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PARAQUAT TONGUE: CASE OF PARAQUAT POISONING AND REVIEW OF LITERATURE

General Surgery

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ABSTRACT

We herein report a rare case of Paraquat poisoning which presented with multiple buccal mucosa and labial ulcers. He complained of burning pain in the mouth which increased on eating, along with difficulty in complete mouth opening. The trismus progressed gradually from 4 fingers to 2 fingers breadth, over 2 days. The patient also had multiple episodes of vomiting with contents mainly being mucous secretions as the patient was nil per oral. Radiographic features including the imaging of the barium swallow of this case are discussed together with the pathomechanics of the poison. A comprehensive overview of the biochemistry and pharmacodynamics of Paraquat has been given as well. Understanding the mechanism of action of Paraquat will help to explain the manifestations of the poisoning and its subsequent treatment. Medical management was undertaken with the imperative step being the use of pulsatile steroid therapy. Supportive care and oral exercises were advised simultaneously to ensure optimum recovery. We looked at previously published literature to assess the proposed management protocols in the absence of a definitive antidote, leading to high mortality rates.

KEYWORDS

Paraquat, Poisoning, Pesticide, Toxicology, Pulmonary fibrosis

INTRODUCTION:

Paraquat or N, N′-dimethyl-4, 4′-bipyridinium dichloride is a commonly used herbicide in India. It is an effective albeit highly toxic quaternary ammonium with the absence of any specific antidote. The diagnosis of poisoning is often difficult in the absence of proper history, nonspecific clinical features, and lack of diagnostic tests. We found a dearth of an evidence-based management protocol to manage cases of paraquat poisoning thereby leading to high mortality rates.

Case:

We present a case of a 34-year-old male, with an alleged history of ingestion of herbicide containing paraquat, with the intent of self-harm, 2 days ago. He complained of burning pain in the mouth which increased on eating, along with difficulty in complete mouth opening. The trismus progressed gradually from 4 fingers to 2 fingers breadth, over 2 days. The patient also had multiple episodes of vomiting with contents mainly being mucous secretions as the patient was nil per oral. No history of dysphagia, dyspnoea, tachypnea, hemoptysis, hematemesis, or malena. On examination, multiple buccal mucosa and labial ulcers were present (Fig 1). Barium swallow (Fig 2) did not reveal any stricture. On 70° laryngoscopy, bilateral vocal cords were normal, with whitish slough visible in the post-cricoid region and pyriform fossa. The patient was managed with topical NSAIDS: choline salicylate and benzalkonium chloride gel for oral ulcers, chlorhexidine gluconate (0.2%) mouth wash, and injection intravenous dexamethasone 8 mg thrice daily, for 3 days and then tapered gradually. The patient was counseled to do active oral exercises. He showed clinical improvement with 3-4 fingerbreadth mouth opening (Fig 3), tolerated oral feeds, and was thus discharged.

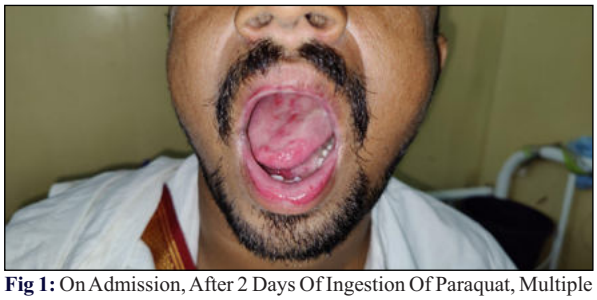

Fig 1: On Admission, After 2 Days Of Ingestion Of Paraquat, Multiple Ulcers Over The Buccal Mucosa And Labia With Areas Of Active Bleed Over The Anterior Two-thirds Of The Tongue Are Seen.

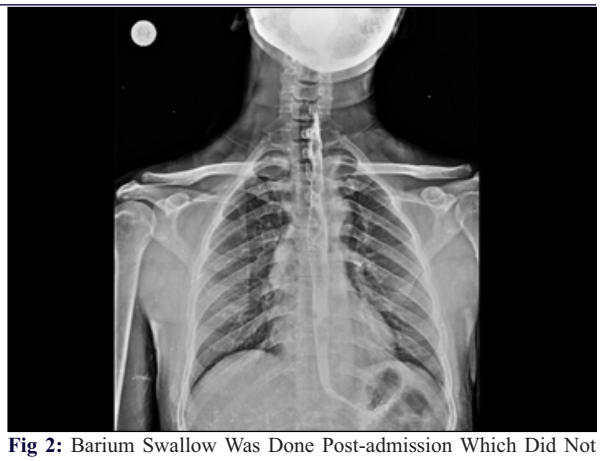

Fig 2: Barium Swallow Was Done Post-admission Which Did Not Reveal Any Strictures.

