Case report

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Propanil induced haemolytic anaemia

de Alwis J P N[1], Hathurusingha H M P W[1], Hassan A H M A[1], Rathnayaka R M S K[2]

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Introduction

Propanil is a herbicide used widely in agriculture. Poisoning by propanil is a rare occurrence with most of these incidents being reported from Sri Lanka due to self-ingestion[1]. It is categorized as a low to medium toxic compound. Severe poisoning is well known to cause methaemoglobulinaemia and tissue hypoxia. Yet the incidence of haemolytic anaemia following propanil poisoning has only been reported in only a few instances[1,2,6]. We present a patient who developed haemolytic anaemia 19 days after ingestion of propanil.

Case report

A 48-year-old previously healthy male was admitted to the casualty medical ward 6-8 hours after ingestion of propanil containing liquid. The amount of propanil taken was approximately 30-40 milliliters. The patient did not suffer from dyspnoea, chest pain, nausea or vomiting. He had a pulse rate of 96 beats per minute with a blood pressure of 90/60 mmHg. He was neither drowsy nor disoriented. He had no respiratory distress and lungs revealed vesicular breathing.

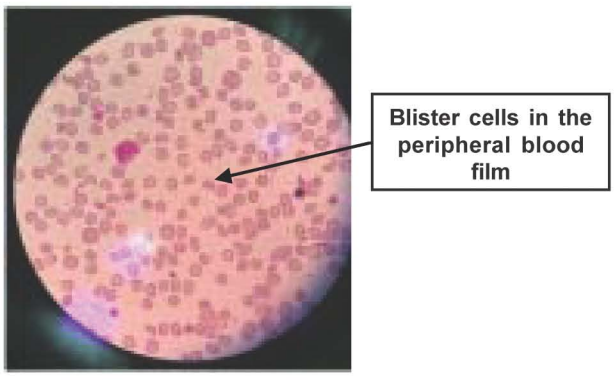
Pulse oximetry showed an oxygen saturation at room air between 75-80%. It did not improve with oxygen therapy via face mask. The arterial blood gases did not reveal an acid-base imbalance and the partial pressure of oxygen was 85mmHg with carbon dioxide 38mmHg. His venous blood showed a methaemoglobin level of over 40%. The level was determined by a colorimetric method.

The patient was given 7.5 ml (0.1ml/Kilogram body weight) of methylene blue which is the recommended antidote in propanil poisoning. During infusion and soon afterwards the oxygen saturation in pulse oximetry improved to normal levels. Yet the saturation dropped 3-4 hours later and the patient required repeated infusions of methylene blue of the same amount. The antidote was given for a total of 6 days before the pulse oximetry oxygen saturations became stabilized to normal levels. Throughout the duration of treatment the patient did not develop respiratory depression, confusion or cardiac compromises which are complications of severe methaemoglobulinaemia.

The basic investigations which included the full blood count (FBC), serum electrolytes (SE), renal function tests (RFT) and liver function test (LFT) were normal from initial presentation till the patient was discharged 8 days following admission.

Eleven days later the patient got re-admitted to the ward complaining of worsening lethargy for five days duration with dyspnoea on exertion. On examination the patient was pale and had yellowish discolouration of the eyes. The patient was haemodynamically stable and lungs were clear. Abdominal examination did not reveal hepato-splenomegaly.

Initial blood investigations showed a haemoglobin of 5.3g/dL and a MCV of 131.2fl. The reticulocyte count was 8% (normal 0.5-2.5%) with a reticulocyte index of 3.21. Serum total bilirubin was 40.6umol/L (5-21) with a predominant indirect bilirubin fraction. The conclusion of the blood picture was of an ongoing haemolysis with an underlying inflammatory process.



Oxidant induced haemolytic anaemia was confirmed due to the presence of blister cells and bite cells in the blood picture. The direct antibody test (Coomb's test) was negative and thus excluded an autoimmune cause for the

[1] *Registrar in Medicine, Teaching Hospital, Anuradhapura.*

[2] *Consultant Physician, Teaching Hospital, Anuradhapura.*

Corresponding author: de Alwis JPN

E-mail: jerome.dealwis@gmail.com

http://orcid.org/0000-0002-6554-2738

haemolytic anaemia. The patient was transfused three packs of red blood cells and on discharge the haemoglobin was 9g/dL. The Glucose-6-phosphate dehydrogenase deficiency was excluded by the screening method (Brewer's test) done 6 weeks following the last transfusion. High performance liquid chromatography (HPLC) of the patient did not reveal abnormal haemoglobins. History did not reveal any haemoglobinopathies or haemolytic anaemias in the family. The anaemia was resolved at the follow up visits done at 4 weeks and 2 months interval with a haemoglobin of 13.4g/dL.

Discussion

Propanil (3,4-dichloropropionanilide) is an arylamide compound which is extensively used in agriculture specially paddy farming. Occupational poisoning due to this compound is very rare or unheard of as only a small amount will enter the body[3]. Most cases of poisoning are due to self-ingestion of this toxic compound. Gastrointestinal irritation and systemic effects of methaemoglobin are well known to occur with ingestion of large doses of this herbicide.

The mechanism behind haemolytic anaemia following propanil ingestion is a point of interest. Certain texts attribute the pathology to a Heinz body formation giving rise to intravascular haemolysis causing anaemia[4]. Heinz body formation is caused by the damage to the haemoglobin molecule which occurs due to direct oxidative stress exerted on the red blood cell. The oxidant insult can be neutralized by NADPH and Glutathione peroxidase which are in limited supply in red blood cells. The stores of NADPH and glutathione peroxidase is depleted when there is an overwhelming amount of oxidants which in turn leaves the red cell membrane vulnerable to injury by reactive oxygen species. These oxygen radicals will result in severe cell membrane damage and leads to premature haemolysis in the intravascular compartment. When the oxidant induced haemolysis over takes the rate of erythropoiesis, the patient will develop anaemia. In this patient the blood picture revealed that the haemolysis was oxidant induced. The history did not reveal exposure to any substance that can lead to oxidant induced haemolysis other than propanil. The culprit oxidant is N-hydroxy-3,4-dichloroaniline. Studies done on rats have resulted in the conclusion that the haemolysis in propanil poisoning is mediated by N-hydroxy-3,4-dichloroaniline[5] which is synthesized in the liver from the parent compound propanil. It is then taken up by the erythrocytes to undergo oxidation. Unfortunately there are no resources available to measure the N-hydroxy-3,4-dichloroaniline levels in Sri Lanka.

There are currently no studies stating the onset of haemolysis in propanil poisoning. A case report from 2003 describes a patient who presented with haemolytic anaemia just a day after ingestion of propanil[6]. In this patient the anaemia took place almost 3 weeks following ingestion. Another field of interest was that this patient required methylene blue for 6 days duration. Methylene blue an oxidant in itself can lead to haemolysis in susceptible patients such as with Glucose-6-phosphate dehydrogenase deficiency (G6PD). The treatment in this situation was supportive with blood transfusions to improve oxygenation of tissues.

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