Intravenous Paraquat Poisoning

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Paraquat is a substance that is highly poisonous to humans. Oral ingestion is the most common pathway of poisoning. Intravenous paraquat poisoning is rare and is strongly associated with attempted suicide. The clinical presentations of such a scenario would appear to be quite different from those of oral ingestion. Herein, we present a case of an intravenous drug abuser who injected paraquat in an effort to commit suicide. He received hemoperfusion and intravenous cyclophosphamide treatment and parenteral pulse therapy with methylprednisolone. Nevertheless, he suffered from dyspnea at around 48 hours post-exposure. His condition improved transiently, but he eventually died from severe hypoxia. The findings from our case and those of previously reported cases indicate the grave prognosis and lack of effective management of intravenous paraquat poisoning. [*J Chin Med Assoc* 2009;72(10):547–550]

Key Words: hemoperfusion, herbicide, intravenous poisoning, paraquat, suicide

Introduction

Pesticide poisoning is common in Taiwan, and a suicide attempt is the most common reason for pesticide exposure.[1] Oral ingestion is the most common pathway of poisoning.[1] Herbicide is a type of pesticide, and paraquat is a widely used herbicide. Patients with paraquat exposures have a high mortality rate in Taiwan.[1] Paraquat is highly toxic to humans after oral ingestion. The initial clinical features of paraquat ingestion include oral ulcer, nausea, vomiting and diarrhea. The patient will usually die from multiorgan failure, such as metabolic acidosis, depression of myocardial and respiratory function with pulmonary fibrosis, and renal or hepatic failure. To the best of our knowledge, intravenous paraquat poisoning is rare,[2–6] and the clinical presentation and prognosis of such a scenario would appear to be quite different from that of oral ingestion.[2–6] Only 1 case of survival has been reported.[4] Herein, we present a patient who attempted suicide by means of intravenous paraquat injection.

Case Report

This 28-year-old male was an intravenous drug abuser. He had attempted suicide several times previously, and had received treatment for major depression. He diluted 10 mL of 24% paraquat solution with normal saline and injected it into a superficial vein in his left forearm. Whilst the toxic substance was infusing, the skin along the infused vessel developed an erythematous appearance and the injection site became painful. The patient was quickly sent to our emergency department, approximately 2 hours post-exposure. At this time, the patient's consciousness was clear and he had vital signs with a pulse of 74 beats/min, a respiratory rate of 23 breaths/min, and blood pressure of 101/65 mmHg. He had low body temperature (34.9°C). The abnormal physical findings for this young man were left arm erythema and induration. Initial complete blood counts and biochemical data, including electrolytes, liver- and renal-function tests, revealed normal results, and subsequent urinalysis did not reveal any abnormalities. The patient's arterial blood-gas assessment displayed a PaO_2 of 120 mmHg in room air. A qualitative urine test confirmed the presence of paraquat, and plasma paraquat concentration (6 hours after injection) was 2.38 μg/mL.

The patient received 6 consecutive 8-hour sessions of hemoperfusion with activated charcoal; thereafter, urine paraquat level became negative. Intravenous cyclophosphamide treatment (1 g) and parenteral pulse therapy with 1 g methylprednisolone daily for 3 days

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were undertaken at the same time as hemoperfusion. The erythematous change, pain and induration of the patient's left arm progressed gradually. Some blisters appeared 4 days after poisoning (Figure 1). The patient suffered from dyspnea around 48 hours post-exposure, and his respiratory rate was 32 breaths/min. At this time, his arterial blood gas displayed a PaO_2 value of 49.8 mmHg in room air. Follow-up chest X-ray revealed increasing infiltration over bilateral lower-lung fields (Figure 2). Intubation with mechanical ventilator support was then performed for acute hypoxic respiratory failure. The patient's dyspnea subsided gradually, and the hypoxemia and chest X-ray results (Figure 3) also appeared to reverse following hemoperfusion and methylprednisolone pulse therapy. Unfortunately, the patient complained of dyspnea on the 10th day of admission. The degree of hypoxemia (PaO_2 of 51.6 mmHg) worsened. At this time, chest X-ray revealed the presence of diffuse fibrotic changes (Figure 4). Pulse therapy was therefore repeated with 1 g/day of methylprednisolone for 3 consecutive days in an attempt to suppress the inflammation. In addition, we prescribed oral dexamethasone subsequent to the pulse steroid therapy. Although he received this aggressive management, the hypoxemia progressed. On the 21st day subsequent to paraquat poisoning, our patient eventually died from severe hypoxemia.