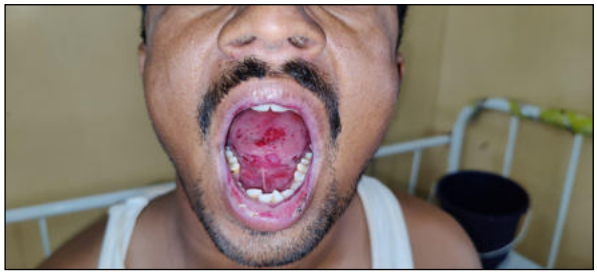

Fig 3: On discharge, the patient showed clinical improvement with 3-4 fingerbreadth mouth opening.

DISCUSSION:

Poisoning is a crucial public health issue, which ranks 45th in total deaths worldwide. It is estimated that intentional ingestion of pesticides causes 3,70,000 deaths each year. Of these deaths, 84% have been shown to occur in low- and middle-income countries (LMICs). [1]

The incidence of poisoning in India is among the highest in the world. More than 50,000 people die every year from toxic exposure. According to the National Poisons Information Centre, New Delhi,

analysis of poisoning calls showed that the highest incidence of poisoning was due to household agents (44.1%) followed by drugs (18.8%), agricultural pesticides (12.8%), industrial chemicals (8.9%), animal bites and stings (4.7%), plants (1.7%), unknown (2.9%) and miscellaneous groups (5.6%). The commonest cause of poisoning in developing countries is pesticides which include organophosphates, carbamates, chlorinated hydrocarbons, pyrethroids, and aluminum or zinc phosphide. The reason behind this upsurge is the agriculture-based economy, poverty, unsafe practices, lack of policies and enforcement, ignorance, illiteracy as well as the easy availability of highly toxic pesticides.

Paraquat is a deadly chemical that is widely used as an herbicide, primarily for the control of weed and grass. [2] The Pesticide Action Network (PAN) and the Berne Declaration have been calling upon governments for a global ban on paraquat, and industry leaders to halt the production and sale of this hazardous pesticide. In countries like the US and China, its use has already been restricted due to its deleterious effects. Nonetheless, paraquat is one of the world's most widely used herbicides, especially in an agrarian country like India, where its use leads to the poisoning of a multitude of farmers. [3]

It has been hypothesized in previous studies that paraquat pulmonary toxicity is caused by the cyclic reduction-oxidation of paraquat and subsequent generation of superoxide radicals along with the singlet oxygen with the initiation of lipid peroxidation.[4] Paraquat generates reactive oxygen species which causes cellular damage via lipid peroxidation, activation of NF-κB, mitochondrial damage, and apoptosis in many organs.

It has low but rapid gastrointestinal absorption but an overall low absorption through the skin. Following ingestion, the peak plasma concentration occurs in less than two hours. A two-compartment model can be used to explain the distribution of Paraquat in the target cells. [5] Paraquat is actively transported to alveolar cells, where it is reduced to form highly reactive free radicals. It is actively taken up against a concentration gradient into lung tissue leading to pneumonitis and lung fibrosis. It also causes renal and liver injury. [5] Generally, paraquat is not metabolized to any large extent. In previous animal studies, the metabolites have been detected in urine, possibly resulting from the action of intestinal microflora. [6]

The toxicity is caused because of the redox-cycling and subsequent generation of reactive oxygen species (ROS). Its metabolism generates a paraquat mono-cation radical (PQ.+). Inside the cell, PQ.+ rapidly gets re-oxidized to PQ2+, and in the process, it generates superoxide (O2.−). O2 acts as an electron acceptor and NADP as an electron donor in this reaction, which further causes the formation of the hydroxyl free radical (HO.) in the presence of iron. NO. combines with O2.− to generate peroxinitrite (ONOO-) which is a very strong oxidant and a nitrating intermediate. NO. is enzymatically produced from L-arginine by NO synthase, and PQ also directly or indirectly induces NO synthase-mediated nitric oxide production The toxicity is particularly severe in the lungs as explained by the mechanism of absorption. [5] A paraquat blood level of >1.6 μg/mL 12 h after ingestion is universally lethal. [7]

In the lungs, it causes acute alveolitis. Further effects include diffuse alveolar collapse, vascular congestion, and adherence of activated platelets and polymorphonuclear leucocytes to the vascular endothelium which leads to apoptosis of the cells.

The major target of toxicity in the lung is the alveolar epithelium. In the initial 'destructive phase' both type I and type II pneumocytes demonstrate swelling, vacuolation, and disruption of mitochondria and the endoplasmic reticulum. Sloughing of the alveoli causes pulmonary edema. This phase leads to a proliferative phase in which the alveolar space gets filled with mononuclear profibroblasts which mature into fibroblasts followed by fibrosis of the lungs. When the renal system is involved, large vacuolation in proximal convoluted tubules (PCT) is visualized in the kidneys which leads to necrosis. Hepatocellular injury caused by paraquat poisoning is due to degranulation of the rough and smooth endoplasmic reticulum as well as mitochondrial damage. Pathologically, it takes a few hours to days for the changes to be seen.

