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Organophosphorus (Chlorpyrifos) Toxicity Causing Delayed Induced Neuropathy and Myelopathy - Rare Case Report

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Abstract

Organophosphate (OP) poisoning is the most common poisoning in India, accounting for almost half of the hospital admissions due to poisoning. 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 report of 35year old male who came to our hospital with delayed neurological manifestations of organophosphorus poisoning, which came out to be OP-induced neuropathy and myelopathy after detailed analysis and evaluation

Keywords: Organophosphate, Neuropathy, Myelopathy

Introduction

Organophosphate (OP) poisoning is known to cause varied neurological presentations in the form of acute, intermediate, and delayed neuropathy. Many organophosphorus esters cause acute cholinergic neurotoxicity. Some of these compounds are capable of producing organophosphorus ester–induced delayed neurotoxicity. Chlorpyrifos 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. The prevalence of OPIDN is variable; however, it occurred in 22% of patients with OP poisoning in a recent study. 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 Report

A 35 year old male presented to causality with a history of consumption of poison at 1pm in farm about 50-100ml following which the patient started vomiting. It was noticed by a neighbour in the field and patient was brought to the PHC. Primary care was provided and the patient was shifted to tertiary care center the same day in the evening. When he arrived the patient had difficulty in breathing and complained of pain abdomen and one episode of loose stool.

On examination the patient was unconscious, pupils pinpoint, typical garlic odor was present, fasciculation's present, secretions present. GCS was E1, V1, M1. Patient was intubated and put on ventilator support. Patient was on ventilator support for 8 days, treated with PAM, Atropine, Antibiotic, Proper Physiotherapy and was discharged, total duration of hospital stay was 10 days. At the time of discharge patient had normal power and no focal neurological deficit and other systems were normal and had mild change in voice.

Patient was apparently alright and doing all his routine activities for 6 days after discharge, on the 7th day he noticed weakness of both the feet but he was able to get up from squatting position. Next day morning he was unable to get up from squatting position and weakness progressed in one day that he was not able to move both his lower limbs. Patient came to the tertiary care center in medicine opd with history of weakness in both lower limbs past 2 days. There was No history of weakness in upper limb, truncal muscle weakness, no sensory loss, cranial nerve involvement, bowel and bladder involvement. No h/o of backache, fever.

On Examination

BP -130/70 mmhg

PR- 80 BPM

Sp02- 98% under room air

Systemic Examination

CVS - S1 S2 Present

R/S - B/L Air Entry Present

P/A - Soft Non Tender

CNS: - Conscious, Oriented to Time, Place, Person.

Pupil equal and reactive to light

Speech comprehensive

Cranial nerve examination - Normal

Sensory system examination - Normal

Bowel bladder - Normal

Motor system examination

		Left	Right
Power:	Upper limb (Proximal Ms)	5/5	5/5
	(Distal Ms)	5/5	5/5
	Lower limb (proximal Ms)	2/5	2/5
	(Distal Ms)	0/5	0/5
Tone:	Upper limb.	Normotonic	Normotonic
	Lower limb	Hypotonic	Hypotonic
Plantar:		Absent	Extensor
DTR:	Upper limb	+2	+2
	Lower limb		
	Ankle	0	0
	Knee	+3	+3

Other Superficial Reflexes within Normal Limit No nuchal rigidity.

Cerebellum system examination- Normal

Investigations

Investigations	Result	
CBC	Normal	
HB	14.1mg/dl	
Peripheral smear	Normal blood picture	
Sr. Creatinine	0.6mg/dl	
Urea	14mg/dl	
CPK	100 (Normal)	
LFT	Normal	
Sr.Calcium	8.4mg/dl	
Sr. Sodium	145mEq/l	
Sr. Potassium	3.65mEq/l	
Sr. Vitamin B12	2000ug	
ANA PROFILE	Normal	
HIV	Non-Reactive	
Hbsag	Non-Reactive	
HCV	Non-Reactive	

CSF analysis

PROTEIN	200mg/dl
SUGAR	54mg/dl
CELL COUNT	5cell/cc
CELL TYPE	100%Lymphocytes
GRAM STAIN	NORMAL
ZN STAIN	NORMAL
KOH	NORMAL
ADA	NORMAL
VDRL	NEGATIVE

MRI Spine- Normal

Nerve conduction study- severe axonal motor neuropathy, Sensory nerve conduction parameters within normal limits in the nerve sampled.

CXR- Normal

Sonography Abdomen- Normal

Nerve biopsy- could not be done

Coarse during hospitalization - Patient was admitted for 40 days and supportive treatment was given. Patient was treated with vitamin B12,B1,B6 and physiotherapy. Neurology opinion was taken and advised to continue the same treatment. The Patient's power started improving. He was able to walk with a walker but had a bilateral foot drop present. At time of discharge the patient had 4/5 power in proximal muscle and distal muscle 2/5. Patient was discharged with multivitamins' and advised for physiotherapy and asked to follow up in opd after 15 days.

