Rare fatal poisoning through dermal exposure to paraquat

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Abstract
Paraquat skin contact occurs less frequently and is rarely fatal. This article reports a case of a 45-year-old man who presented with dysphagia, respiratory distress and grade two, and third skin burns focusing on the upper body after accidental exposure to paraquat. He was admitted to the hospital 6 days after the first contact. The urine sodium dithionate test was strongly positive. The O₂ saturation at admission was 52%, which reached 91% with a bag valve mask. Rising blood liver enzymes, urea, creatinine, and respiratory acidosis in the venous blood gas analysis were observed in the lab data. In the course of hospitalization, the patient was intubated due to oxygen level dropping. Evidence of acute respiratory distress syndrome and decreased level of consciousness was also observed. However, despite treatment with corticosteroids, antioxidants, and hemodialysis, he died on the fourth day of hospitalization. It is concluded that dermal exposure with paraquat could be life-threatening if the patient presented late with organ involvement.

Keywords
Poisonings, paraquat, dermal exposure, fatal

Date received: 5 February 2022; accepted: 31 October 2022

Case report

A 45-year-old farmer with a body mass index = 22.1 (BMI = weight (kg)/height² (m)) who was referred to the poisoning emergency center of Khorshid Hospital affiliated to Isfahan University of Medical Sciences about 6 days after the skin exposure through accidental spraying PQ 20% solution on his face and body. He suffered from dysphagia, two episodes of hemoptysis containing clear blood clots, and respiratory distress which was started 3 days after exposure.

Although severe cases of PQ poisoning occur after ingestion, however, there are also reports of systemic involvement after skin exposure to PQ. This study also reports a case of severe systemic involvement and death after dermal exposure.
exposure. All of the history related to the patient was obtained from his mother.

At admission, vital signs were axillary temperature, 36.7°C; heart rate, 107/min; respiratory rate, 30/min; blood pressure, 111/50 mm Hg; and O₂ saturation, 52% which reached 91% with a bag valve mask. On initial physical examination, the patient was confused and he had second- and third-degree burns and multiple ulcers focusing on the body (face and around and in the mouth, forehead, neck, shoulders and axillary, elbows, trunk, hands, and feet) with yellow and green serous discharge. There was an ulcer and erosion in the oral cavity as well.

In first visit, Glasgow Coma Scale (GCS) recorded by physician in medical record. Physical examination of the lungs showed a decrease in the sound of the left lung. The volume of urine was reduced and changed to brown. In addition, the urine sodium dithionate test for PQ on the first day at admission was strongly positive and defined as purple-colored urine. In his past medical history, the patient had a history of addiction to methadone and opium inhalation.

Based on the local protocol for PQ management, for those patients who present late after exposure, the gastrointestinal endoscopy is not performed. In the initial tests of the patient, an increase in blood liver enzymes, urea, creatinine, as well as respiratory acidosis in the venous blood gas analysis was seen. Table 1 shows the patient’s laboratory tests patient during 4 days of hospitalization in the intensive care unit (ICU).

Three hours after admission to the emergency room, O₂ saturation without oxygen was 30% and after receiving oxygen with bag valve mask, it reached 60%. At this time, the patient was intubated and transferred to the ICU. Dialysis access was placed in the left femoral vein.

The patient was treated with fluid hydration, oxygen supplement, antioxidants including Vitamin E 300 units daily (Osvah Pharmaceutical Company, Tehran, Iran) intramuscular, Vitamin C 2 g intravenous (IV) infusion, and then 150 mg/h daily infusion for 2 days (Daroupakhsh Pharmaceutical Company, Tehran, Iran), methylprednisolone 1 g IV infusion on the first day and then 500 mg daily infusion (for 3 days) (Jaber Pharmaceutical Company, Tehran, Iran), N-acetylcysteine 300 mg/kg/day IV infusion for 1 day (Aurum Pharmaceuticals Limited, Romford Essex, England). After consultation regarding body burns, tetracycline skin ointment was given daily. He underwent hemodialysis two times, 8h each time (the first and third day of hospitalization) due to a positive dithionite test and renal failure. On the third day of hospitalization, potassium chloride 15% was prescribed due to reported hypokalemia.

