Abstract:
Organophosphorus compounds are common insecticidal agents used in India. Their use as a suicidal agent is also well known often leading to massive organophosphorus-compound intoxication. Although uncommon, delayed neurotoxicity has been consistently reported in literature probably related to the inhibition of neurotoxic esterase. This mechanism is implicated not only in damaging peripheral nervous system but also in causing central processes leading to Myelopathy. We describe a patient who had a classic acute cholinergic crisis after exposure to organophosphates, with the subsequent development of organophosphate-induced delayed neuropathy. Magnetic resonance imaging (MRI) showed diffuse spinal cord atrophy that persisted long after the cholinergic effects had subsided.

Keyword: Chloropyriphos, Organophosphorus, Delayed Myelopathy, pure motor, peripheral nervous system

CASE REPORT:
An 18-year-old girl attempted suicide by drinking 100 ml of a mixture containing Chloropyriphos 50% (O,O-diethyl O-3,5,6-trichloropyridin-2-yl phosphorothioate) and Cypermethrin 5% a synthetic Pyrethroids which acts as an axonic poison. She developed classical features of organophosphate poisoning with loss of consciousness, pin-point pupils and profuse oral secretions. She was treated with gastric lavage, atropine infusion and other supportive measures. She did not require ventilation and over the next one week made an uneventful recovery and was discharged without any neurological deficits. The patient was asymptomatic over the next 2 months after which she developed progressive spasticity of both lower limbs which progressed over the next 4 months and since then has remained static. Currently, she is independent for almost all her ADLs except walking for which she requires one person support. Clinically she had features of bilateral pyramidal tract involvement in the lower limbs (spasticity, brisk deep tendon jerks, extensor
plantars and ankle clonus). She also had mild wasting of distal lower limbs. There was no evidence of spinothalamic tract or posterior column involvement. The bedside autonomic function tests were normal including postural blood pressure, isometric hand grip test, cold-pressor test, and valsalva maneuver. She had no urinary symptoms. Vision was normal and there were no degenerative retinal changes. No in-coordination in upper limbs was noted. Family history was negative for adult onset ataxias. Gadolinium enhanced MRI of the spine and brain showed diffuse thinning of the dorsal cord without signal changes (Fig: 1).

Nerve conduction studies showed motor axonal neuropathy with evidence of chronic reinnervation in lumbosacral myotomes (L4, L5 and S1 myotomes). Visual Evoked Potential (VEP) were normal. SSEP tibial (somatosensory evoked potential) showed dorsal column dysfunction. SSEP median was normal. The CSF was normal (4 cells and protein of 27mg%). Viral marker (multiplex PCR) in CSF was negative. Blood investigations showed normal B12 and folate levels. Markers for vasculitis and detailed autoimmune panel was also non-contributory. Her retroviral status (HIV as well as HTLV 1) were negative. The patient had marginal improvement with muscle relaxants and physiotherapy. She is under follow up there has been no worsening since then.

**Discussion:**
Organophosphate induced delayed neurotoxicity (OPIDN) affects peripheral as well as central nervous system. Extrapyramidal manifestations (3) and behavioral and psychologic changes (4), (5) are well described delayed central nervous system manifestations. To the best of our knowledge, there are only few reports of myelopathy occurring as a complication of OP Poisoning. Here we have described a patient, who after recovering from the acute cholinergic crisis of organophosphorous poisoning presented with a late onset delayed myelopathy. Investigations revealed motor axonal polyneuropathy which indicates that this patient had an organophosphorous induced delayed polyneuropathy (Type II paralysis) which in this patient had remained sub-clinical. Similar to the case in question, one report describes pyramidal signs and central nervous system involvement, with partial functional recovery, after severe organophosphate-induced delayed neuropathy. (6) Thirunavukkarasu et al (7) had reported a similar case of a young girl with Chlorpyrifos poisoning who developed a spastic paresis after 6 weeks. Similar to our patient the electrophysiological studies showed a pure motor neuropathy and there was thoracic cord atrophy on MRI spine. Chuang et al described a case that had symptoms of neuropathy on day 17th and later on went on to develop a spastic myelopathy after 18 months (8). The mechanism of delayed toxicity due to organophosphates is unclear. One postulated mechanism is
phosphorylation of the enzyme Neuropathy targetesterase by organophosphates (9), (10). This enzyme is present in the brain, spinal cord and the peripheral nervous system. Chlorpyrifos is classified as 'Moderately Hazardous (Class II)' as per the WHO Organophosphorus Compound Classification. The risk of developing OPIDN is independent of the severity of acute cholinergic toxicity. Some organophosphorus agents, such as parathion (WHO Class Ia), are potent cholinergic agents but are not associated with OPIDN. Others, such as triorthocresyl phosphate (TOCP), produce few clinical signs of cholinergic excess but are frequently implicated in OPIDN (figure 2). Carbamates are only rarely associated with the development of OPIDN (11), (12)

Fig 2:

Another hypothesis suggests organophosphate induced increased aberrant protein kinase mediated phosphorylation of cytoskeletal proteins resulting in the destabilisation of microtubules and neurofilaments which would lead to axonal dysfunction. Studies in chicks with organophosphate-induced delayed neuropathy (13) have shown severe damage in the ventral and lateral tracts of the thoracic and lumbar spinal cord. The same neuropathological changes may have been associated with the prominent diffuse spinal cord atrophy, especially in the thoracic column, that we observed in our patient.

This case describes rare manifestations of chronic neurotoxicity of organophosphate poisoning. Awareness of the natural history of neurotoxicity of a given compound helps to establish prognosis and management. Spastic myelopathy due to dorsal cord involvement can be a delayed complication of organophosphorus compounds. A history of exposure of organophosphorus compounds should be sought in such patients without other definite etiology.

References:


