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Olgu Sunumu / Case Report

Alcohol Withdrawal Mimicking Organophosphate Poisoning

Organofosfat Zehirlenmesini Taklit Eden Alkol Yoksunluğu

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ABSTRACT

Organophosphates are widely used insecticides in southern Turkey which can cause occupational poisoning due to inappropriate personal protective measures. Therefore, the classical clinical findings of this cholinergic poisoning which are myosis, excessive secretions, bradicardia and fasciculations are easy to be recognized in our region. Diseases and conditions related to alcoholism such as mental and social impairments, coma, toxicity, withdrawal, and delirium are frequent causes of emergency visits of patients. Here we present a case diagnosed and treated as organophosphate poisoning although it was an alcohol withdrawal in the beginning and became delirium tremens due to overlooking.

Key Words: Alcohol withdrawal, delirium tremens, organophosphate, poisoning.

ÖZET

Kişisel koruyucu önlemler alınmadığında mesleki zehirlenmeye neden olabilen organofosfatlar, Türkiye'nin güneyinde oldukça sık kullanılan insektisitlerdir. Bu nedenle bizim bölgemizde tanınması kolay olan bu kolinerjik zehirlenmenin klasik klinik bulguları, miyozis, sekresyonlarda artma, bradikardi ve fasikülasyonlardır. Alkolizme bağlı mental ve sosyal uyumsuzluk, koma, zehirlenme, yoksunluk ve deliryum gibi hastalık ve durumların birçoğu sık acil servis başvurularının nedenleridir. Burada atlandığı için organofosfat zehirlenmesi tanısı ile takip ve tedavi edilirken deliryum tremense ilerleyen bir alkol yoksunluğu olgusu tartışılmıştır.

Anahtar Kelimeler: Alkol yoksunluğu, deliryum tremens, organofosfat, zehirlenme

INTRODUCTION

Organophosphate (OP) insecticides are over the counter chemicals that are frequently used in agriculture, animal care and pest control in living areas in Turkey. Poisoning with OPs is not difficult to diagnose when patients have the history of exposure in any route with the obvious physical findings such as fasciculation, diaphoresis, bradicardia, myosis, and other cholinergic manifestations. Alcohol consumption is one of the frequent habits1 which needs to be questioned while obtaining clinical history of any patient since alcohol intoxication or withdrawal may mimic serious conditions in the ED as well as these two entities may be misdiagnosed. Here we present a case diagnosed and treated as OP poisoning with proper history of exposure because of similar clinical manifestations although it was an alcohol withdrawal.

CASE

A-60-year-old farmer admitted to emergency department (ED) of a university based hospital with the complaints of nausea, perspiration, shivering

and fatigue 3 hours after spraying OP insecticide in a farm. He added he had discomfort after smelling the sour smell of the insecticide and curious about being poisoned. His past medical history included hypertension, nephrolithiasis and prostate hypertrophia with ongoing antihypertensive medication and a scheduled prostate operation. He was asked about the habits, alcohol consumption and smoking were noted without frequency and amounts. The initial physical examination of the patient revealed diaphoresis and fasciculation of the tongue with a Glascow Coma Scale score of 15. His initial vital signs were: Blood pressure: 140/80 mmHg, pulse rate: 96/minute, body temperature (axillary): 36,9 oC, respiration rate: 22/minute, O2 Saturation by pulse oxymetry: %98. His clothes were removed, his body was rinsed with soap and washed to decontaminate and 2 mg atropin intravenously (IV) was given to dry mucous membranes. The serum pseudocholinesterase level was 2,3 KU/L (normal value: 4.9-11.9 KU/L), so he was started additional atropin as daily infusion (5 mg/day) and 1400 mg PAM as antidote. He was taken to observation room where his urine output, cardiac rhytm and pulse oxymetry monitorizations were performed. The haematologic and biochemical tests revealed no abnormality except high MCV (Tables 1 and 2). Diaphoresis became obvious again on the second day and his atropin infusion dose was doubled. He experienced delirium which was attributed to atropin, he took out his foley catheter, was agitated and aggressive with rapid, insulting and scurrilous speech, so his atropin infusion was stopped. The patient's pulse rate was 100-110/minute with no new neurological signs, no screened fewer or blood pressure changing. On the 3rd day of hospitalization, sedation with benzodiazepines was planned, but was unsuccessful despite recurrent doses of midazolam then haloperidol (5 mg IV) was given. His diaphoresis and spitting on people around made us to think cholinergic manifestations of OP poisoning because of low serum pseudocholinesterase level, thus atropin was given again. He had no other findings such as decreased pulse O2 saturation, pulmonary edema, respiratory deppression or diarrhea that made us to reassess the diagnose of OP poisoning. Paroxysmal screaming and fluttering were added to clinical findings on the 4th day although atropin was stopped. A CT scan of the cranium in which no abnormality was found and blood tests for metabolic parameters that are completely normal were performed to rule out intracranial lesions, infections (ie.encephalomyelitis) and other metabolic causes of delirium. It was difficult to manage the patient's agitation, midazolam, thiopental sodium and haloperidol one by one and in combination were uneffective to sedate, then haloperidol and chlorpromazine combination was tried and succeeded. On the 5th day of hospitalization, with ongoing sedation and anxiolysis there was a decrease in serum pseudocholinesterase level with no clinical worsening in cholinergic signs, he had tachycardia, hypertension (blood pressure: 160/90 mmHg, pulse rate: 120-130/minute) with a long QT interval that was thought to be anticholinergic effects of atropine, haloperidol and chlorpromazine and was corrected with NaHCO3 infusion for 5 hours. There was a decrease in agitation and involuntary movements. He was totaly awake, cooperated, able to eat and talk on the sixth day when it was noticed that he had tremors on hands. He was asked about alcohol consumption frequency and amount, the answer was "I consume for nearly 40 years, everynight and day for the last couple of years, but the last night before poisoning I did not drink since I was trying to give up.".

The patient was started thiamin and multivitamine replacement. He was willing to be discharged before physchiatry consultation. He was discharged with recommendation for admitting to a clinic for treatment of substance addiction.

Table 1. Haematologic parameters of the patient.

	On admission	Control (Day 2)
WBC (4.3-10.3 µL)	7400	8200
Hgb (13.6-17.2 g/dL)	14.5	14.3
Hct (39.53-50.33 %)	42.1	42.6
MCV (80.7-95.5 fL)	98.2	99.2
Plt (156-373.3 uL)	274000	256000
PT (11-15 sn)	11.3	12.0
INR (0.85-1.2)	0.98	0.99
aPTT (22-34.6 sn)	19.2	20.1

aPTT: Activated partial thromboplastin time, **Hct:** Hematocrit, **Hgb:** Hemoglobin, **INR:** International normalization ratio, **MCV:** Mean corpuscular volume, **Plt:** Platelet, **PT:** Prothrombin time, **WBC:** White blood cell, **(-):** not repeated

Tablo 2. Biochemical parameters of the patient.

	Day 1	**Day 2**	**Day 3**	**Day 4**	**Day 5**	**Day 6**
Glu (70-105 mg/dL)	92	-	-	-	73	-
AST (0-40U/L)	17	-	-	-	-	-
ALT (0-40U/L)	14	-	-	-	-	-
T.Bil. (0-1 mg/dL)	0.5	-	-	-	-	-
D.Bil.(0-0.2 mg/dL)	0.1	-	-	-	-	-
BUN (8-25 mg/dL)	8	-	14	16	13	10
Cr (0.9-1.3 mg/dL)	0.62	-	0.81	0.73	0.67	0.5
Na (135-145 mmol/L)	138	-	139	137	143	139
K (3.5-5.1 mmol/L)	4.5	-	3.8	3.7	3.7	3.4
PcHE (4.9-11.9 KU/L)	2.3	2.2	2.3	2.1	2.0	1.8

ALT: Alanine transaminase, **AST:** Aspartate transaminase, **BUN:** Blood urea nitrogen, **CPK:** Creatine phosphokinase, **CK-MB:** Creatine phosphokinase MB isoenzyme, **Cr:** Creatinin, **D.Bil.:** Direct Bilirubin **Glu:** Glucose, **K:** Potassium, **Na:** Sodium, **PcHE:** Pseudocholinesterase, **T.Bil.:** Total Bilirubin, **Tr-T:** Troponin-T, **(-):** not repeated.