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High-resolution computed tomography (HRCT) and chest X-rays (CXRs) of the patient were reported in Figure 1. In the HRCT, alveolar opacity by air bronchograms of both lungs with evidence of acute respiratory syndrome was seen. In addition, increased lung opacity was defined in the CXR report.

**Table 1.** Laboratory tests of the patient during 4 days of hospitalization in intensive care unit.

| Laboratory test | Time | Fourth day | Third day | Second day | First day |
|----------------|------|------------|-----------|------------|-----------|
| Hematology     |      |            |           |            |           |
| Hb (g/dL)      |      | 10.2       | 10.7      | –          | 12.8      |
| WBC (×10⁹/L)   |      | 13.8       | 7.9       | –          | 8.5       |
| PLT (µL)       |      | 220        | 237       | –          | 279       |
| Liver          |      |            |           |            |           |
| AST (IU/L)     |      | 720        | 740       | 375        | 385       |
| ALT (IU/L)     |      | 920        | 880       | 445        | 475       |
| ALP (IU/L)     |      | 1210       | 1264      | 1210       | 1407      |
| BILL. T (mg/dL)|      | 10.35      | –         | 7.35       | 6.8       |
| BILL. D (mg/dL)|      | –          | –         | 5.93       | 2.9       |
| PT (s)         |      | >60        | 11.7      | 11.6       | 12.7      |
| PTT (s)        |      | >120       | 26        | 30         | 84.4      |
| INR            |      | >6         | 1.17      | 1.16       | 1.27      |
| Blood sugar    |      |            |           |            |           |
| BS (mg/dL)     |      | –          | 214       | 254        | –         |
| Kidney         |      |            |           |            |           |
| BUN (mg/d)     |      | 26         | 83        | 57         | 135       |
| Cr (mg/dL)     |      | 1.5        | 4.86      | 3.91       | 6.5       |
| Electrolyte    |      |            |           |            |           |
| Na (mEq/L)     |      | 140        | 145       | 14.17      | 130       |
| K (mEq/L)      |      | 3.5        | 4.5       | 4.2        | 5         |
| VBG            |      |            |           |            |           |
| pH             |      | 7.36       | 7.19      | 7.27       | 7.24      |
| PCO₂ (mm Hg)   |      | 57.2       | 58.3      | 60.9       | 66.2      |
| HCO₃ (mEq/L)   |      | 31.7       | 21.8      | 27         | 27.5      |

Hb: hemoglobin; WBC: white blood cell; PLT: platelet; AST: aspartate aminotransferase; ALT: alanine transaminase; ALP: alkaline phosphatase; Bill. T: bilirubin total; Bill. D: bilirubin direct; PT: prothrombin test; PTT: partial thromboplastin time; INR: international normalized ratio; BS: blood sugar; BUN: blood urea nitrogen; Cr: creatinine.
The level of patients’ consciousness decreased 16 h after admission with GCS 4/15 (no eye contact and no response to painful stimulation and intubation). On the fourth day of hospitalization, the patient gradually developed sinus bradycardia, with O₂ saturation of 35%–40% with FIO₂ of 100%. Finally, the cardio-respiratory arrest occurred, and the patient died despite cardiopulmonary resuscitation.

**Discussion**

PQ is a highly toxic compound and has a high mortality rate in poisoning due to the lack of a specific antidote. Although severe cases of poisoning are usually the result of ingestion; however, one of the most important routes of exposure is dermal. In our case, PQ poisoning was confirmed by positive urine sodium dithionate test. As the absorption of PQ from the skin is low and takes time, the urine sodium dithionate test may become positive even after several days based on exposure amount.