The Initial management of paraquat poisoning focuses on the principle of decontamination of the gastrointestinal system and prevention of further absorption. Adsorbents like activated charcoal (1-2 g/kg) and Fuller's earth (1-2 g/kg); with a cathartic such as 70% sorbitol should be given immediately. There isn't any concrete data to support the use of hemoperfusion to improve the survival of patients but it has been shown to decrease paraquat levels in humans if initiated within 4 h of ingestion. It is used only as a supportive treatment for patients who develop kidney failure.

There is no specific antidote for paraquat which makes it extremely dangerous. In a study by Afzali et al., the therapeutic effect has been reported with high dose cyclophosphamide and glucocorticoid where survival was about 75%. Supportive management has been used to tackle these cases as there is a lack of evidence-based standardized guidelines. Different studies provide varying approaches to these cases, none of which can be agreed upon by most clinicians. A previous study demonstrated that pulse therapy with cyclophosphamide and methylprednisolone (MP) might be effective in preventing respiratory failure and reducing mortality in patients with moderate to severe poisoning by suppressing ROS production by neutrophils and macrophages. Corticosteroids were administered to our patient after which rapid improvement in their condition was observed. Dexamethasone 8 mg was given intravenously thrice a day for 3 days then tapered gradually to twice a day for 3 days followed by once a day for 3 days after which it was stopped. [8]

A recent Cochrane meta-analysis concluded that patients who received glucocorticoid with cyclophosphamide in addition to standard care had a lower risk of death at final follow-up than those receiving standard care only (risk ratio 0.72; 95% confidence interval 0.59–0.89). [9]

Desferrioxamine has shown to be effective due to its protective mechanism by chelating iron and by blocking the uptake of paraquat by the type II alveolar cells of the lungs. Vitamin E (a-tocopherol) is a well-known antioxidant that works by scavenging free radicals and stabilizes membranes that contain polyunsaturated fatty acids (PUFA), which may prevent the cytotoxic effects of paraquat.

N-acetyl cysteine (NAC) has also been used with success in massive paraquat poisoning. It is converted in the body into cysteine, the rate-limiting amino acid for glutathione synthesis, thereby enhancing detoxification, and acting directly as a free radical scavenger. It also helps in delaying inflammation.

Other supportive care includes fluid and electrolyte balance and pain management. Oxygen supplementation should be avoided because it can worsen paraquat-induced lung injury. Oxygen is indicated when a patient develops hypoxia. Since our patient did not complain of dysphagia, an Esophagogastroduodenoscopy was not indicated in this case. A barium swallow was done to rule out any strictures and its subsequent complications. The role of surgery is limited and may only play a role when the patient develops complications like esophageal strictures.

The variation in approach and lack of standard guidelines in different hospitals makes managing cases of Paraquat poisoning difficult to manage, even in well-equipped tertiary care centers. Thereby, making it essential to identify poisoning due to ingestion of paraquat as soon as possible. Early intervention can be lifesaving and drastically reduce mortality rates. Management initially starts with the administration of steroids in pulsatile form followed by medical and surgical treatment. Treating patients with steroids must be done as soon as possible to reduce the effects and complications by delayed management of paraquat poisoning. The lack of an effective antidote makes steroids the best conservative method of management of a case of paraquat poisoning.

REFERENCES:

1. Asawari R, Atmaram P, Bhagwan K, Priti D, Kavya S, Jabeen GA. Toxicological pattern of poisoning in urban hospitals of western India. J Young Pharm. 2017;9(3):315-320.
2. Facts About Paraquat. Cdc.gov. https://emergency.cdc.gov/agent/paraquat/basics/facts.asp. Published May 16, 2019. Accessed September 18, 2021.
3. Iuf.org. https://www.iuf.org/wp-content/uploads/attachments/Joint%20paraquat%20study%20India_0.pdf. Accessed September 18, 2021.
4. Bus JS, Aust SD, Gibson JE. Paraquat toxicity: proposed mechanism of action involving lipid peroxidation. Environ Health Perspect. 1976;16:139-146.
5. Gawarammana IB, Buckley NA. Medical management of paraquat ingestion: Medical management of paraquat ingestion. Br J Clin Pharmacol. 2011;72(5):745-757.
6. Donaldson C. Paraquat. In: Small Animal Toxicology. Elsevier; 2013:731-739.
7. Hart TB, Nevitt A, Whitehead A. A new statistical approach to the prognostic significance of plasma paraquat concentrations. Lancet. 1984;2(8413):1222-1223.
8. Ping SH. 2011 Jun - Improved survival in severe paraquat poisoning with repeated pulse

therapy of cyclophosphamide and steroids. Hksccm.org. https://www.hksccm.org/index.php/professional/journal-news-update/92-intensive-care-medicine/2380-201 1-jun-improved-survival-in-severe-paraquat-poisoning-with-repeated-pulse-therapy-of-cyclophosphamide-and-steroids. Accessed September 18, 2021.
9. Janeela MA, Oommen A, Misra AK, Ramya I. Paraquat poisoning: Case report of a survivor. J Family Med Prim Care. 2017;6(3):672-673.