CASE REPORT

Chlorpyrifos-induced Delayed Myelopathy and Pure Motor Neuropathy: A Rare Case Report

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Abstract

Organophosphate (OP) poisoning is known to cause delayed neurological manifestations. Chlorpyrifos, an OP, causes a delayed syndrome that is characterized by motor sensory polyneuropathy. Pure motor neuropathy with intact sensory conduction is rarely documented. Rapidly evolving delayed myelopathy is extremely uncommon. A healthy 46-year-old male, known alcoholic and smoker without any comorbidities was admitted to the hospital with a cholinergic crisis due to ingestion of chlorpyrifos (OP). He was on mechanical ventilation for 20 days and treated with atropine, pralidoxime, and other supportive measures. After his sensorium improved, he noticed a flail type of weakness in both lower limbs. He also noticed weakness, thinning, and clawing in both hands. No history of (h/o) muscle twitching, bowel and bladder disturbances, and sensory system involvement. After 1 week, patient noticed truncal weakness and also stiffness in both lower limbs. On examination (o/E) he had spasticity in all four limbs. All reflexes are brisk with absent ankle reflex and bilateral extensor plantar. Electrophysiological studies revealed pure motor neuropathy. A spine magnetic resonance imaging (MRI) showed atrophy of the entire spinal cord. Other causes of myelopathy and neuropathy were excluded. The pathology of OP-induced delayed neuropathy (OPIDN) involves a central-peripheral distal axonopathy. The axonopathy is thought to be attributed to the inhibition of neuropathy target esterase (NTE) by phosphorylation and subsequent aging of NTE, causes Wallerian-type degeneration of the axon, followed by myelin degeneration of long and large diameter tracts of the peripheral and central nervous systems. Peripheral distal axonopathy results in predominantly motor polyneuropathy. Axonopathy of the central nervous system results in myelopathic features. Pure motor neuropathy with intact sensory conduction is rarely documented. Rapidly evolving delayed myelopathy is extremely uncommon which makes for a poorer prognosis.

Keywords: Case report, Chlorpyrifos, Myelopathy, Organophosphates poisoning, Pure motor neuropathy.

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Introduction

Organophosphates (OP) compounds are used mainly in agricultural fields as herbicides and pesticides and it is well known to cause toxicity on exposure. Most organophosphate (OP) compounds cause acute cholinergic neurotoxicity but only certain OP compounds cause delayed toxicity which occurs after a latent period of nearly 2–3 weeks.[1] Chlorpyrifos is an organophosphate compound recognized as causing acute toxicity, intermediate, and delayed neurological manifestations, or organophosphate-induced delayed neuropathy (OPIDN) also known as type III syndrome.[2,3] Organophosphate-induced delayed neuropathy (OPIDN) seen frequently in patients who consumed large amounts of chlorpyrifos or were exposed for a long time and in situations in which therapeutic agents were used to treating the cholinergic toxicity.[3,4] The pathomechanism involves a central and peripheral distal axonopathy which is caused by a Wallerian-type degeneration of the axon, followed by myelin degeneration of long and large diameter tracts of both peripheral and central nervous systems (CNS).[1,3] Here we described a rare presentation of OPIDN as myelopathy in the CNS and pure motor neuropathy without affecting the sensory system.

Case Vignette

A 46-year-old male, known alcoholic and smoker without any comorbidities was brought to the hospital due to ingestion of chlorpyrifos OP. In view of the cholinergic crisis, he was intubated and connected to mechanical ventilation for 20 days, and treated with atropine, pralidoxime, and other supportive measures. After his sensorium got improved, he noticed a flail type of weakness in both lower limbs. He also noticed weakness, thinning, and clawing in both hands which are shown in Figure 1. There was no history of (h/o) muscle twitching, bowel and bladder disturbances, and sensory system involvement. One week later patient noticed truncal weakness and also stiffness in both lower limbs. On examination (o/E), he had spasticity in all four limbs. All reflexes are brisk except the ankle reflex and bilateral extensor plantar. The sensory system and cranial nerves examination were entirely normal. Magnetic resonance imaging (MRI) brain was normal. MRI spine was taken which showed atrophy of the entire spinal cord as shown in the

