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CASE REPORT

Heavy hemolysis after organophosphate poisoning by chlorpyrifos ethyl

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Abstract

Organophosphates (OPs) inactivate the acetylcholinesterase enzyme, thus increasing the cholinergic effect. In a clinical setting, patients with OP poisoning may experience nausea and vomiting, diarrhea, and abdominal pain, or in severe cases respiratory failure, seizures, and death. Rarely, acute hemolysis has also been observed. The existing literature contains few descriptions of several delayed diseases associated with OP poisoning. This article presents the case of a patient who experienced severe hemolysis approximately one week after OP exposure. Only a small number of similar cases have been previously examined.

Keywords: Hemolysis, Organophosphate Poisoning, Chlorpyrifos Ethyl.

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INTRODUCTION

Organophosphates (OPs) are often used as insecticides in agricultural areas. Mortality and morbidity rates are high in cases of OP poisoning caused by suicidal or accidental exposure. The primary target of OPs is the acetylcholinesterase (AChE) enzyme. The inhibition of AChE by OPs causes the accumulation of acetylcholine in cholinergic synapses and the overstimulation of muscarinic and nicotinic cholinergic receptors. It has three clinical manifestations: cholinergic syndrome, intermediate syndrome, and delayed polyneuropathy (1). Rarely, acute hemolysis has also been observed (2). The existing literature contains few descriptions of several delayed diseases associated with OP poisoning. In rare cases, such as ours, OPs may cause life-threatening hemolysis in the subacute poisoning period.

CASE REPORT

A 45-year-old male patient was admitted after presenting with weakness, fatigue, and an icteric appearance. He was hospitalized with a provisional diagnosis of autoimmune hemolytic anemia upon detection of the following values: WBC:4.4 K/uL, Hgb = 10.4 gr/dl; Plt = 148 K/uL; reticulocyte = 1.56%; total bilirubin = 10.8 mg/dL; indirect bilirubin = 9.71 mg/dL; and LDH = 459 U/L, macro & micro spherocytes were found in the peripheral smear. He declared no disease except immune thrombocytopenia (ITP), which was in remission with no continuing treatment. The patient was administered a 250-mg pulse methylprednisolone treatment. However, a direct coombs test was negative. The tests for paroxysmal nocturnal hemoglobinuria (PNH) and ADAMTS13 were normal. G6PD was normal. Haptoglobin could not be studied.

Despite the treatment, the patient's Hgb value decreased to 3.9 g/dl on the second day of hospitalization. On the third day, rapid increases were observed in total bilirubin (to 82 mg/dl) and indirect bilirubin (to 45 mg/dl). Therefore, a total plasma exchange process was started. Since hemolytic anemia had not been proven, a bone marrow (BM) biopsy was performed. The aspiration of BM showed incremental and significant dysplasia of the erythroid lineage (M/E ratio = 1/3; **Figure 1**). When a more thorough anamnesis was conducted, the relatives of the patient revealed that the patient had sowed seeds with the OP pesticide chlorpyrifos ethyl (CPF) about one week before the onset of the disease, and he had subsequently washed the device that he used by spraying it with water.

The patient's cholinesterase level was normal. However, since time had passed since the event, subacute OP poisoning was considered a diagnosis. The total bilirubin of the patient, who underwent a total of four plasmapheresis treatments, declined to 17 mg/dl and then continued to regress spontaneously without further plasmapheresis. Nine units of erythrocyte suspension replacement were provided. The reticulocyte level increased to 8.29% on the 10th day of hospitalization, and the Hgb level began to stabilize around 9.5 g/dl without transfusion. The LDH level decreased from 1,034 to 593 U/L. In the first month following discharge, the patient's Hgb level was 13 g/dl, and bilirubin levels were normal. In the second month, a control bone marrow aspiration showed a significant decrease in erythroid dysplasia (**Figure 2**) and the Hgb level increased to 15 g/dl.

