The combination of acute pancreatitis and toxic hepatitis developing secondary to exposure to malathion : a case report

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Abstract

Organophosphate(OPH) compounds are cholinesterase-inhibiting chemicals used as pesticide. Pancreatitis secondary to malathion toxicity is rare and toxic hepatitis has been reported in only one case. In this paper, we report the case of the combination of acute pancreatitis and toxic hepatitis, which developed in a 30-year old farm worker and the mechanism is discussed in this first report of its kind. Awareness of this complication should prompt earlier investigation because early diagnosis coupled with timely therapeutic measures may improve patient prognosis. (Acta gastroenterol. belg., **2018**, 81, **333-335**).

Key words : malathion, organophosphate, pancreatitis, toxic hepatitis

Introduction

Organic phosphate compounds (organophosphates) are the most widely used pesticide group and constitute more than 80% of the pesticides in use worldwide (1). According to World Health Organisation (WHO) data, there are approximately 3 million cases of pesticide poisoning per year, and of these 220,000 result in death. Although there are regional differences, organophsphate (OPH) poisoning is frequently seen in Turkey. According to 2008 data of the National Poison Consultation Centre, 8% of all cases of poisoning were of pesticide origin (2).

Malathion (ML) (O,O-dimethyl-S-1.2-bis ethoxycarbonyl ethyl phosphorodithioate), as a compound with OPH, is a widely used form of pesticide especially in agricultural countries battling with insects (3). In ML intoxication, an accumulation of acetlycholinesterase (ACHE) in the post-synaptic spaces causes overstimulation in post-synaptic receptors and associated with this, persistent stimulations occur in skeletal muscle, the central nervous system (CNS) and the autonomic nervous system (ANS) (4). Following exposure to ML, apart from cholinergic and muscarinic symptoms, occasional cases of acute pancreatitis have been seen, but to the best of our knowledge there have been no reported cases of toxic hepatitis in humans. All the available data have come from a limited number of animal experiments (5-7). To date, there has only been 1 reported case of toxic hepatitis related to agricultural OPH insecticides and the substance in that case was parathion.

In this paper, a case of toxic hepatitis is presented, which was seen together with pancreatitis that developed secondary to ML intoxication.

Case

A 30-year old male presented at the Internal Diseases polyclinic with complaints of nausea, headache, lethargy, fatigue, abdominal pain striking the back, and diarrhoea, which had been ongoing for 3 days. There was a strong anamnesis of exposure to agricultural pesticides. The patient was a farm labourer and 2 days previously had been engaged in applying pesticides. The complaints started immediately after the pesticide application process and it was learned that the necessary protective measures had not been taken during the process. The pesticide packaging was requested and it was determined that the patient had been exposed to a type of OPH pesticide containing ML. The patient had no history of alcohol consumption and no chronic disease or related medication use. Within the previous 12 months, the patient had taken no analgesic or anti-inflammatory drugs, had no blood transfusion, no contact with jaundice and no tooth extraction. In a general check-up 3 months previously, the liver function test results of the patient were normal.

The vital signs of the patient were body temperature:37.3ºC, pulse:62 bpm, blood pressure:115/70 mm/hg. In the physical examination, the respiratory sounds were equal bilaterally and normal, and there was minimal sensitivity and no defence or rebound in the mid-epigastrum. No pathology was determined in the other system examinations. In the biochemical blood tests, the values were recorded as fasting blood glucose (FBG) : 145 Mg/Dl(75-110), aspartate transaminase (AST) : 995 IU/L(5-40), alanine transaminase (ALT) : 1086 IU/L(5-40), gamma glutamyl transpeptidase (GGT) : 563 U/L(7-49), alkaline phosphatase (ALP) : 237 IU/L(30-128), Amylase : 1442 U/L(24-125), Lipase : 265 U/L(10 -140), lactate dehydrogenase (LDH) : 289 U/L(0-248), Total Cholesterol : 153 mg/dl(110-200), Triglyceride :

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57 mg/dl(50-200), Total Bilirubin : 8.21 mg/dl (0.2-1.2), Direct Bilirubin 4.78mg/dl (0-0.5), Albumin : 4.5 G/Dl (3.5-5). In the full blood count, the leukocyte, erythrocyte and thrombocyte counts were normal. The full urine analysis, cardiac markers, prothrombin time and renal function tests were within normal limits.