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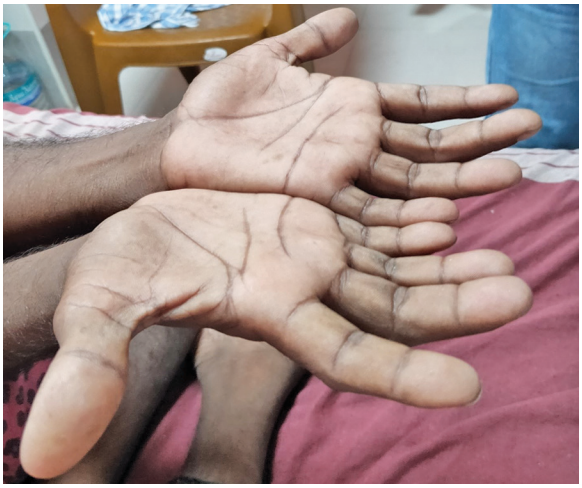

Fig. 1: Wasting and clawing of both hands

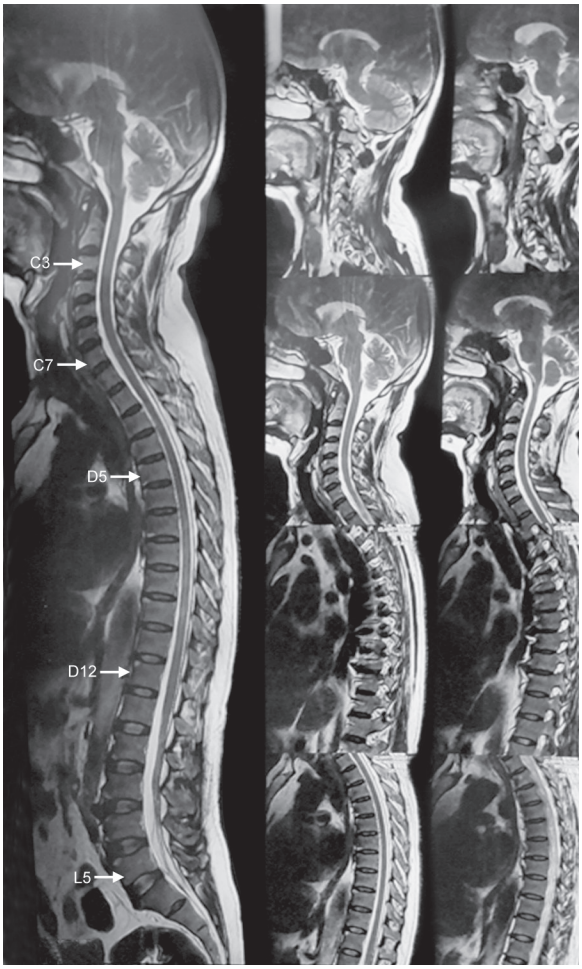

Fig. 2: MRI spine showing thinning of the entire spinal cord

Figure 2. Nerve conduction studies (NCS) were done which revealed absent compound muscle action potential in all four limbs. Sensory nerve action potentials (SNAP) were normal in both upper and lower limbs. Electromyography (EMG) revealed symmetrical denervation changes in all four limbs. Cerebrospinal fluid (CSF) analysis was normal. Investigations like complete blood picture, LFT, RFT, ESR, C-reactive protein, serum electrolytes, vitamin B12 levels, ANA and ENA screening, viral markers, and VDRL, were done for the exclusion of other causes of non-compressive myelopathy and which were normal. He was treated with supportive medication and given physiotherapy.

