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Case Report

Rapid Progression of Multiple Organ Dysfunction Caused by High-dose Diquat Poisoning in a Teenager

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Abstract Diquat is one of the most commonly used herbicides in the world. Since paraquat, another widely used herbicide, was banned in the Chinese market in 2016, the use of diquat in China has been increasing. In recent years, cases of diquat poisoning, either in accidents or in suicide attempts, are more frequently seen in the clinic. Herein, we report a rare case of acute high-dose diquat poisoning in a previously healthy 17-year-old male teenager. He was admitted to the emergency department in our hospital 30 minutes later after ingesting 20 grams (100ml) of diquat solution during a suicide attempt. His blood laboratory tests suggested rapid development of liver and kidney dysfunction, along with acute myocardial injury, coagulopathy, and elevation of inflammatory markers. After he was admitted to the emergency department, he received treatments including gastric lavage, forced diuresis, hemoperfusion, fluid and electrolyte replacement, and administration of cathartics, antioxidant compounds, and glucocorticoids. However, despite prompt and aggressive treatments, his condition did not improve and he passed away 40 hours after diquat ingestion. This rare case report in a male teenager represents the rapid progression of high-dose diquat poisoning and highlights the need for seeking preventive response measures and effective treatments.

Keywords:Diquat, Poisoning, Herbicide, Multiple organ dysfunction syndromes, Anti-oxidant

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Introduction

Diquat (1,1'-ethylene-2,2'-bipyridinium) is a non-selective, fast-acting herbicide widely used in many countries for weed control in agriculture. It belongs to the bipyridyl class, a group of redox-active compounds that can cause strong oxidative damage (1, 2). Diquat is considered moderately toxic; however, if swallowed, inhaled, or absorbed through the skin in large amounts, it can be extremely harmful to humans and can even cause multiple organ failures and death (3). Since the withdrawal of another widely used herbicide, paraquat, from the Chinese market in 2016, the use of diquat in China has gradually increased and several cases of rapid acute diquat poisoning with different symptoms and disease courses have also been reported (4-6). However, to date, the management of diquat poisoning remains a challenge in the clinic and its toxicokinetics and clinical features are not fully understood.

The mechanisms of toxicity of diquat have been reviewed in several reports (1, 3). Briefly, diquat acts as a powerful redox cycler and can convert to free radicals. Therefore, it could exert toxic effects on human cells by generating reactive oxygen species (ROS) and reactive nitrogen species (RNS), which leads to oxidative stress and eventually cell death. Although diquat can be absorbed by dermal, ocular, pulmonary, and oral routes, most severe poisoning cases are reported in those who ingested concentrated formulations, and mortalities are often seen in

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those ingested volumes greater than 15 mL of 20% concentrated formulations (3). The reported clinical manifestations vary in patients ingested different doses. Patients who ingested less than 1 g of diquat (20%) usually have gastrointestinal tract symptoms and putative development of kidney function impairment; fully recover is possible when urgent medical care is provided. Multiple organ dysfunction and rhabdomyolysis can be seen in those who ingested 1 to 12 g diquat (20%) and most patients could still recover after treatments (6). The mortalities occur in most patients who ingested over 12 g diquat (20%); investigations on effective treatments or preventive measures for this group of patients are particularly needed. Current therapeutic strategies focus on reducing absorption and enhancing the elimination of diquat, as well as symptomatic treatment and supportive care for the patients. No antidote for diquat poisoning is available so far.

In this report, we presented a case of a 17-year-old male teenager who self-administered 20 g of diquat solution during a suicide attempt. He developed multiple organ dysfunction within 24 hours and his blood tests suggested acute severe inflammatory responses. Despite the extensive treatments including gastric lavage, forced diuresis, hemoperfusion, fluid and electrolyte replacement, and administration of cathartics, antioxidant compounds, and glucocorticoids, the patient's condition did not improve and he passed away 40 hours after diquat ingestion. This rare case represented the rapid progression of high-dose diquat poisoning and addressed the need for seeking preventive measures and effective treatments.

Case presentation

A 17-year-old previously healthy male teenager presented after ingesting approximately 100 mL of diquat (20g/100ml) with suicidal intent after relationship conflicts with his girlfriend. After 30 minutes later, he experienced restlessness and numbness and was sent to the emergency department of our hospital. The patient was in good health condition and denied having a medical history of other diseases such as diabetes, hypertension, and cardiovascular diseases. At the emergency room, his vital signs were as follows: pulse rate 97 beats/min, blood pressure 141/95 mmHg. His mind was clear, and his spirit was slightly irritable. His cardiopulmonary examination showed no abnormality in the heart and lungs. No abdominal tenderness and rebound pain, and no abnormal positive signs for the nervous system were detected. His laboratory tests are shown in Figure 1. After admission to the hospital, the patient immediately received the treatments including gastric lavage (10000 ml water), mannitol catharsis, massive fluid replacement, diuresis, antioxidants (Vitamin C and Glutathione), gastric mucosal protection, and hemoperfusion (3.5h).