DISCUSSION

Alcohol withdrawal is a serious clinical entity that is sometimes fatal because of misdiagnoses. The neurotransmitter level alterations (enhance in excitators and reduction in inhibitors) result in cognitive, sensorial and autonomic function impairments in an individual who abruptly stops or reduces his drinking after a heavy and prolonged alcohol consumption[2]. It is not a rule to experience withdrawal since this do not happen to all heavy drinkers when they do stop drinking. DSM-IV-TR criteria for the diagnosis of alcohol withdrawal and alcohol withdrawal delirium is used and two or more of the symptoms among those described must be present to meet the diagnostic criteria[3]. The symptoms may vary due to the time passed after last drink. In a chronic heavy drinker who does not drink for 6-36 hours mild withdrawal symptoms includes hand tremors, headache, mild anxiety, loss of appetite, diaphoresis, tachycardia, nausea and vimiting may be seen[4]. As alcohol-free-interval gets longer generalized tonic-clonic seizures and status may be added. While withdrawal lasting 12-48 hours may cause hallucinations, those lasting 48-96 hours may cause “delirium tremens” which is characterized by acute and fluctuating disturbances such as tachycardia, hypertension, agitation, fever, diaphoresis, hallucinations and delirium[5]. Patients may develop life-threatening electolyte, metabolic and fluid imbalances. Co-morbidities such as hypoglycemia, toxic alcohol ingestion, pneumonia, urinary tract infections, sepsis, intracranial hemorrhagias, meningitis, trauma, pancreatitis, hepatitis, gastrointestinal bleeding, hypertension may cause or facilitate delirium and morbidity from it as well[6].

The main aim of the treatment is to cease the symptoms of alcohol withdrawal, to prevent serious and fatal complications and to keep the patient awake and cooperative[4]. Thus a-long active benzodiazepine[7] to substitute alcohol and supportive care are needed. The main steps include IV crystalloids for hydration and dextrose for hypoglycemia, 100 mg IV thiamin for 3 days, 1 mg/day folate and multivitamin replacements. The presence and severity of seizures, agitation and delirium influence the type of anxiolytic and antipsychotic used. Sometimes combination of two or more drugs is needed to sedate patient properly. The first choice is chlordiazepoxide 25-100 mg orally or 1-4 mg lorazepam oral/sublingual/IV/IM 4-6 times a day. Chlordiazepoxide is preferred over lorazepam because of its long half-life in patients with smoother withdrawal clinic where lorazepam is preferred in those with hepatic failure-metabolism is not hepatic dependant. The parenteral administration availability of lorazepam makes it safer to use in those with aspiration pneumonia risk who can not take oral medications due to altered mental status. Lorazepam is also preferred in patients who received the maximum dose of chlordiazepoxide (600 mg/day) but sedation was not achieved. Propofol is also an agent to be used for patients refractory to high doses of benzodiazepines[8]. Haloperidol is a better choice than repeated doses of benzodiazepines in patients presenting primarily with agitation, disorientation or hallucinations without autonomic dysfunction[9].

OP compounds are widely used insecticides in agriculture, animal care and living areas for pest control. OPs bind to and inhibit the enzyme acetylcholinesterase (which breaks down acetylcholine to acetic acid and cholin) irreversibly, resulting in accumulation of acetylcholine in synapses and neuromuscular junctions[10]. Nicotinic manifestations of poisoning are fasciculation, muscle weakness, hypertension and tachycardia where muscarinic manifestations are result of parasympathetic activity in all smooth muscles (exocrin glands, gastrointestinal trunk, bladder, etc.) causing secretions and bradycardia. The dominance of any nicotinic or muscarinic effects

determines the clinical manifestation and severity of poisoning. Acutely poisoned patients may have anxiety, insomnia, emotional lability, jerks, headache, dizziness, confusion, delirium and hallucinations. Depression of respiration and circulation may result in coma. Muscarinic effects are usually dominant and many patients experience salivation, diaphoresis, lacrimation, urinary incontinence, diarrhea, emesis and bradycardia. Tachycardia, mydriasis, hypertension and palor may also be clinical findings due to adrenergic stimulation. Bronchospasm, bronchorrhea, hypoxemia, tachycardia and myosis are parasympathetic effects. Bronchorrhea and respiratory muscle paralysis may result in death unless proper treatment and care are given. The diagnose is based on clinical findings. Serum pseudocholinesterase level (PcHE) is indicative but not equally valuable as erytrocyte cholinesterase which is not essayed in routine laboratory studies. Although low PcHE level is poor prognostic in organophosphate poisoning, it is not an indicator of atropine treatment dosing or mechanical ventilation support necessity. PcHE levels may be low in patients with cronic exposure, genetic disorders, cronic diseases, hepatic failure, cirrhosis, malnutrition, low serum albumine, neoplasias, infections and pregnancy[11].

Treatment of OP poisoning includes spesific antidotes and supportive measures[10-12]. Atropine is given to resolve muscarinic manifestations where oximes are antidote of nicotinic effects. Pralidoxime (2-PAM) is the most preferred oxime that has to be given immediately before aging (completion of irreversible phosphorilation of acetylcholinesterase). The dose regimen of atropine depends on the patient. It is usually given as intravenous boluses repeatedly until all secretions are dried out. If frequent boluses are needed, intravenous infusion of atropine is also preferred. The initial dose of atropine is 0.05-0.1 mg/kg, but there are many poisoned patients received hundreds of miligrams of atropine to manage secretions. Pralidoxime is given as intravenous infusion over 30 minutes at a dose of 20-40 mg/kg in normal saline and may be repeated within 4-6 hours period. Hydration, nutrition, benzodiazepines for agitation and seizures, mechanical ventilation support and extracorporeal methods such as plasmapheresis hemoperfusion and hemodialysis may be added to treatment if needed[13,14].

