J Med Sci* 2012; 37(2): 74–91.