A Tragic Outcome: Paraquat Poisoning in a Teenage Boy Using Marijuana

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Introduction

Paraquat (N, N’-dimethyl-4,4’-bipyridinium dichloride) is used in agriculture as an herbicide for grass control. Poisoning by pesticides and other agricultural chemicals is a significant public health problem worldwide, especially in developing countries. Paraquat poisoning can occur either by inhalation, ingestion, or direct contact which can cause local as well as systemic toxicity. Accidental or deliberate ingestion stays the major cause of poisoning with increased risk for fatality. Studies show a variable case fatality rate of 50% to 90%. Therefore, it has been restricted in many parts of the world. In rural areas, Paraquat poisoning usually results from suicidal exposure, occupational exposure, or accidental exposure.

The lethal dose of paraquat for humans is around 10 to 20 ml of 20% solution. Paraquat mainly exerts its toxicity by the formation of intracellular reactive oxygen species (ROS), which cause cellular damage affecting multiple organs including lungs, kidneys, heart, liver, adrenal glands, central nervous system, muscles, spleen, etc. There is no specific effective antidote available for paraquat poisoning which is why the outcome solely depends upon early diagnosis, decontamination and aggressive symptomatic management.

We report a rare case of paraquat poisoning in a cannabis user as per the CARE 2020 Guidelines. It is one of the first reported case of accidental ingestion of paraquat under the influence of marijuana.

CASE PRESENTATION

An 18-year-old man who had been using marijuana for a year showed up at the emergency room supposedly under the effect of marijuana and having consumed 10–15 ml of 24% paraquat four days earlier. The day after the ingestion, he had many episodes of vomiting mixed with blood and food particles. Other complaints he reported included heartburn, trouble swallowing, and decreased urine production. There was no past history of fever, seizure-like movement, coughing, chest pain, shortness of breath, yellowing of the eyes, and abdominal distension. When he revealed the ingestion to his guardians following three days of ingestion of paraquat, they immediately brought him to the closest hospital. Upon arrival at the hospital intravenous fluid and proton pump inhibitors were administered.

At the emergency department, his GCS was 15/15 with a pulse rate of 79 beats per minute, blood pressure of 120/70 mm Hg, a respiratory rate of 20, and oxygen saturation of 94% in room air. On chest examination, a bilateral equal breath sound was heard, and there were no crepitations or heart murmurs. The abdominal examination was normal. However, he had intraoral mucosal erosion with hemorrhages (Fig. 1). His chest X-ray revealed infiltration (Fig. 2. a), and he was admitted to the ICU. He was managed conservatively along with intravenous Dexamethasone.

On the third day of ICU admission, the patient had gradual decline in oxygen saturation along with decrease in urine output. Arterial Blood Gas (ABG) analysis showed a PaO₂/FiO₂ ratio of <100. His creatinine
and liver enzymes were elevated. Chest X-ray showed diffuse infiltration with the reticulonodular pattern (Fig 2.b). The patient continued receiving oxygen via a non-rebreathing mask, intravenous dexamethasone, vitamin C, and vitamin E. His creatinine rose to 14.5mg/dl with ALT/AST up to 272/157 IU/L.

Fig 1: Clinical photograph showing ulceration and sloughing of the oral cavity
The patient's condition began to improve as evidenced by an increase in urine output and a decrease in creatinine level. There was also an improvement in the levels of aminotransferases. However, the patient's oxygen requirement did not improve significantly and an arterial blood gas analysis showed a PaO2/FiO2 ratio of less than 100. A high-resolution computed tomography (HRCT) scan revealed diffuse ground glass opacity with infiltration. The treatment plan included intravenous cyclophosphamide, but unfortunately the patient chose to leave against medical advice (LAMA) and subsequently died on the second day after leaving.

Table 1: Lab value of patient

<table>
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<tr>
<th>Parameters</th>
<th>Values</th>
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Total Leucocyte Count 8400 /cumm 4000-11000
Neutrophils 80% 40-70
Lymphocytes 12% 20-40
Eosinophils 0% 2-6 %
Monocytes 10% 2-10 %
Basophils 0% 0-1 %
Hemoglobin 13.6 g/dl 12-16 gm/dl
Platelet count 190000/cumm 150000-350000 /cumm
PT 11.1 sec
INR 0.93
BT 3 2-7 Min
CT 7 min 6-12 min
Phosphorus 8.1 mg/dl 3.0-5.0
Serum creatinine 10.1 mg/dl 0.4-1.4
Blood Urea 283.6 mg/dl 15-46 mg/dl
Sodium 135 mmol/l 135-150 mmol/L
Potassium 5.9 mmol/l 3.5-5.5 mmol/l
Serum bilirubin 0.8 mg/dl 0.1-0.4 mg/dl
SGPT 161 IU/l 5-40 IU/L
SGOT 110.9 IU/l 5-35 IU/l
Serum phosphatase 301.6 U/L 30-120 U/l

Discussion
Paraquat (N, N’-dimethyl-4,4’-bipyridinium dichloride ), is an effective herbicide that is a brown syrupy liquid with a strong odor. It accounts for 13% of all deaths due to poisoning.6 For this reason, the use has been restricted in many parts of the world. However, cases are largely reported from areas where agriculture is practiced by a majority of population. It may be due to easy availability and accessibility of paraquat in those regions. It is rapidly deactivated in contact with soil which makes it easier to handle.7 However ingestion of even a small amount (i.e., 10 to 20 ml of 20% solution) is considered lethal. A plasma concentration of >1.6 pg/ml, 12 hours after administration, has been determined to be always lethal. In our case, the patient accidentally consumed paraquat under the influence of marijuana.