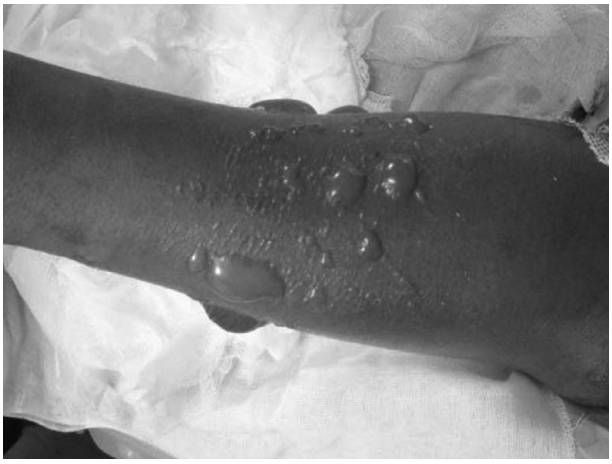

Figure 1. Four days following paraquat poisoning. Several vesicles featuring erythematous and indurated changes have developed around the paraquat-infused vessel in the patient's forearm.

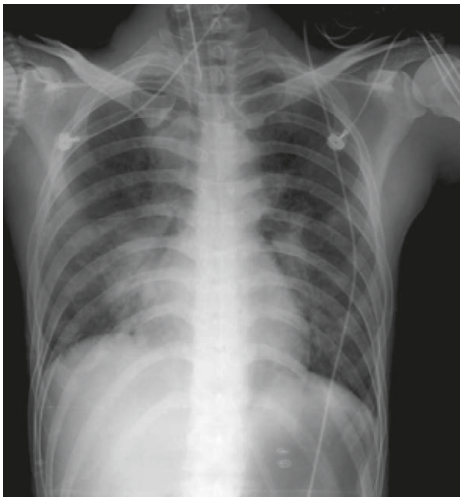

Figure 2. Chest radiograph of the patient taken on the 3rd day of hospitalization shows ill-defined alveolar infiltration predominant in bilateral lower-lung fields with patch consolidation in the right middle lobe of the lung.

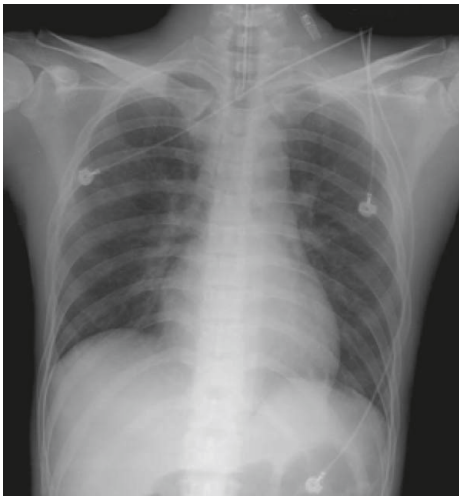

Figure 3. Chest radiography taken on the 5th day of hospitalization depicts great improvement in the patient's lungs (compared with Figure 2).

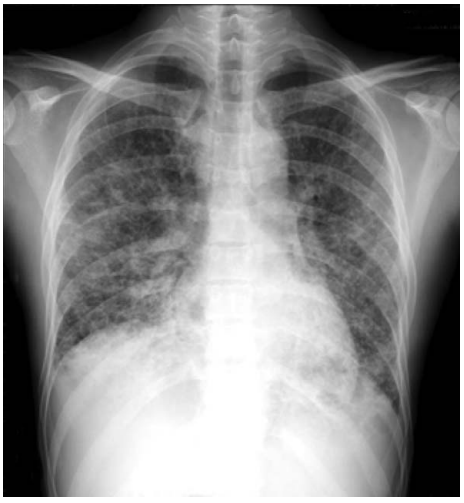

Figure 4. Chest radiography taken on the 10th day of hospitalization demonstrates diffuse fibrotic change and reticulonodular opacities in bilateral lungs.

Discussion

Paraquat (1,1′-dimethyl-4,4′-dipyridylium) is an effective herbicide; it is highly toxic to humans and most animals. Unintentional and intentional oral ingestion are the most common pathways of paraquat poisoning in humans. According to a search of the related literature, intravenous paraquat injection is extremely rare. MEDLINE was searched from 1966 to 2008 for cases of intravenous paraquat poisoning in the English-language literature. Only 6 cases were found.[2–6] The available medical data for the 6 patients and our patient (total, 7 cases) are summarized in Table 1.

