Late-onset distal polyneuropathy due to acute organophosphate intoxication case report

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Intoxications due to organophosphate insecticides are common in our country, since agriculture has an important place. Besides the well known acute cholinergic toxicity, these compounds may cause late-onset distal polyneuropathy occurring two to three weeks after the acute exposure.

An eight-year-old boy and a 13-year-old girl admitted to the hospital with gait disturbances.

Beginning 15 and 20 days, respectively, after organophosphate ingestion. Neurologic examination revealed bilateral dropped foot, absent Achilles tendon reflexes and peripheral sensory loss. Electromyography demonstrated motor weighed sensory-motor polyneuropathy with axonal degeneration significant in the distal parts of bilateral lower extremities. Biochemical, radiological findings and magnetic resonance imagings were normal. The two cases were taken under a physiotherapy program.

The two cases are presented here since organophosphate poisonings are common in our country, and since late-onset polyneuropathy is not a well known clinical presentation as acute toxicity.

Key words: acute organophosphate intoxication, late-onset distal polyneuropathy.

Organophosphate compounds cause acute toxicity and cholinergic crisis by acetylcholinesterase inhibiton. Some organophosphates, on the other hand, inhibit a protein called "neuropathy target esterase" and lead to a rather rare late-onset polyneuropathy. This clinical presentation, though not frequently seen as cholinergic reactions, is an important cause of morbidity in organophosphate intoxication due to sequelae development[1-3].

An eight-year-old boy and a 13-year-old girl admitted to the hospital with complaints of walking difficulties beginning 15 and 20 days respectively, after acute organophosphate poisoning. The two cases were diagnosed as distal polyneuropathy occurring late after organophosphate intoxication. Organophosphate poisonings are frequently seen in our country based on our agricultural economy[4-8]. We present here these two cases to emphasize the importance of raising families' awareness of the potential chronic neurological complications due to this condition.

Case Reports

Case 1

An eight-year-old boy admitted to the hospital because of walking difficulty. One month before admission to our hospital, the boy had accidentally ingested an agricultural organophosphate product and had been treated for five days in a community hospital where he was brought in comatose. Pralidoxime (30 mg/kg every 12 hours for 24 hours) and atropine had been administered. At the 15th day after intoxication, walking difficulty had begun and worsened with time. History and family history associated with a neurologic disease were negative.

Physical examination findings: weight 30 kg (3-10 p), height 134 cm (25-50 p), blood pressure 100/70 mmHg, body temperature 36.5°C.

Neurologic evaluation revealed bilateral dropped foot, absent Achilles tendon reflexes, sensory impairment of peripheral type in the lower extremities, no deep sensory involvement,

normal muscle strength in upper extremities and 2/5 in lower extremities and no cranial nerve involvement. The other systems were normal.

His laboratory investigations, including complete blood cell count, urinalysis, blood glucose, electrolytes, and liver and renal function tests were normal.

Electromyography (EMG) revealed electrophysiological findings referring to symmetrical sensory-motor polyneuropathy (predominantly motor involvement) with significant distal axonal degeneration in the lower extremities. Thoracolumbosacral magnetic resonance imaging (MRI) was normal.

Case 2

After one day of treatment in a private hospital, a 13-year-old girl who had ingested organophosphate insecticide in a suicide attempt was admitted to our hospital. She was given pralidoxime (1 g every 12 hours for 24 hours) and atropine and was discharged at the 8th day. She suffered from gait disturbance at the 20th day after acute intoxication and was rehospitalized. History and family history associated with a neurologic disease were negative.

Physical examination findings: weight 60 kg (50-75 p), height 155 cm (25-50 p), blood pressure 110/70 mmHg, body temperature 36°C.

Neurologic evaluation revealed bilateral dropped foot, bilateral absent Achilles tendon reflexes, sensory impairment of peripheral type in the lower extremities, no deep sensory involvement, normal muscle strength in upper extremities and 2/5 in lower extremities and no cranial nerve involvement. The other systems were normal.

Laboratory tests: Routine urine analysis, complete blood cell count, blood glucose, electrolytes, and liver and renal function test results were normal.