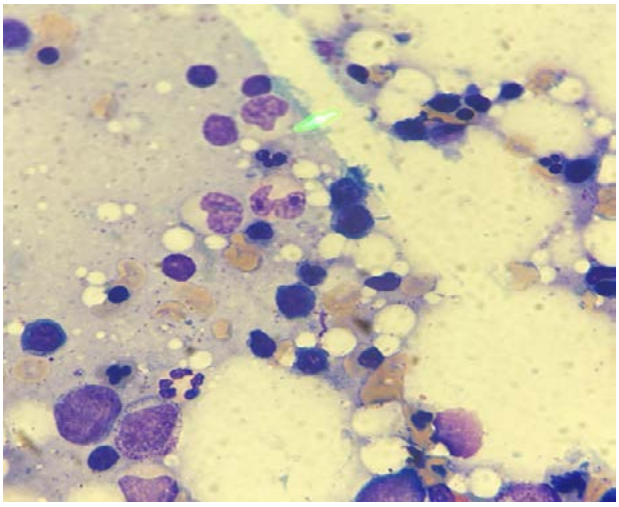

Figure 1: Dysplasia of erythroid lineage

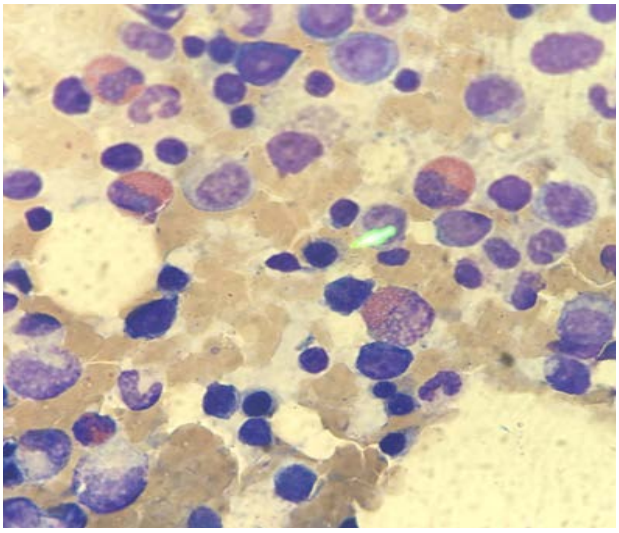

Figure 2: Control bone marrow aspiration

DISCUSSION

Organophosphates inhibit the function of carboxylic ester hydrolases, such as chymotrypsin, AChE, plasma, or butyrylcholinesterase (BChE), plasma and hepatic carboxylesterase (aliesterase), paraoxonase (esterases), and other non-specific esterases within the body. However, the most prominent clinical effects of poisoning with OPs result from their inhibition of AChE.

It is suggested that oxidative tissue damage plays a role in the pathogenesis of toxic effects (neurotoxicity, hepatotoxicity, immunotoxicity, embryotoxicity and genetic toxicity) resulting from acute and chronic OP applications (3). It has also been noted that free radicals, especially DNA, proteins, and cell phospholipids, form as a result of oxidative stress and have the ability to react with many organic and inorganic compounds, especially polyunsaturated fatty acids (4). These free radicals cause the exhaustion of the enzymatic and nonenzymatic antioxidant systems that protect the cell. It has been suggested that lipid peroxidation of cells, DNA damage, and changes in proteins occur due to oxidative damage resulting from these effects.

As a lipophilic molecule, CPF enters the cytoplasm of cells and begins to damage the cellular molecules inside the cells. It demonstrates its main toxic effect through its metabolite, chlorpyrifos-oxon (CPO), to which it is converted by cytochrome p-450. This metabolite carboxylesterase binds to AChE with high affinity, as in butyrylcholinesterase, and produces toxic effects by inhibiting AChE (5). Acute CPF toxicity includes other mechanisms that are unrelated to AChE inhibition, including oxidative stress. Oxidative damage begins primarily with the production of reactive oxygen species and causes damage to macromolecules such as lipids, DNA, and proteins.

The clinical picture depends on the specific agents, the amount that was absorbed, and the mode of exposure. If the amount absorbed in OP poisoning is high enough, the effects may be apparent within minutes. Most patients begin to show symptoms within 8 to 24 hours after intake. Parasympathomimetic effects are dominant and may include salivation, lacrimation, sweating, urinary incontinence, diarrhea, vomiting, bradycardia, bronchospasm, bronchorrhea, hypoxia, and miotic pupil. OP poisoning has also been associated with certain delayed manifestations, such as OP-induced delayed neuropathy, myonecrosis, personality changes, schizophrenia, and pancreatitis (6,7). However, the development of hemolysis occurs less frequently. In their case report, Kadeli and Hanjagi observe that hemolysis developed after one week (2). Similarly, in our case, hemolysis developed one week after exposure. Our case is similar to the other case in the literature in terms of the age and gender of the patient, and a significant decrease in hemoglobin levels and an increase in LDH levels were observed in both individuals. It was thought that the reticulocyte count was normal due to dysplasia in the bone marrow. However, in our case, the cholinesterase level was normal since it was measured after plasmapheresis.

Thus, it should be noted that OP poisoning may have unusual clinical manifestations. It should also be considered in the differential diagnosis of antiglobulin negative hemolysis. Ultimately, a physical examination and a detailed anamnesis are always the best guides.

Declarations

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Ethical Committee approval was not required. Informed consent was obtained from all participants.

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