Intermediate Syndrome with Delayed Distal Polyneuropathy Folowing Chlorpyrifos Ingestion

Kloroprifosa Maruziyetten Sonra Gelişen Geç Distal Polinöropati ile Birlikte İntermediate Sendrom

Aynur Akın
Assoc. Prof., M.D.
Department of Anesthesiology and Reanimation
Erciyes University Medical Faculty
aaynur@erciyes.edu.tr

Aliye Esmaoğlu
Prof., M.D.
Department of Anesthesiology and Reanimation
Erciyes University Medical Faculty
ealiye@erciyes.edu.tr

Recep Aksu
Assist. Prof., M.D.
Department of Anesthesiology and Reanimation
Erciyes University Medical Faculty
raksu@erciyes.edu.tr

Işın Güneş
M.D.
Department of Anesthesiology and Reanimation
Erciyes University Medical Faculty
isingunes@yahoo.com

Sümeyra Türk
M.D.
Department of Anesthesiology and Reanimation
Erciyes University Medical Faculty
smyr_turk@yahoo.com

Abstract
Intermediate syndrome with delayed distal polyneuropathy is an uncommon clinical condition due to organophosphates following accidental or suicidal exposure. Features of intermediate syndrome develop 24 to 96 h and delayed distal polyneuropathy develops 7-12 days postingestion. We describe a case of intermediated syndrome with delayed polyneuropathy that occurred in a 54 year-old, female patient after exposed to chloropyrifos. Patients who recover from initial acute cholinergic crisis should be closely monitored for the development of delayed distal polyneuropathy.

Key words: **Chlorpyrifos; Polyneuropathy**

Özet
Distal nöropati ile ilişkili intermediate sendrom , organofosfatlara kazara veya intihar amaçlı maruz kalma nedeniyle görülen nadir bir klinik durumdur. İntermediate sendrom tipik olarak 24-96 saat içinde gelişir ve distal nöropati alımdan sonra 7-12 gün içinde gelişir. Bu yazıda kloroprifosa maruziyetinden sonra polinöropati ile ilişkili intermediate sendrom gelişen 54 yaşında bayan sunulmuştur. Bizim rapor ettiğimiz hastada olduğu gibi akut kolinerjik kriz tablosuyla gelen hastalarda distal polinöropati gelişmesi açısından yakın monitörizasyon ile takip gerekir.

Anahtar kelimeler: **Kloroprifos; Polinöropati.**

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Corresponding Author:
Doç. Dr. Aynur Akın
Department of Anesthesiology and Reanimation
Faculty of Medicine University of Erciyes
Kayseri, Turkey

Telephone : +90 - 352 4374937-24039
E-mail : aaynur@erciyes.edu.tr

Introduction

Acute organophosphate poisoning is a significant cause of morbidity and mortality in Turkey and developing countries (1). Acute manifestations include miosis, salivation, lacrimation, sweating, pulmonary edema, bradycardia or tachycardia, muscle weakness with fasciculations and changes in mental status (2). Intermediate syndrome (IS) with delayed distal polyneuropathy is an uncommon clinical condition due to organophosphates following accidental or suicidal exposure. Even though the etiology of IS is unknown, there are numerous theories about this life threatening condition. These are inadequate oxime therapy, induced organophosphates and desensitization of pre-and postsynaptic acetylcholine receptors (3-6).

We are reporting a case who had intermediate syndrome and delayed polyneuropathy occurred after being exposed to chloropyrifos. We also aimed to discuss the clinical features of this uncommon condition.

Case Report

A 54year-old, unconscious, female patient was brought to our hospital by her relatives, following oral intake of a high dose of chloropyrifos. In a suicide attempt she had taken 100 cc commercial formulation of chloropyrifos (480 g/L) four hours before the admission to the hospital. On admission, the patient was comatose, unresponsive to deep pain. Fasciculation of the eyelids and lips, twitching of the extremities, hypersalivation and miosis were noted. Heart rate was 60/min, blood pressure was 110/60 mmHg. Her complete blood count, biochemical parameters, chest radiography and electrocardiogram were normal. Plasma pseudocholinesterase activity was 350 U/I (normal, 4000 to 12600 U/I). An endotracheal tube nasogastric tube and gastric lavage were performed. The loading dose of pralidoxime was 30 mg/kg delivered over half an hour then administered at 2 g a day divided into four doses. A continuous infusion of atropine was started at 0.02-0.08 mg/kg per hour and activated charcoal was performed. The patient presented respiratory fatigue followed by respiratory insufficiency, and mechanical ventilation was required. On the 3rd day secretions decreased, muscle tone improved and endotracheal tube was removed. However; on the 9th day of hospitalization severe stridor and respiratory distress began. Reintubation was accomplished with difficulty without upper airway edema and required mechanically ventilated.Therapy with pralidoxime was discontinued after 12 days. The patient was able to be weaned from the ventilator on 23th day. Left vocal cord paralysis was recognized during direct laryngoscopy on day 23. The neurological examination revealed distal motor deficit in upper and lower limb (1/5, 3/5) and Achilles tendon reflex was absent. Babinski sign was not observed. Cranial nerves were not involved. Hypoesthesia and pain were present at bilaterally lower limbs. Electromyography demonstrated an absence of voluntary motor units. The findings were consistent with a predominant motor axonal polyneuropathy involving mostly the lower limbs. She was treated with gabapentin (600 mg/d), thiamin (300 mg/d) and physiotherapy, which resulted in a partial control of the pain.

Discussion

Organophosphate esters are used as insecticides, petroleum additives, modifiers of plastics, antioxidants and flame-retardants (7). On the other hand, half of the admissions to emergency services with acute poisoning are due to organophosphates following accidental or suicidal exposure. Three well defined clinical phases has been described in organophosphate poisoning: acute cholinergic crisis, the intermediate syndrome and delayed polyneuropathy (OPIDP) (7, 8). After ingesting chloropyrifos, our patient presented all symptoms of the three phases of intoxication. Although, the treatment was continued, the patient had a relapse of acute cholinergic crisis at day 4. The acute poisoning phase was followed by an intermediate syndrome and delayed distal polyneuropathy.

The clinical findings of acute cholinergic crisis are a mixture of muscarinic effects resulting from the excitation of postganglionic parasympathetic activity, nicotinic effects resulting from accumulation of acetylcholine at neuromuscular junctions and consequent depolarization and central nervous system effects causing initial excitation and subsequent inhibition of all central nervous activity (8). Acute manifestations include miosis, salivation, lacrimation, sweating, pulmonary edema, bradycardia or tachycardia, muscle weakness with fasciculation and changes in mental status (2).

Intermediate syndrome is characterized by respiratory paralysis, proximal muscle weakness, and motor cranial nerve palsies. It was first described by Senanayake and Karalliedde in 1987 (9). Its incidence in different studies has been reported to be between 20-68% (10) This

syndrome has been shown to be commonly associated with organophosphorous compounds like diazinon, dimethoate, methylparathion, methamidaphos, monocrotophos, fenthion and ethylparathion. It develops 12-96 hours after exposure and reflects a prolonged action of acetylcholine on the nicotinic receptors. Prolonged suppression of the enzyme acetylcholinesterase is seen during this stage (8).

Kusu et al (11) reported that plasma pseudocholinesterase levels markedly decrease during organophosphate poisoning. Plasma pseudocholinesterase activity was found low in our patient and began to rise after 45th day of ingestion and reached 2301 U/L at the end of second month.

Organophosphate induced delayed polyneuropathy occur in after a period of 7-21 days of exposure and causes significant morbidity. Clinical manifestations characterized with a distal, symmetric, predominantly motor polyneuropathy. Foot drop, weakness of the intrinsic hand muscles, absent ankle jerks and weakness of hip and knee flexors were seen. There may be signs of pyramidal tract and central nervous system involvement. Functional recovery can take place, but residual deficits commonly remain. OPIDN is common following exposure to organophosphate compounds which have weak anticholinesterase activity such as chloropyrifos and triorthocresylphosphate. However, following exposure to the presently available organophosphate compounds which have strong anticholinesterase activity, it is distinctly uncommon (3,7,8). Our patient showed left vocal cord paralysis, muscle weakness, foot drop, and urinary incontinence. Although it is uncommon in OPIDN, Aiuto et al (2) described persisted bilateral recurrent laryngeal nerve paralysis resulting in paralysis of the vocal cords as a delayed complication in organophosphate poisoning in 1993.

In conclusion, we described a case who was exposed to chloropyrifos and had all three phases of organophosphate intoxications. We recommend that all patients who exposed to low toxicity organophosphates and had manifestations of IS should be monitored for the development of OPIDN.

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