In the patient above, although proper medical treatment of OP poisoning was initiated, clinical improvement was not satisfying since neurologic and behavioral detoriation occured. Obtaining past medical history including habits, allergies and substance addiction is extremely important in the management of patients. It is sometimes difficult to get medical data of intoxicated patients in emergency clinics because of depressed conciousness or unwilling to tell adequate and true medical histories. But as in our patient, although being informed of alcohol consumption, overlooking the real diagnose among other possible differential diagnoses is easy if clinican focuses on a spesific diagnose.

Organophosphates are widely used insecticides and misused in suicide attempts in our region. These compounds are also responsible for accidental poisoning since exposures happen among farmers or any other farm workers. The patient had admitted with the suspicion of poisoning, and decreased PcHE levels might have let clinician to diagnose OP poisoning without revising other possible diagnoses. Overlooking withdrawal caused not initiating proper treatment such as benzodiazepines and thiamine supplement that ended with delirium. The nonspesific complaints of the patient including of nausea, perspiration, headache and fatigue also fulfills the diagnose of mild alcohol withdrawal as well as OP poisoning. Fasciculation and perspiration may be seen in OP poisoning, but not spesific for. Neuromyotonia, diseases of the lower motor neuron, magnesium deficiency, myalgic

encephalomyelitis, rabies, benzodiazepine and alcohol withdrawals are other causes of fasciculation[15]. Excessive perspiration or diaphoresis is a nonspesific finding, may be seen normally in a hot weather or in a cholinergic overstimulation process such as OP poisoning. Other abnormal causes of diaphoresis are hyperthyroidism, hypoglicemia, shock, drugs such as caffeine, morphine, alcohol, certain antipsychotics, sympathetic nervous system stimulants such as cocaine and amphetamines, pheochromocytoma, hearth attack, serotonin syndrome, neuroleptic malign syndrome, infections such as malaria and tuberculosis. Even leukemia may cause diaphoresis. Withdrawal from alcohol and benzodiazepines or narcotic painkillers in dependent patients may also cause diaphoresis[15]. Chronic exposure of OP compounds may cause low serum PcHE levels[11]. As it is in our patient, alcoholism, malnutrition and chronic OP exposure are causes of low serum PcHE levels.

Alcohol consumption anamnesis of the patient was obtained but frequency, amount and alcohol free interval were not asked. After the full recovery of the patient, remarkable hand tremours made us to investigate alcohol addiction so having not drinken the previous night of hospitalization was learned. During delirium state, he was evaluated for intracranial pathologies such as encephalomyelitis and for other metabolic reasons of delirium. He was given benzodiazepines, haloperidol and chlordiazepoxide one by one and in combination to be sedated. Before delirium tremens was diagnosed, he was not started thiamine. In medical schools, we are taught to ask, learn and assess the medical histories of patients, habits and drug abuses, addicitons and allergies. Anyone can not find out something that he does not look for. If we have doubts about diagnoses, then we will investigate more. Or if we are certain, then start treatment and wait for clinical recovery. It is the low PcHE levels with diaphoresis and fasciculation of the tongue that made emergency resident to misdiagnose the case as OP poisoning. There will be a tendancy to overdiagose if any diseases are seen widely in an area and differential diagnoses are not checked scrupulously. OPs are widely used in our city and accidental poisonings are common among farmers. Intentional poisonings are also frequently seen in our clinic. Anyone can argue that it was really a poisoning. Since we can not assay erhytrocyte cholinesterase, low PcHE levels and clinical findings support this diagnose. In that situation, our conclusion will be the time interval after hospitalization caused first withdrawal then delirium since the patient did not drink alcohol during hospitalization and as time passed thiamine deficiency and prolonged alcohol free interval caused delirium.

In conclusion, it is wise to evaluate a patient entirely. When clinical recovery is delayed, revising possible diagnoses is essential. The possibility of misdiagnose and overlooking comorbities may be detrimental. Any patient should be evaluated again and again regarding past medical histories, habits, drug addictions and allergies. Alcohol withdrawal is extremely important and may mimic many other conditions. If overlooked, diagnostic confusions may let fatalities due to delirium tremens.

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