Discussion

In India, OP compounds are among the most commonly used agents for suicidal poisoning. Organophosphate (OP) poisoning is known to cause delayed neurological manifestations. Chlorpyrifos, an OP, causes a delayed syndrome that is characterized by a motor sensory polyneuropathy is well known. Rapidly evolving delayed myelopathy is extremely uncommon. There are only few reports describing pyramidal signs and central nervous system involvement, with partial functional recovery, after severe organophosphate-induced delayed neuropathy. Studies related to organophosphate-induced delayed neuropathy have shown severe damage in the ventral and lateral tracts of the thoracic and lumbar spinal cord. But article published in NEJM showed spinal cord atrophy. One of the study showed normal MRI spine which was similar to our study. The clinical manifestations of OPIDN are not caused by acetylcholine excess at the myo-neural nicotinic receptors. OPIDN is probably caused by phosphorylation and inhibition and subsequent ageing (dealkylation) of a protein enzyme called neuropathy target esterase (NTE) in the nerve cells. This enzyme is present in the brain, spinal cord, and peripheral nerves as well as in non-neural tissues and cells such as spleen, muscle, and lymphocytes.

Neurotoxic effects have also been linked to poisoning with OP pesticides causing four neurotoxin effects in humans: cholinergic syndrome, intermediate syndrome, organophosphate-induced delayed polyneuropathy (OPIDP), and chronic organophosphate-induced neuropsychiatric disorder (COPIND). These syndromes result after acute and chronic exposure to OP pesticides. OPIDP occurs in a small percentage of cases, roughly two weeks after exposure, where temporary paralysis occurs. This loss of function and ataxia of peripheral nerves and spinal cord is the phenomenon of OPIDP. Once the symptoms begin with shooting pains in both legs, the symptoms continue to worse for 3–6 months. In the most severe cases quadriplegia has been observed.

Paraoxonase (PON1) is a key enzyme in the metabolism of organophosphates. PON1 can inactivate some OPs through hydrolysis. PON1 hydrolyzes the active metabolites in several OP insecticides such as chlorpyrifos, oxon, and diazoxon. The level of PON1 plasma hydrolytic activity provides more protection against OP pesticides. Animal experiments indicate that while PON1 plays a significant role in regulating the toxicity of OPs its degree of protection given depends on the compound (i.e. Chlorpyrifos oxon or diazoxon). The higher the concentration of PON1 the better the protection provided.

The occurrence of OPIDN is said to follow the phosphorylation and subsequent ageing of an enzyme in axons called as Neuropathy Target Esterase. The occurrence of OPIDN is said to follow the phosphorylation and subsequent ageing of an enzyme in axons called as Neuropathy Target Esterase.

Very few cases like this one have been described in literature following chlorpyrifos exposure. The earlier hypothesis of inhibition of neurotoxicity target esterase as a causative factor is being replaced by implication of aberrant phosphorylation of cytoskeletal proteins leading to axonal instability and degeneration. The combination of upper and lower motor neuron features in our patient bears superficial resemblance to the motor neuron disease. The possible link may be paraoxonase enzyme which is required for chlorpyrifos oxon hydrolysis and its mutation has been linked to the motor neuron disease.

Recovery from the intermediate syndrome is normally complete and without any sequelae. The usefulness of oximes during the IMS remains uncertain. In animal experiments, very early administration of oximes has prevented the occurrence of myopathy. The distribution of the weakness in human cases of the IMS, in general, parallels the distribution of the myopathy observed in a number of studies in experimental animals. This has led to speculation that myopathy is involved in the causation of the IMS. However, while myopathy and the IMS have a common origin in acetylcholine accumulation, they are not causally related to one another.

Organophosphates inhibit AChE, causing OP poisoning by phosphorylating the serine hydroxyl residue on AChE, which inactivates AChE. AChE is critical for nerve function, so the irreversible blockage of this enzyme, which causes acetylcholine accumulation, results in muscle overstimulation. This causes disturbances across the cholinergic synapses and can only be reactivated very slowly, if at all. The onset and severity of symptoms, whether acute or chronic, depends upon the specific chemical, the route of exposure, the dose, and the individuals ability to degrade the compound, which the PON1 enzyme level will affect.

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Conclusion

Chlorpyrifos induced delayed neuropathy is common complication but presence of UMN sign in lower limb suggest spinal cord involvement. All patients presenting with neuropathy or myeloneuropathy should be screened for possible exposure to organophosphates or other toxins.

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