Discussion

Organophosphate-induced delayed neuropathy is classified into four stages which are the latent period, the progressive phase, the stationary phase, and the improvement phase.[1,3] The "latent period" is a delay between the onset of neurological deficits after exposure to OP's. Based on the factors like amount, the route and the duration of exposure, chemical composition, and frequency of exposure the latent period ranges from 2 to 3 weeks.[3,5]

The second stage is the "progressive phase", in which the patient presents with rapidly progressing sensory and motor polyneuropathy usually affecting the lower limbs more than the upper limbs. Almost all the patients present with sensory symptoms and signs and their absence is very rare like in our case. The most common sensory symptoms are tingling and numbness of feet and legs, cramps, and burning sensation in the calves. Sensory signs include "glove-and-stocking" sensory loss and a positive Rhomberg phenomenon.[2,3] Motor signs are predominant in lower limbs starting distally as foot drop and later progressing proximally as flaccid paralysis of all limbs. Bladder disturbances may see in some patients. After the "progressive phase", the third stage is the "stationary phase" in which the progression of the symptoms stopped and becomes static.[3] The fourth stage is "improvement phase," in which sensory symptoms improve first than motor symptoms, with faster recovery in upper limbs than the lower limbs.[3] In OPIDN the improvement starts first in the PNS, due to which CNS damage becomes evident and which manifests as spasticity with exaggerated deep tendon reflexes.[3]

In our case patient initially presented with lower motor symptoms and signs and within a short period of time he developed upper motor neuron signs and was the predominant clinical feature. This suggests greater effect of chlorpyrifos on the CNS compared with the peripheral nervous system and which was explained by the finding of spinal cord atrophy as shown in Figure 2, which was taken after 3 months of consumption.

This type of predominant CNS effect due to chlorpyrifos and other OP compounds have been reported previously. Agapejev et al. reported a case series involving >200 patients who had more predominant effects on CNS than PNS after op poisoning.[5] A study from Sri Lanka reported around 20 young females with op poisoning among which more than half of them are readmitted with CNS involvement with predominant pyramidal signs.[6]

The pathophysiology of delayed neurotoxicity after OP poisoning is not yet clearly known. It is hypothesized to involve neuropathy target esterase (NTE) enzyme which is present in the central nervous system (the brain and spinal cord) and the peripheral nervous system.[3,7] In OP poisoning the phosphorylation of NTE and cleavage of the lateral side chain from the phosphorylated NTE are thought to inhibited which results in axonapathy.[7]

Though all neurotoxic OP's inhibit NTE, some OP's doesn't result in OPIDN. The degree of NTE inhibition and the source of NTE vary with different op compounds and were proposed to have a different mechanisms.[8] Significant amounts of phosphorylated NTE and cleaved NTE is necessary for the occurrence of neurotoxicity in op compounds and the relative ratio of the same for chlorpyrifos

is 0.07:3.[3,8] A study on Hens revealed that the susceptibility of NTE inhibition is different from different op compounds and the decreasing order of the susceptibility is noted to be brain NTE, spinal cord NTE followed by nerve NTE and This might be the possible explanation for the greater CNS involvement in our patient as more amount of NTE inhibition occurred in the spinal cord than peripheral nerves.[3,8]

The prognosis of OPIDN is based on the amount of axonal degeneration that occurred in both CNS and PNS. In severe cases that cause predominant CNS axonal degeneration, the neurological deficits will persist as regeneration does not happen in CNS but reversible changes like edema may decrease as time progress.[1,3]

Conclusion

Organophosphate-induced delayed neuropathy (OPIDN) is dependent on several factors like the type of compound, ingested amount or duration of exposure, and the drugs that are given for acute toxicity. The pathomechanism of delayed neurotoxicity involves central and peripheral distal axonopathy. Peripheral involvement causes sensory-motor polyneuropathy whereas CNS involvement results in myelopathic features. The prognosis was poor in patients with predominant CNS involvement.

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