The symptoms in patients with poisoning include local and systemic toxicological effects. The local clinical presentations of intravenous paraquat poisoning differ from those of oral poisoning. Patients with oral paraquat ingestion suffer from oral ulcers, hemoptysis and gastrointestinal (GI) symptoms such as nausea, vomiting, diarrhea and GI bleeding.[7] These symptoms are caused by direct mucosal irritation.[7] Patients with intravenous paraquat poisoning do not have direct mucosal irritation, but they might have some GI symptoms such as nausea and vomiting,[2,5,6] which may be explained by the systemic effect of paraquat on the central nervous system.[5] Patients with intravenous poisoning have local skin or vessel symptoms.[2,5,6] In our patient, the injection site developed an erythematous condition, and tissue swelling was initially apparent around the site of the injected vessel. Then, several vesicles of varying sizes appeared. Such findings have also been reported by Hsu et al.[5] The skin presentation may be explained by local reaction due to the occurrence of trivial extravasation of paraquat solution to adjacent soft tissue, and/or by local blood-vessel injury, such as phlebitis, related specifically to paraquat injection. The systemic toxicological effects, such as renal hepatic or pulmonary damage, come later than local effects, and are suspected to be dose-dependent and lethal.[7] The systemic toxicological effects are also suspected to have faster onset in patients with intravenous poisoning than in patients with oral ingestion.[5,6]

Although there is no definitive treatment for paraquat poisoning, patients with oral paraquat poisoning require immediate treatment that includes: (1) preventing GI absorption; (2) increasing plasma elimination; and (3) preventing pulmonary damage.[7] Several methods are suggested to prevent pulmonary damage, including immunosuppressive therapy, vitamin E, deferoxamine, and *N*-acetylcysteine.[7] Although there is a lack of good evidence of the clinical efficacy of immunosuppressive therapy with glucocorticoids and cyclophosphamide in a systematic review,[8] a current meta-analysis suspects that immunosuppressive therapy is likely to decrease lung fibrosis and mortality.[9] No treatment protocol was suggested for patients of intravenous paraquat poisoning. Because of the limited number of cases (Table 1), there are no existing treatment protocols to improve the grave outcome for patients with paraquat injection.

Proudfoot et al were the first to suggest that paraquat concentration-time ratio before treatment

Table 1. Summary of clinical manifestations and outcomes of patients with intravenous paraquat poisoning

Patients	Age (yr)	Sex	Plasma paraquat concentration (μg/mL) (hours after injection)	Predictive survival rate (%)*	Management	Outcome
Harley et al[2]	24	F	NA	NA	Forced diuresis + ascorbic acid + superoxide dismutase + α-tocopherol + steroid	Died after 20 d
Hendy et al[3]	42	M	2.3 (4)	30–50	Hemoperfusion × 2	Survived
Fernandez et al[4]	21	M	0.62 (6)	50–70	Hemoperfusion + propranolol	Died after 15 d
Hsu et al[5]	35	F	18 (5)	< 10	Hemoperfusion × 2 + cyclophosphamide + pulse therapy	Died after 4 d
Hsu et al[5]	37	M	19.6 (1)	< 10	Hemoperfusion × 2 + cyclophosphamide + pulse therapy	Died after 5 d
Choi et al[6]	31	F	21 (10)	< 10	Hemoperfusion × 2	Died after 3 d
Present case	28	M	2.38 (6)	20–30	Hemoperfusion × 6 + cyclophosphamide + repeated pulse therapy	Died after 21 d

**According to the formula of Hart et al.[12]*

could predict the outcome of poisoning.[10] Several prediction methods were developed. Five methods were compared in a large cohort study, and these methods are likely to be accurate in predicting death for patients with paraquat poisoning.[11] Hart et al created a nomogram with 6 concentration-time curves of about 10–90% survival probability,[12] and the nomogram is easy to use in the emergency department. Sawada et al presented a severity index of paraquat poisoning (SIPP) which was calculated according to the serum level of paraquat,[13] and the serum concentrations were lower than plasma concentration.[7] We could not calculate the SIPP because we only have the plasma paraquat concentrations of the 6 patients with intravenous paraquat from published reports. Jones developed an equation to predict the probability of survival for any specific time,[14] but it is too complex to be of practical use in the emergency department. Because paraquat enters the body more rapidly by intravenous injection than by oral exposure, the prognosis of intravenous paraquat poisoning might be worse than that of oral poisoning. We tried to predict the mortality rate of the 6 patients with intravenous paraquat according to the formula of Hart et al,[12] and 5 of the 6 patients were considered to have a very high mortality rate (Table 1).[2–6] Six of the 7 patients (including the present case) did not survive after aggressive treatment (Table 1).[2–6] Only 1 miraculous case survived from severe pulmonary damage due to paraquat administered intravenously and orally.[2] The predictive mortality method according to the formula of Hart et al[12] seems to be suitable for use with cases of intravenous paraquat. However, as there is an inadequate number of cases who survived, we cannot test the survival prediction ability of Hart et al's nomogram.

In conclusion, intravenous paraquat poisoning is rare, and patients may manifest with a variety of symptoms including initial dermal changes. These symptoms often appear immediately subsequent to paraquat injection. The prognosis of intravenous paraquat poisoning is graver than that of oral poisoning. Further experimental and clinical trials are required to search for an effective treatment for patients suffering from intravenous paraquat poisoning.

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