Myeloneuropathy in organophosphorous compound poisoning

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Abstract:
Organophosphorous compounds are commonly used pesticides and are consumed by humans with suicidal intention. It causes various neurological complications in the form of acute, intermediate and delayed syndromes. Organophosphorous induced delayed syndrome occurs only in certain organophosphorous compounds. In some patients with time when the lower motor neuron involvement features improves, the upper motor neuron involvement becomes evident. Recognition of upper motor neuron involvement is important as it is helpful for prognostication. We report two cases of organophosphorous compound poisoning with upper motor neuron involvement seen at our institute.

Keyword:
Organophosphorous compound poisoning, Myeloneuropathy, Upper motor neuron, Prognostication, Organophosphorous induced Delayed syndrome

Introduction
Organophosphate compounds (OPCs) are used as pesticides, petroleum additives, plastic modifiers, antioxidants, flame retardants and lubricants. They are absorbed through the respiratory, skin and gastrointestinal tracts. Suicidal ingestion is the common mode of OPC poisoning in India. The severity of poisoning depends on the type and the dose of organophosphate compound. Early manifestations of organophosphorous compound poisoning are caused by accumulation of acetylcholine resulting in depolarisation block at the muscarinic and nicotinic receptors due to phosphorylation and inhibition of the enzyme acetylcholinesterase. Common clinical syndromes that are seen in patients with organophosphate poisoning include

1. Acute muscarinic syndrome (type I syndrome)
2. Intermediate nicotinic syndrome (type II syndrome) and
3. Organophosphorous induced delayed syndrome (type III syndrome) Rare manifestations such as organophosphorous induced Guillain Barre like syndrome, extrapyramidal syndrome,
dual neurotoxicity and chronic neuropsychiatry disorder have also been reported. The term organophosphorous induced delayed syndrome includes polyneuropathy and myeloneuropathy. Delayed syndrome occurs only in certain OPCs such as triorthocresylphosphate, leptophos, trichlorfon, dichlorvos, and mipafox. Upper motor neuron involvement occurs in only in half the cases of the delayed neuropathy and in that many of them are masked. Prompt recognition of upper motor signs is important by careful neurological examination so as to provide functional outcome in a patient with delayed syndrome.

Case 1
A 25-year-old male, consumed around 30 ml of an organophosphate compound (trichlorfon) with suicidal intent and was hospitalised in an unconscious state with cholinergeric crisis and respiratory failure. He was treated with gastric lavage, injection atropine and pralidoxime (PAM) apart from ventilatory support. He regained consciousness within 24 hours of initiating treatment, but remained restless and agitated for the next 24 hours. He however became fully conscious and was taken off ventilatory support by day four. By day six he became ambulant and was discharged on day eight with no motor or sensory deficit. He remained relatively asymptomatic for the next three weeks, but then started noticing burning sensation with difficulty in appreciating hot and cold water sensation in both legs. This was accompanied by a progressive difficulty in using both lower limbs in the form of difficulty in gripping slippers and tripping of toes while walking. All the symptoms progressed over a period of 4 weeks, and subsequently remained static over the next 2 weeks. On examination his vitals were stable, and systemic examination was normal. On neurological examination, there were normal higher mental functions and intact cranial nerves. On spinomotor system examination, tone was reduced distally in both lower limbs and there was a minimal wasting of the foot, leg, and hand muscles with bilateral foot drop. Power in the upper limb was normal except for mild weakness of hand grip and small muscles of the hand. Where as in lower limb power was normal proximally but knee and ankle showed MRC grade 4 and 3 respectively. The abdomen and cremasteric reflexes were absent, plantars were bilateral extensor and all deep tendon reflexes (DTRs) were brisk except ankle jerk which was absent. On sensory examination, all modalities of sensation impaired bilaterally in distal graded fashion in glove and stocking pattern. On investigation, haemogram, blood sugar, LFT, RFT, serum electrolytes, ECG, X-ray chest and MRI spine were normal. Nerve conduction studies revealed distal symmetrical sensory and motor axonal neuropathy with lower limb more affected than upper limb. EMG revealed denervation pattern in the form of fibrillation potentials and reduced interference in the distal muscles. Patient was followed up with physiotherapy for next 6 months but did not show much improvement in functional impairment.

