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Case Report

An interesting case of organophosphate induced delayed polyneuropathy

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Abstract

Organophosphate induced delayed polyneuropathy is a rare clinical manifestation resulting from exposure to certain organophosphorus esters.[1] It is characterized by degeneration of both peripheral and central nervous system axons occurring 1-4 weeks after a single or short term exposure.[2] This syndrome is due to inhibition of neuropathy target esterase (NTE). It usually starts with cramping muscle pain in both lower limbs, distal numbness and paresthesia, followed by progressive weakness which may become irreversible.[2] Decreased or absent deep tendon reflexes in both the lower limb is usually seen, rarely even upper limbs may be affected.[3] We report a rare case of organophosphorus induced delayed polyneuropathy overlapping with intermediate syndrome with possible features of non compressive myelopathy.

Keywords : organophosphates; organophosphate induced delayed polyneuropathy; axonal degeneration; neuropathy target esterase; nerve conduction study; paraplegia

Introduction

Organophosphates (OP) are among the commonly used pesticides across the world.[4] Organophosphorus poisoning can present as three different manifestations, namely acute cholinergic crisis, intermediate syndrome and organophosphate induced delayed neuropathy.[4] [5] Organophosphate induced delayed polyneuropathy (OPIDP), usually occurs 1-4 weeks after either a single or short term exposure and it may be progressive.[5] OPIDP is not related to acetylcholinesterase inhibition but it is due to inhibition of a special type of esterase named Neuropathy Target Esterase (NTE) present in nerve tissues.[6][7] For OPIDP to be initiated, phosphorylation and subsequent ageing of at least 70% of NTE is necessary and for this to happen usually a large amount of OP compound must be ingested.[8] However, there have been many case reports where delayed polyneuropathy has been reported following prolonged exposure to OP compound.[9] Here we describe a case who developed OPIDP following a single exposure to dimethoate superimposed on intermediate syndrome.

Case Report

A 48 year old male patient was referred to us 8 days after consumption of Dimethoate after having been treated in another hospital initially. He had presented to the EMR there 3 hours after consumption of organophosphorus compound and was managed with decontamination, anticholinergics, oximes and other supportive measures. He was intubated and initiated on ventilatory support the same day in view of impending respiratory failure. He had 2 episodes

of seizures following which anti-epileptics were started. MRI brain done was unremarkable. He developed features of intermediate syndrome from day 4 onwards, which was managed with anticholinergics and supportive measures. He developed ventilatory associated pneumonia (VAP) 5 days after initiation of ventilation which was managed with appropriate antibiotics. Patient was continued on ventilatory support and other supportive measures. By this time patient had developed extensive muscle weakness involving all 4 limbs. In anticipation of prolonged ventilatory support and ICU stay, tracheostomy was done on day 8 and was referred to our centre.

Patient was continued on ventilatory support, antibiotics and other supportive measures. Patient started improving slowly by the end of 2nd week onwards and underwent spontaneous breathing trials by 3rd week. However, patient continued to remain paraplegic with increased secretions and ptosis. All the correctable causes of weaning failure including metabolic, electrolyte disturbances, nutritional deficiencies and any other rare central causes were evaluated and ruled out. Antibiotics were rationalized as per culture reports and stopped after a course of 10 days. Patient showed marginal improvement by 4th week onwards and started having good cough reflex, sustained hand grip and neck extension. Patient was eventually weaned off ventilatory support by day 44. By this time, power in both the upper limbs had increased to 3/5, though he remained in flaccid paralysis of both lower limbs with power 0/5.

MRI whole spine screening in T2 weighted scan revealed increased signal intensities from distal thoracic cord to conus medullaris with secondary changes in vertebral bodies, which were consistent with features suggestive of non-compressive myelopathy. Further evaluation with nerve conduction study of motor nerves showed prolonged distal latencies with normal Compound muscle action potential (CMAP) amplitude and normal conduction velocities in both median nerves. However, CMAP was absent in both peroneal and tibial nerves bilaterally. Sensory nerve conduction study of both median and ulnar nerves showed prolonged distal latencies, normal amplitudes and reduced conduction velocities. These features were suggestive of demyelinating motor and sensory polyneuropathy.

A provisional diagnosis of Organophosphate induced delayed polyneuropathy was made and managed with physiotherapy and supportive measures. Patient improved further and tracheostomy was decannulated by day 50. He was discharged with comprehensive neuro rehabilitation care plan including physiotherapy and other supportive measures on day 57.

On 10 days follow-up, he remained paraplegic with slight improvement in lower limb powers (2/5) and normal upper limb powers. One month later, patient still has persisting weakness in both the lower limbs with power 3/5 and normal reflexes. Therefore, keeping in view the history of organophosphorus poisoning followed by signs of motor neuropathy with axonal degeneration, a diagnosis of organophosphate induced delayed polyneuropathy was established.

Discussion

Organophosphate compound poisoning manifests as three well defined clinical patterns. The initial phase constitutes an acute cholinergic crisis. This occurs 24– 48 hours following consumption due to inhibition of enzyme acetylcholinesterase leading to accumulation of acetylcholine in the synaptic junction causing excessive stimulation of cholinergic receptors resulting in respiratory failure.[10] Intermediate syndrome typically occurs 48-96 hours following an intense period of cholinergic symptoms and signs. Clinical features comprise of muscle weakness affecting proximal muscles, neck flexors and respiratory muscle. The clinical course usually lasts from 7 to 21 days.[11] Third is the Organophosphorus induced delayed polyneuropathy which develops three to four weeks after the initial symptoms. It is characterized by distal motor axonal neuropathy.

Weakness initially develops in distal leg muscles causing foot drop. It usually starts with cramping muscle pain in both lower limbs, distal numbness & paresthesia followed by progressive weakness. [12] [13] The pathogenesis of OPIDN involves phosphorylation and inhibition of neuropathy target esterase (NTE).[13] This enzyme is present in brain, spinal cord, peripheral nerve and other non-neural tissues. [14] Inhibition

of NTE causes degeneration of predominantly long axons with loss of myelin and macrophage accumulation in nerves leading to motor axonal neuropathy. The classical clinical features include muscle weakness with gradual progression proximally mimicking Guillain-Barre Syndrome (GBS).[14][15] Pure motor or sensory-motor neuropathy is common. However, pure sensory neuropathy is not seen in OPIDP. Diagnosis is usually made by typical clinical features and nerve conduction study which reveals classical prolonged distal latencies of affected nerves with decreased sensory and motor action potential.

However, global involvement of all limbs and cranial nerve involvement is also seen and not uncommon. In our case, there was sensory motor polyneuropathy in all four limbs which is similar to the findings seen in many earlier published case reports.[16] Surprisingly, MRI whole spine screening in T2 weighted scan showed altered signal intensities extending from thorax to conus medullaris with secondary changes in vertebral bodies which is usually seen in myelopathies. However, increased signal intensities could just be a manifestation of CNS lesion because of NTE inhibition. Treatment largely remains supportive though trials with steroids, thiamine and immunoglobulin have been done with varying outcome.[16] Our case remained paraplegic even after 70 days following exposure and started showing some improvement first in upper limb and later in lower limb during further follow up. The prognosis in mild neuropathy is good but with severe neuropathy, partial recovery occurs in 6-12 months, most of them may be left with permanent deficits.

Conclusion

OPIDP is relatively rare but not an uncommon manifestation of OP compound poisoning. Anticipation and prompt evaluation leads to timely diagnosis. Superimposed and atypical presentations can also occur. However, treatment remains largely unsatisfactory with no proven benefit with many regimen and still remains primarily supportive.

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