In general, the diagnosis is often made on circumstantial evidence and clinical symptoms. History of paraquat exposure, empty pesticide bottles, suspicious residue, odor, or color can be a diagnostic clue. In doubtful cases, the Urinary dithionite test can be done at the bedside. In an alkaline medium, sodium dithionite reduces paraquat to a blue radical 8. Toxicity is mainly due to its ability to redox-cycling and subsequent production of increased Reactive Oxygen Species (ROS) 8. It increases oxidative stress and leads to lipid peroxidation, finally disrupting biological membranes leading to apoptosis.

Poisoning can be either through the topical route or by ingestion. Clinical manifestations that follow paraquat poisoning depend upon the route of ingestion and the amount quantity. Ingestion of large amounts results in fulminant organ failure and the prognosis is universally poor8. It can involve multiple organs causing pulmonary oedema, cardiac, renal and hepatic failure and convulsions due to CNS involvement.

Lung manifestations are severe because pneumocytes uptake the paraquat by an active polyamine uptake pathway leading to a very high concentration of paraquat in the lung parenchyma (10-20 times greater than in plasma) 9. In type 1 pneumocytes, it leads to impaired oxygenation and capillary exchange while in type 2 pneumocytes, it causes Increased surface tension and subsequent fluid accumulation causing pulmonary oedema and hemorrhage. Infiltrations of inflammatory cells develop subsequently leading to lipid peroxidation-induced pulmonary fibrosis. Spontaneous pneumothorax or pneumomediastinum are poor prognostic markers8. Most fatalities were from respiratory failure9. Studies have shown that approximately 20% of patients develop pneumomediastinum as a complication with a mortality rate of approximately 100%. It

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is believed that pathological repair at the alveolar level leads to interstitial widening, alveolar congestion, collagen deposition, and microthrombi formation, which can cause the early development of secondary pulmonary hypertension and an obvious consequence of pneumothorax and pneumomediastinum called “Daisley Barton syndrome”.6

There is usually a delay of several days before the onset of respiratory symptoms following ingestion as seen in this case. Nonetheless, once infiltrates appear on the chest X-ray, the condition is usually progressive and soon respiratory failure ensues.11. Routine use of supplemental oxygen is not recommended in mild-to-moderate hypoxia as it can further aggravate lung injury. The hypoxemic strategy has been shown to reduce the production of ROS. Oxygen therapy should be reserved only for severe hypoxemia.

The unavailability of a specific antidote and lack of definitive treatment for paraquat toxicity has led to a high case fatality rate of around 50% to 90%1. Symptomatic treatment remains the mainstay treatment, focusing mainly on decontamination and stabilization of the patient. Gastric decontamination is beneficial in those patients who present within 1-2 hours of ingestion. Activated charcoals can be used. However, lavage is contraindicated due to its corrosive nature12.

In a study by Lin et al 10, Pulse therapy with cyclophosphamide and methylprednisolone has shown effective in preventing respiratory failure and reducing mortality by 25%. Pulse therapy, along with antioxidants such as N-acetyl-cysteine, and vitamin C has shown efficacy in preventing ongoing inflammation and pulmonary fibrosis with varied outcomes 12. A few case reports also suggest lung transplantation after paraquat poisoning11. Few studies also show salicylate significantly reduced oxidative stress in animal models, however, benefits in humans are not established yet 8.

Patients developing acute renal failure should undergo hemodialysis until renal functions returns to normal. In our patient, Liver Function Tests, Renal Function Tests and Pulmonary Function Tests were deranged. The patient showed improvement in the liver and kidneys functions but the pulmonary injury was ongoing.

Conclusion
To date, there is no specific antidote to paraquat poisoning. The focus should be on preventive measures and in case of exposure, prompt decontamination and stabilization should be done. Oxygen therapy is only recommended for severely hypoxic patients. Pulmonary insults are the main causes of mortality in the majority and despite aggressive management, mortality rates are high.

Consent
Written consent was obtained from the patient for the publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-chief of this journal on request.

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Authors Contribution

MY, NAS, SL, SKJ prepared the original manuscript. MY, NAS, SL, SKJ reviewed and edited the manuscript. SL, SKJ reviewed the manuscript. MY, NAS, SL, SKJ were in charge of the case.

References:


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