The HBs Ag, anti- HBc IgM, anti-HCV, anti-HAV IgM, anti-HEV, and CMV IgM values were determined to be negative. Anti-HbsAg antibody was positive, and the anti-nuclear antibody (ANA), anti-mitochondrial antibody (AMA), anti-smooth muscle antibodies (ASMA), anti-liver-kidney microsome-1 antibodies (ALKM-1), and perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) were negative. Serum iron, iron-binding capacity, ferritin, free T4 and thyroid stimulating hormone values were found to be normal. On transabdominal ultrasonography (USG), there was increased echogenity in the pancreas and the liver, and swelling was observed in the pancreas. On the magnetic resonance cholangiopancreatography (MRCP), no pericholecystic fluid or stones within the lumen were observed. No dilatation or filling defect was determined in the intrahepatic or extrahepatic bile ducts. When the anamnesis, physical examination, laboratory results and imaging results were evaluated together, although there was no liver biopsy as conclusive evidence, the strong exposure history and the clinical course of the patient led to a diagnosis of acute pancreatitis and toxic hepatitis associated with exposure to ML. Although the patient had muscarinic findings of nausea and diarrhoea, as there were no clinical symptoms of bradycardia, myosis, hypotension, bronchorrhea or severe respiratory problems, and as a long time (approximately 72 hours) had passed since the exposure, pralidoxime and atropine treatment was not administered.

Conservative treatment was applied to the patient with daily monitoring of full blood count and biochemical values. The biochemical markers, which had been high, started to return to normal on the second day of hospitalisation. On the 7th day, the patient had recovered clinically and the biochemical values were within the normal ranges, so he was discharged. At the follow-up examinations 1 month and 3 months after discharge, no abnormal findings were determined in the physical examination, laboratory tests or on USG.

Discussion

Agricultural pesticides containing OPH are in widespread use. Cases of intoxication developing after exposure to these pesticides associated with the widespread use are often seen especially in occupational groups with direct exposure, such as agricultural labourers (8). Exposure to OPH may be through ingestion , respiration or by the transcutaneous route with absorption through the skin (2). Although rare, internal organ damage can develop secondary to intoxication by compounds containing OPH. The immune system, pancreas, kidneys, haematological system, reproductive system and liver tissue may be damaged (9). In the current case, exposure to ML was through the respiratory and transcutaneous routes and it should be emphasised that this is the first case in literature in which acute pancreatitis and toxic hepatitis have been seen together.

Acute pancreatitis (AP) is defined as serum lipase or amylase activity at a level at least 3 times greater than the normal upper limit together with sudden onset abdominal pain and radiological changes in the pancreas determined on contrast-enhanced computed tomography (CECT) or less commonly, on magnetic resonance imaging (MRI) or transabdominal USG (10).

A very limited number of ML intoxication-related cases of AP has been reported in literature (11,12). The mechanisms held responsible for AP after exposure to agricultural pesticides with OHP are hyperstimulaton, ductular hypertension and increased oxidative stress in the pancreatic aciner cells caused by increased ACHE expression as a result of over-stimulation of the interpancreatic nerves (4).

The liver is a major site for the biotransformation, accumulation, and excretion of exogenous chemicals and it is therefore a primary target for toxic substances. Tissue damage may be identified by certain serum enzymes (13).

Three conditions are necessary for a diagnosis of occupational toxic hepatitis. These are, i) the development of liver damage following exposure to a substance required by the occupation, ii) an increase in liver enzymes of at least 2-fold more than the normal limit and iii) the discounting of other causes of liver damage (14).

To the best of our knowledge, there has been only one case reported in literature of toxic hepatitis which developed after exposure to agricultural pesticides containing OPH (15). All the remaining data are limited to rat studies. In those rat studies, OPH was seen to have caused abnormal liver function tests, hepatic necrosis, mid-zonal type liver necrosis and fatty changes (3,5,7). Hepatocyte membrane damage associated with increased oxidative stress has been held responsible for the development of hepatic damage (3).

The systemic toxication symptoms of OPH may be masked by the clinical findings of AP, which can make diagnosis more difficult and in related studies it has been stated that one of the symptoms on presentation is abdominal pain which strikes the back, as seen in the current case (16,17). The cause of hyperglycaemia in the current case seemed to be that the ML-induced pancreas cell damage and stopped the stimulaton of metabolic pathways in the brain, skeletal muscle and the liver (4). The WBC value was normal in the current case. In a previous study, leukocytosis was found to be a prognostic marker in acute OPH intoxication and this increased proportionally with the degree of intoxication. As the clinical findings in the current case were not severe, it was normal that there was no increase in WBC (9).

Mortality rates of AP and toxic hepatitis are high. Due to the systemic effects of OPH intoxication, it must be kept in mind by clinicians that the signs of these complications could be masked. Early diagnosis and early intervention will be life-saving. Therefore, biochemical parameters related to acute pancreatitis and toxic hepatitis must be examined without delay and when necessary, imaging methods must be applied.

The case presented here can be considered of value as the first reported case of pancreatitis and toxic hepatitis together.

The authors have no conflict of interests to declare.

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