Electromyography (EMG) revelaled electrophysiological findings referring to symmetrical sensory-motor polyneuropathy (predominantly motor involvement) with significant distal axonal degeneration in the lower extremities. Thoracolumbosacral MRI was normal.

Discussion

Three million people in the world suffer from intoxication due to organophosphate compounds annually and approximately 220,000 of them die. Organophosphates cause acute symptoms by the inhibition of acetylcholinesterase[9]. Several organophosphate compounds additionally lead to polyneuropathy by a different route: inhibition of neuropathy target esterase. But inhibiton of neuropathy target esterase is not enough for the development of neurotoxicity. In the experimental trials it was demonstrated that pohsphonate, carbamate and sulfonate inhibited neuropathy target esterase but neuropathy did not occur. It was even shown that these agents, occupying the catalytic region of neuropathy target esterase, avoided the neuropathic inhibitor binding and played a preventive role against neuropathy development. Data from the experimental studies and case reports demonstrated that phosphates, phosphoamidates and phosphonates were the ones that were neurotoxic esterase inhibitors leading to polyneuropathy[10-14].

Symptoms appear two to three weeks after the ingestion of toxic material. Onset of the symptoms changes according to the dose and route of exposure. The onset may be delayed with the chronic exposure. Initial symptoms are generally cramps in legs. Subsequently distal paresthesia and sensory loss, and progressive weakness at the lower extremities occur and deep tendon reflexes become hypoactive. Similar symptoms may become evident in the forearm and hands. Sensory loss is mild. Occasionally mild pyramidal findings may accompany the clinical presentation[2,15]. The initial neurologic symptom in our cases was gait disturbance which manifested 15 and 20 days after the acute exposure, respectively, and progressed.

Electrophysiologic studies demonstrate distal symmetrical, generally motor type polyneuropathy particularly at the lower extremities. In our patients, the neurologic and electrophysiological findings were limited to the lower extremities and upper extremities were normal. This is probably because long fibers with breader diameters are more susceptible than the narrow and short ones. Degeneration in the anterior columns of thoracic and lumbar parts of the spinal cord has been reported as central nervous system involvement[2,13]. Late-onset polyneuropathy caused by organophosphate compounds is diagnosed by history and clinical findings. Senanayake et al.[16] defined a clinical picture appearing one to four days after intoxication with organophosphates such as phention, dymetoate, monochrotopos. They termed this condition "intermediate

syndrome". The most striking clinical finding in this syndrome is muscle weakness. Despite late-onset polyneuropathy, proximal muscles of the extremities and flexors of the neck are particularly involved. Cranial nerve palsies are common. Respiratory muscle involvement may be lethal.

There is no specific therapy for the late-onset polyneuropathy due to organophosphate compounds. Physiotherapy is effective. Pralidoxime that reactivates cholinesterase in the acute phase, fails to reactivate neuropathy target esterase. Prognosis is variable. Peripheral nerve destruction may cause atrophy, dropped foot, claw hand. Central nervous system involvement may result in spasticity and ataxia. In general, severity of the pyramidal involvement predicts the prognosis.

In our cases physical examination findings and electrophysiological studies revealed distal symmetrical sensory motor polyneuropathy at the lower extremities. For the differential diagnosis thoracolumbosacral MRI gave normal images. Both of them were taken under a physiotherapy program.

Studies have shown that years after acute intoxication with organophosphates, memory and cognitive functions might be defective and vibrotactile sensitivity might be decreased, indicating the presence of peripheral neuropathy, although neurologic examination and electroencephalography (EEG) findings were normal[17-20]. Similar findings were reported in cases who had suffered from low-dose chronic exposure to organophosphate insecticides[21]. These studies conclude that chronic or subclinic defects may be seen in the central and peripheral nervous system after either acute or chronic organophosphate intoxications.

In our country based on agriculture, intoxications due to organophosphate insecticides are common. Besides well known and potentially lethal acute cholinergic toxicity, chronic neurologic effects causing important morbidity must be considered; patients and families must be informed of this kind of chronic toxicity.

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