Case 2
A 40-year-old male, who had consumed unknown quantity of organophosphorus compound [leptophos] with suicidal intent and was hospitalised in conscious state. He was found to have cholinergeric crisis and was treated with gastric lavage, injection atropine and pralidoxime (PAM). His symptoms subsided in next three days. At the time of discharge on day seven, there was no motor or sensory impairment. He was back to his job and was asymptomatic for next 2 months. Then he noticed a insidious onset and rapidly progressive weakness and wasting.
of all four limbs and became bedridden in next two months. On examination his vitals were stable, and systemic examination was normal. On neurological examination, the higher mental functions were normal and cranial nerves were intact. On motor examination, tone was reduced in all four limbs and there was a severe wasting of the foot, leg, and hand muscles with bilateral foot drop and claw hand. Power was decreased in all four limbs bilaterally distal more than proximal weakness and lower limb more affected than upper limb in the range of MRC grade 2 to 3. All deep tendon reflexes (DTRs) were brisk except ankle jerks which were absent, abdomen and cremasteric reflex were absent and the plantars were extensor. Sensory examination revealed sensory impairment in distal graded fashion in glove and stocking pattern.

On investigation, haemogram, blood sugar, LFT, RFT, serum electrolytes, ECG, X-ray chest and MRI spine were normal. Nerve conduction studies showed distal symmetrical sensory and motor axonal neuropathy with lower limb more affected than upper limb. EMG revealed denervation pattern. This case also showed poor recovery and left with severe functional deficit even after six months of follow up with physiotherapy.

**Discussion**

Organophosphorus compound induced delayed syndrome is because of central and peripheral axonopathy. Axonopathy of the central and peripheral nervous system causes myelopathy and polyneuropathy respectively. The clinical manifestations of organophosphorous compound induced delayed syndrome are not due to acetylcholine excess. The mechanism of delayed neurotoxicity is currently not known. One hypothesis suggests phosphorylation and cleavage of the lateral side chain of Neuropathic Target Esterase (NTE), an enzyme that is present both in central and peripheral nervous system. Another hypothesis suggests an increased aberrant protein kinase mediated phosphorylation of cytoskeletal proteins leading on to destabilisation of microtubules and neurofilaments which leads to an axonal dysfunction. The organophosphorous compound induced delayed syndrome usually progresses through following four stages namely latent, progressive, stationary and improvement phases. Features of polyneuropathy are marked during the progressive phase, where as upper motor neuron features are unmasked during improvement phase of delayed syndrome. Koc reported latent period of 1 to 26 weeks for developing delayed polyneuropathy after exposure to organophosphate compounds in 22% of cases with organophosphorous poisoning. In our study, one was 3 weeks and other was 16 weeks later developed delayed syndrome after organophosphorous poisoning.

Organophosphorous induced delayed neuropathy is a predominantly motor, distal dying back axonopathy and are characterised by cramps in the calves, distal paraesthesias and limb weakness with foot drop and intrinsic hand muscle wasting. One of our patient had burning sensation in both legs and both patients had wasting and limb deformity similar to previous studies. One of the cases in this study had proximal weakness in concordance with Wadia who had reported 40% of cases with proximal weakness in delayed syndrome. In our study both of them had pyramidal tract involvement in the form of brisk reflexes with
bilateral plantar extensor and absent abdominal and cremasteric reflexes compared to Senanayake’s series where 50% of patients had evidence of pyramidal tract dysfunction. Involvement of upper motor neurons becomes evident when the peripheral neuropathy improves. In our study, however both of the patient had corticospinal tract involvement along with polyneuropathy at the time presentation itself. Glove and stocking sensory impairment has been encountered in 46.5% of cases in a study conducted by wadia et al. In our study, however, both of our patient showed glove and stocking sensory impairment. We encountered distal symmetrical sensory motor axonal neuropathy in both of our patients in electrodiagnostic studies in concordance with previous reports. Studies by vasconcellos have shown that patients with superimposed myelopathy on neuropathy had poor recovery compared to neuropathy alone. Similar findings were noted in our patients where both patient had pyramidal tract involvement and did not show much improvement and left with significant functional deficit. There is however, no specific therapy for organophosphate-induced neuropathy or myeloneuropathy available till date. Physiotherapy remain the main stay of therapy for organophosphorous induced delayed syndrome.

**Conclusion:**
In organophosphorous compound poisoning polyneuropathy is uncommon where as myeloneuropathy is still more uncommon. Myeloneuropathy is underreported compared to polyneuropathy due to unawareness of this entity and also classical signs of upper motor involvement such as pyramidal pattern of weakness spasticity, exaggerated reflexes and extensor plantar are easily masked by neuropathy.

References:

