Two Serious Complications of Organophosphate Poisoning in the Same Patient: Acute Pancreatitis and Late-Onset Polyneuropathy: Case Report

Organofosfat Zehirlenmesinin Aynı Hastada Görülen İki Ciddi Komplikasyonu: Akut Pankreatit ve Geç Başlangıçlı Polinöropati

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ABSTRACT Organophosphorus compounds and carbamates are cholinesterase inhibitors which are widely used as pesticides and insecticides. There is an increased risk for accidental human intoxication among farmers and their families. Acute pancreatitis and late onset polyneurophaty are rare and serious side effects of organophosphate poisoning. A 13-year-old farmer's boy was taken to the hospital after playing around and eating fruits in a field which has just been applied pesticide. He was hospitalized with vomiting and loss of consciousness. The case was diagnosed as acute pancreatitis which can be obscured by severe systemic effects of organophosphate poisoning. Three weeks later he was admitted to hospital again and diagnosed with organophosphate-induced delayed polyneuropathy.

Key Words: Poisoning; pancreatitis; polyneuropathies

ÖZET Organofosfat ve karbamatlar, sık kullanılan pestisid ve insektisitlerden olup kolin esteraz inhibitörleridir. Özellikle çiftçi ve ailelerinde kazayla alım nedeniyle intoksikasyon riski yüksektir. Akut pankreatit ve geç başlangıçlı polinöropati, organofosfat zehirlenmesinin nadir görülen ciddi komplikasyonlarıdır. Kusma ve bilinç kaybı şikâyetleri ile hastaneye getirilen 13 yaşındaki erkek çocuğun pestisid ile ilaçlanmış bir meyve bahçesinde dolaşıp, ilaçlanmış meyvelerden yediği öğrenildi. Olgu organofosfat zehirlenmesinin ağır sistemik etkileri tarafından maskelenmiş olan akut pankreatit tanısı ile yatırıldı. Üç hafta sonra tekrar hastaneye başvuran olguda bu kez organofosfat zehirlenmesinin neden olduğu geç başlangıçlı polinöropati gelişti.

Anahtar Kelimeler: Zehirlenme; pankreatit; polinöropati

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Organophosphate (OP) and carbamate insecticides are widely used in commercial agriculture and home gardening.[1] They are absorbed through the skin, lungs and gastrointestinal tract, distributed widely in tissues and slowly eliminated by hepatic metabolism; and thereafter they act by inhibiting the enzyme acetyl cholinesterase, causing an increase in acetylcholine activity at nicotinic and muscarinic receptors.[2,3] OP poisoning can occur in a variety of situations which can be accidental or suicidal. There is an increased risk for accidental human intoxication among farmers and their families. Acute pancreatitis and late-onset neuropathy are rare complications of OP poisoning.

CASE REPORT

A 13-year-old farmer's boy was taken to the hospital after playing around and eating fruits in a field which has just been applied with parathion-methyl (Folidol M-35 Bayer®) as pesticide. He was presented with vomiting and loss of consciousness. He was hospitalized in our pediatric intensive care unit. Physical examination revealed a heart rate of 98 beats per minute, a blood pressure of 115/78 mmHg and a body temperature of 38.3°C. He had miosis, fasciculations, hypersalivation and excessive sweating. Results of his initial laboratory studies were as follows: blood glucose, 247 mg/dL; sodium, 143 mmol/L; potassium, 3.1 mmol/L; blood urea nitrogen, 18 mg/dL; creatinine 0.6 mg/dL; haemoglobin, 12.3 g/dL; and platelet count, 282.000/mm^3. Complete blood count showed an elevated white blood cell (WBC) count (28 x 10^9) with neutrophil predominance (82%). The initial liver function tests and blood gas analysis were normal. Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels were elevated (42 mm/h and 2.3 mg/dL) while pseudo cholinesterase level was low (1.3 kU/L). On admission, gastric lavage was performed and activated charcoal was given via nasogastric tube. The patient's contaminated clothing was removed and exposed areas were washed with soap and water. Three grams of atropine was given until atropinization was achieved and 1.2 g pralidoxime was given until nicotinic symptoms were resolved. The patient became conscious in the first 15 hours. After 30 hours of hospitalization he suffered from epigastric pain and bilious emesis. The findings of abdominal CT were enlargement of the corpus and the tail of the pancreas, peripancreatic exudation and thickening of the anterior pararenal fascia (Gerota's fascia) (Figure 1 and 2). These findings were associated with the high serum levels of amylase, lipase, aspartat aminotransferase (AST), and alanine aminotransferase (ALT).

Patients was treated with parenteral volume replacement, cefotaxime (2 g/day, i.v) and somatostatin (6 mg/day)infusion. Somatostatin infusion continued for two days. Five days later, the level of pseudo cholinesterase and the liver function tests returned to normal (Table 1). The patient was discharged with normal amylase and lipase levels after 10 hospital days.

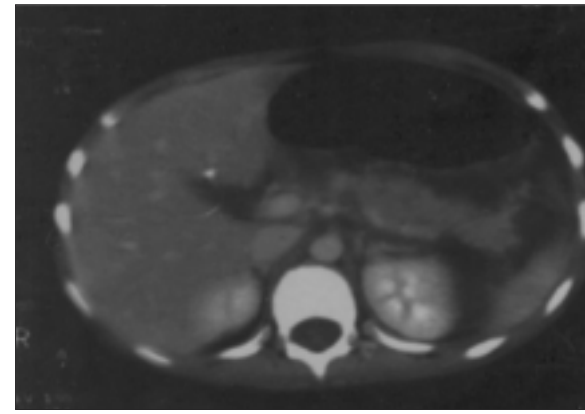

FIGURE 1: Enlargement of the pancreas and peripancreatic edema.

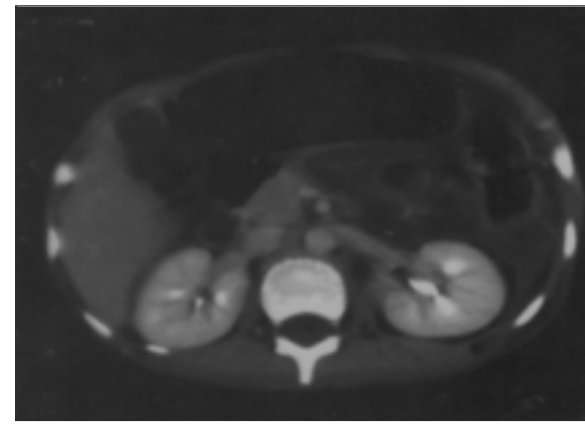

FIGURE 2: Gerota's fascia is thickened and peripancreatic exudation.

However, approximately three weeks later he was admitted to the hospital with difficulty in walking and sensory loss in foot fingers. Neurological examination revealed bilateral dropped foot, absent Achilles tendon reflexes and sensory impairment of peripheral type in the lower extremities particularly in foot fingers. There was no deep sensory involvement. Muscle strength was normal in upper extremities and 3/5 in lower extremities and cranial nerve involvement was not determined. Electromyographical examination demonstrated symmetrical sensory-motor polyneuropathy with

TABLE 1: Laboratory values on admission and 5 days later.

	Units	Reference range	On admission	After 5 days
WBC count	x 10^9 L	3.4-10	28.5	12.4
Neutrophil count	x 10^9 L	2.2-8.6	23.4	9.9
Amylase	U/L	27-102	512	127
Lipase	U/L	8-57	143	76
Pseudocholinesterase	kU/L	7-19	1.3	7.8
AST	IU/mL	5-40	124	24
ALT	IU/mL	5-40	92	36

significant distal axonal degeneration in the lower extremities. The other system examination and laboratory findings (e.g. complete blood cell count, blood glucose, electrolytes, urinalysis, liver and renal function tests) were found to be normal. The patient was subjected to the a physiotherapy program. Clinical and neurological examination findings resolved without any sequelae at the end of the 6th month.

DISCUSSION

Every year three million people in the world suffer from intoxication due to organophosphate compounds and approximately 220.000 of them die. Though the number of children exposed is likely to be greater, awareness of the dangers of pesticides is less in developing countries .[4]

Organophosphates which are absorbed through the skin, lungs and gastrointestinal tract. They widely distribute to the tissues and eliminate by hepatic metabolism. The diagnosis of OP toxicity is based on clinical findings. The measurement of cholinesterase activity confirms the OP poisoning. However, cholinesterase levels do not always correlate with severity of clinical illness.[5] Monitoring of RBC and plasma cholinesterase levels is recommended before and during therapy.[2,6]

The prevalence of pancreatitis in OP poisonings ranged is 0.59-12.7%.[6,7] The diagnosis of acute pancreatitis can be obscured by the systemic effects of OP toxicity. The diagnosis of acute pancreatitis is usually established by the detection of increased level serum amylase values threefold or more above normal and elevated level of serum lipase. The pancreatic enzyme elevations are very modest for acute pancreatitis and hyperamylasemia is well reported after OP poisoning arising from salivary gland hyperstimulation.[6] Serum amylase and lipase elevation with the imaging findings confirmed the diagnosis of acute pancreatitis in our patient.

In addition to clinical manifestations caused by peripheral nicotinic and muscarinic effects, central nervous system (CNS) can be effected. CNS poisoning may cause agitation, seizures and coma. The intermediate syndrome is probably caused by prolonged over stimulation of the neuromuscular junction and may be associated with inadequate oxime therapy. Patients may develop proximal muscle weakness over a few days even after resolution of the acute cholinergic crisis. Firstly neck weakness is observed, and then proximal limb weakness and cranial nerve palsies occur. However some cholinesterase inhibitors may cause a delayed, often permanent peripheral neuropathy.[2]

Several OP compounds additionally lead to polyneuropathy by a different route such as inhibition of neuropathy target esterase (NTE). However the inhibition of NTE is not enough for the development of neurotoxicity.[4] In experimental trials it was demonstrated that phosphonate, carbamate and sulfonate inhibited NTE 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.[6] 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.[8,9] 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.[10] The onset may be delayed with the chronic exposure.[11] Cramps in legs are the common initial symptoms. Subsequently distal paresthesia and sensory loss, and progressive weakness at the lower extremities occur and deep

tendon reflexes become hypoactive.[12] Sensory loss is mild in general. Occasionally mild pyramidal findings may accompany the clinical presentation.[13] The initial neurological symptoms in our case were gait disturbance and sensory loss at food fingers which was respectively manifested 3 weeks after the acute exposure. Electrophysiological studies demonstrated distal, symmetrical sensorymotor polyneuropathy particularly at the lower extremities. In our patient, the neurologic and electrophysiological findings were limited to the lower extremities. This is perhaps because long fibbers with broader diameters are more susceptible than the narrow and short ones.

Late-onset polyneuropathy caused by OP compounds is diagnosed by history and clinical findings.[4,14] There is no specific therapy for the late-onset polyneuropathy due to OP compounds but physiotherapy may be effective.[15] Prognosis is variable. Peripheral nerve destruction may cause atrophy and dropped foot. Generally, severity of the pyramidal involvement predicts the prognosis. In our case physical examination findings and electrophysiological studies demonstrated that distal symmetrical sensory motor polyneuropathy occurs at the lower extremities. This is a possible finding for the late onset polyneuropathy due to OP poisoning. The patient was taken under a physiotherapy program. His clinical findings showed no progression.

Two serious complications of OP poisoning, both acute pancreatitis and late-onset distal polyneuropathy, developed in this case; and it is further reason why this case is presented as an example in this document.

In the countries where economies are based on agriculture, exposures due to OP insecticides are common. The diagnosis of acute pancreatitis can be masked by the severe systemic effects of OP poisoning. Therefore since appropriate treatment could be life-saving in OP poisoning cases, importance should be given to acute pancreatitis. In addition to acute cholinergic toxicity, late onset polyneurophathy should be considered and patients and families must be informed about chronic toxicity. Patients who recover from serious OP intoxications should be closely monitored for acute pancreatitis and the development of OP-induced delayed polyneuropathy.

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