The patient had second- and third-degree burns and multiple ulcers focusing on his body due to PQ spraying. Different people have diverse cutaneous reactions to accidental contact with PQ; some do not react to PQ, or only local lesions on the skin and nails without systemic involvement. Hoffer and Taitelman reported that accidentally exposure through skin and eye in 15 patients during PQ spraying, resulted in only local lesions due to a single contact without systemic involvement. In addition, in the study of Castro-Gutiérrez et al., only 53% of farmers had skin rashes or burns after 2 years of chronic contact with sprayers of toxin.

However, dermal contact with this toxin causes severe systemic reactions and death. The first death from PQ dermal absorption was reported in 1974, followed by at least 11 fatalities and 2 nonfatal cases of systemic poisoning via a dermal route. Various factors contribute to the spreading of toxicity, including inter-individual variability, an increase in the percentage of the body surface exposed to the herbicide, and the presence of injury and skin lesions before exposure to the toxin. Finally, the lack of timely washing of the body, inappropriate protective equipment, and delay in primary treatment management may be responsible for more severe intoxication.

In this case, the report was observed: some of factors that contribute to progression severity such as lack of protective equipment during working and do not wash the body in the early hours of contact with a toxin, and finally, late referral for treatment (6 days after the initial contact with the toxin).

However, this point should be considered that the focus of the lesions was more on the upper body and axillary in the mentioned case, whereas the perineal and axillary skin has smaller and more fragile blood vessels that could be contributed to greater absorption during PQ exposure. Moreover,
pulmonary insufficiency, hypoxia, and kidney failure with strongly positive urine sodium dithionate test could be the factors that caused the patient’s death.

There are some limitations in this report. Our patient had also dysphagia which may be due to entering the PQ into the mouth through the accidental spraying PQ 20% solution on his face. We could not rule out gastrointestinal injury as endoscopy was not performed for the patient based on local protocol as the time elapsed from exposure was 6 days.

Although our patient had respiratory distress, as he did not show other symptoms of COVID-19, we did not perform the test for possible COVID involvement, which was not also available at that time in our hospital. Many ulcers focusing on his body (face and around the mouth, forehead, neck, shoulders and axillary, elbows, hands, and feet) induced by PQ enhance its more absorption and could explain systematic sign and respiratory distress. Also, the volume of PQ was sprayed into the face and body of the patient had not mentioned in the medical record of the patient which may be another limitation of the study to explain the amount of exposure.

Conclusion
In conclusion, dermal exposure to PQ can be fatal, especially when accompanied by significant delays in starting treatment and involving respiratory and renal systems. The exact effectiveness of current medical management in PQ poisoning is controversial. Therefore, it is very important for emergency physicians to suspect PQ poisoning when facing chemical burns and skin lesions, particularly when the skin lesions are associated with systemic symptoms, and to investigate the possibility of poisoning. Considering immediate removal of poison from the skin, hair, and nail contamination, assessment of the severity of skin damage and treatment of burns, and assessment of the risk of systemic absorption (evaluation of lung, kidney, and liver function factors) are important factors. They should use protective equipment when working with PQ, and in case of initial contact of the body with the poison, after rapid body washing with soap and water, they should refer the patient to the relevant medical centers for further investigation.

Acknowledgements
The authors appreciate the patient’s legal guardian for their consent to this research project.

Author contributions
N.E.-M. and Ro.M. developed the idea and design of the study. S.H. and Ra.M. researched the literature and wrote part of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript. Ro.M and Ra.M. acted as the respective authors.

Availability of data and materials
This case report has no restrictions on the availability of data and materials.

Declaration of conflicting interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

Ethical approval
This article is a case of registry design data approved by the Isfahan University of Medical Sciences with code IR.MUI.MED.REC.1400.651.

Human right
All authors adhered to the Helsinki Declaration; patient confidentiality and anonymity were preserved.

Informed consent
Written informed consent was obtained from the legally authorized representative of the patient to publish with anonymized data.

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