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Organophosphorus induced toxic myeloneuropathy

Nitesh Kanwar[1], Neha Patial[2]
MD Medicine, CHC Kotkhai, Himachal Pradesh, India

Abstract
Organophosphate (OP) poisoning is the most common poisoning in India.Organophosphate poisoning (OP) is known to cause various neurological syndrome which include acute toxic effects due to cholinergic crisis and delay-ed syndrome characterised by motor-sensory polyneuropathy. Pure motor neuropathy with intact sensory conduction is rarely documented. Delayed neuropathy is initiated by an attack on a nervous tissue esterase. Although uncommon, delayed neurotoxicity has been consistently reported in literature. This mechanism is implicated not only in damaging peripheral nervous system but also in causing central processes leading to myelopathy. We report a case of patient who came to our hospital with delayed neurological manifestations of organophosphorus poisoning, which came out to be OP-induced myeloneuropathy after detailed analysis and evaluation.

Keywords: myeloneuropathy, nerve conduction velocity, OPIDN, organophosphorus

Introduction
Organophosphate (OP) poisoning is known to cause varied neurological presentations in the form of acute, intermediate, and delayed neuropathy [1] many organophosphorus esters cause acute cholinergic neurotoxicity. Some of these compounds are capable of producing organophosphorus ester–induced delayed neurotoxicity [2] Chlorpyrifos (O,O-diethyl O-3,5,6-trichloro-2-pyridylphosphorothioate) is known to cause a delayed syndrome or type III syndrome also called Organophosphorus-induced delayed neuropathy (OPIDN). It occurs especially in instances of high-dose exposure and in instances in which therapeutic agents were used to resolve acute cholinergic toxicity. The pathology involves a central-peripheral distal axonopathy. This is caused by a Wallerian-type degeneration of the axon, followed by myelin degeneration of long and large-diameter tracts of the peripheral and central nervous systems [3] OPIDN occurs within a period of 1 week to 5–6 months of the ingestion of an OP compound, almost exclusively in patients with preceding acute cholinergic toxicity related to severe acute exposure (to an OP compound). But as the incidence of myeloneuropathy is very rare in OP poisoning, exact incidence is not known.

Case analysis
Case A 26 years old man was admitted to medicine ward and later shifted to ICU with cholinergic crisis due to intentional ingestion of chlorpyrifos. At the time of admission his GCS was 3, with pin point pupils, excessive salivation, hypotension and lacrimation. He was put on mechanical ventilator and treated with atropine. He recovered from acute cholinergic crisis but after 1 month, he developed weakness in legs and bilateral foot drop. There was no weakness of the upper limbs. There was no sensory deficit. Nerve conduction studies (NCS) confirmed the diagnosis of severe axonal pure motor neuropathy with normal sensory response. He noticed improvement in strength in the legs over time but follow-up NCS after 1 year still shows axonal motor neuropathy.

Table 1

Age	**26 yrs**
Sex	male
Occupation	farmer
Duration of poisoning	1 month
Chemical name	Chlorpyrifos
Presentation	Weakness bilateral lower limbs since 2 weeks, insidious in onset, gradually progressive.
	▪ Proximal and distal weakness of lower limbs. ▪ No h/o loss of touch, temperature sensation. ▪ H/o stiffnes of b/l lower limbs. ▪ No H/o any cranial nerve involvement. ▪ No h/o bowel bladder involvement.
Clinical examination	▪ HMF: Normal ▪ Speech: Normal ▪ CN: Normal ▪ Motor: B/L Foot drop present. Bulk: Bilaterally comparable and Normal Tone: Rt side Lt side UL: N UL: N

	L L: ↑ L L: ↑ ▪ DTR: ▪ B T S K A ▪ Rt: 2+2+2+5+5+ ▪ Lt: 2+2+2+5+5+ ▪ Ankle clonus present bilateral sustained. ▪ Plantar B/L Mute.
Blood investigations	▪ normal
MRI Brain and spine	▪ normal
Nerve conduction studies	▪ NCS is suggestive of peroneal and tibial axonal neuropathy.

Discussion

- We described a male patient who developed OPIDN after an acute OP exposure. In our patient, muscle weakness in the lower extremities appeared four weeks after OP exposure. In addition to the distal paraplegia, upper motor neuron signs were also present. Sensorial examination was unremarkable, and electrophysiological findings confirmed pure motor axonal neuropathy. With respect to these findings, we diagnosed him with OPIDN. However, there are only a few case reports of delayed neuropathy following OP insecticide exposure and most cases from India. Type III paralysis or organophosphate induced delayed neuropathy (OPIDN) is a pure motor or predominantly motor axonal neuropathy characterized by wrist drop and foot drop with minimal or no sensory loss which occurs 7-20 days after exposure to an OP agent. The cardinal feature is weakness which appears initially in distal leg muscles followed by small muscles of the hands and later it may extend proximally. Clinical involvement of the corticospinal tracts and the dorsal columns becomes apparent when the peripheral neuropathy improves. Incidence of pyramidal tract involvement is high but presentation is delayed. The main mechanism of OPIDN development is the inhibition of neuropathy target esterase (NTE) via phosphorylation. Neuropathy target esterase is an integrated membrane protein, and present in the endoplasmic reticulum of neurons.[4] Neuropathy target esterase activity is important for axonal maintenance, because it facilitates the transport of macromolecules to the end of axons.[5] Mutations of this protein may contribute to motor neuron diseases such as amyotrophic lateral sclerosis. Also, mutations of NTE may be a facilitating factor for OPIDN development. The pathogenesis of OPIDN is presumed to be due to phosphorylation and ageing of an enzyme in axons called neurotoxic esterase or neuropathic target esterase (NTE). Inhibition of NTE causes degeneration of predominantly long axons, with loss of myelin and macrophage accumulation in nerves leading to motor axonal neuropathy. Commonly implicated OPCs include diazinon, malathion,fenthion, sumithion, chlorpyrifos, tri-orthocresyl phosphate (TOCP), dichlorovos, leptophos.

Conclusion

- OP poisoning is one of the most common hazards seen in Indian households. Delayed myeloneuropathy is one of the complications seen after stabilization in the acute phase. Early diagnosis and adequate therapy can help many young people to fight this irreversible morbidity. Precise reporting of such neurotoxicities of common household toxins may help us in gaining more insight into the mechanism to provide a better therapy in future. Every patient of OP poisoning should be followed up for at least one month and identification of offending chemical. During the rehabilitation process prescription of the appropriate assistive devices, strengthening, and stretching exercises should be applied intensively. Facilitating the functional improvement and achieving independence in activities of daily living should be the main aim. Clinicians should be aware of this rare condition to establish the diagnosis and appropriate treatment protocol.

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Conflicts of interest
There are no conflicts of interest.

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