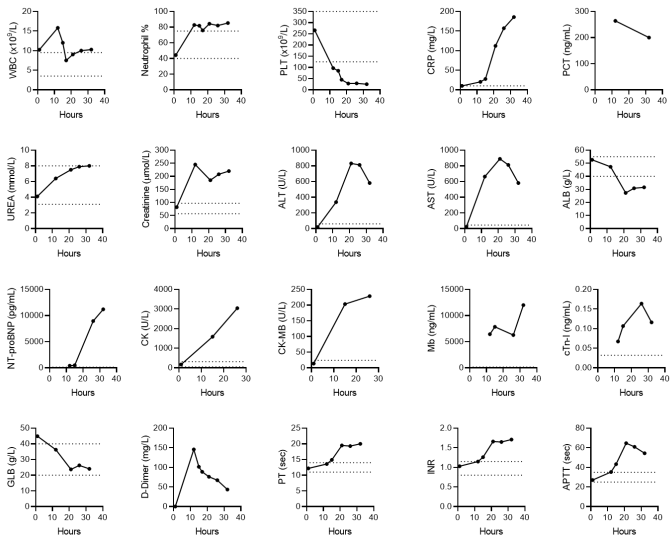

Figure 1. The blood test results of the patient at different hours after ingesting diquat. WBC: white blood cells; PLT: platelets; CRP: c-reactive protein; PCT: procalcitonin; ALT: alanine transaminase; AST: aspartate aminotransferase; ALB: albumin; CK: creatine kinase; CK-MB: creatine kinase-MB; Mb: myoglobin; cTn-I: cardiac troponin I; GLB: globulin; PT: prothrombin time; INR: international normalized ratio; APTT: activated partial thromboplastin Time.

After 3 hours, the patient had symptoms including delirium and high fever and black greenish rotten stools. His vital signs markedly declined 10.5 hours later (pulse rate 157 beats/min, blood pressure 77/33mmHg). His blood pressure recovered to 125/84mmHg after fluid replacement therapy. After 11.5 hours, his blood tests suggested acute kidney and liver injury and potential infections (Figure 1). Due to the rapid progression of his condition, he was transferred to the intensive care unit (ICU) for further treatments. After being admitted to ICU, he was given sedation and analgesia. Later, penicillin, tazobactam sodium, and imipenem cilastatin sodium were successively given for anti-infection. Methylprednisolone 500 mg, cyclophosphamide 0.2g, and ulinastatin were given for anti-inflammation. Transfusions of blood component infusion were given to improve the coagulation function. Continuous veno-venous hemofiltration (CVVH) treatment was also given. However, 20.5 hours later, the patient developed consciousness disturbance and intubation was required. Despite the active treatment, the patient's condition did not significantly improve. His liver and kidney function, respiratory function, and coagulation function continued to decline. His lab test results showed the markers of myocardial injury and rhabdomyolysis were also notably elevated (Figure 1). Clinical death due to circulatory failure was pronounced 40 hours after administration.

Discussion

High-dose diquat (>12 grams) poisoning causes multiple organ injuries and is usually lethal. In 1983, McCarthy et al. reported a case of a 23-year-old man who ingested 300 mL of diquat and died 14 hours post-admission after developing renal and central nervous system symptoms and cardiovascular collapse (7). In 2020, Xing et al. reported a case of a 21-year-old man who ingested 100 mL of diquat (20 g/100 mL) and died 15 days after admission due to multiple organ dysfunction (8). More recently, Yu et al. reported two adult cases who ingested around 100 mL of diquat (20 g/100 mL) and developed encephalopathy; one patient died 18 days after due to cardiac arrest and another patient survived over 3 months (4). These cases, together with our case, highlight the high mortalities caused by high-dose diquat poisoning.

In this case, the patient's digestive tract was damaged to varying degrees after ingesting diquat, which was manifested in injuries to the oral mucosa, esophageal mucosa, and gastrointestinal mucosa. His chest CT report suggested that multiple parts of the esophagus were dilated. After 11 hours, his blood test report showed the elevation of inflammatory markers including neutrophil percentage, c-reactive protein (CRP), and procalcitonin (PCT), suggesting potential infections. Because the patient was healthy and without malignant tumor and blood diseases. Hence, bacterial infection was suspected as a cause for the elevation of blood inflammatory markers. The source of infection was considered to be the gastrointestinal flora. It has been shown that gut bacteria translocation could occur under certain conditions and could lead to the occurrence of sepsis (9).

In addition to the gastrointestinal tract, damage to the liver, kidney, and lung post-diquat injection is also severe in this patient. In the lungs, diquat mainly causes mild reversible damage to type I alveolar cells, but does not cause damage to type II cells. At present, there is no evidence that diquat can lead to pulmonary fibrosis (3, 10, 11), but pulmonary infiltration and exudation or pulmonary edema can occur in patients with acute severe poisoning (12, 13). At present,

most hospitals in China use glucocorticoids or immunosuppressants to treat patients with acute diquat poisoning, but no related basic and clinical studies have shown that the two drugs can improve the prognosis. Glucocorticoids and immunosuppressants are often used in patients with paraquat poisoning due to their effective improvement of pulmonary interstitial edema, prevention of pulmonary fibrosis, and strong anti-inflammatory effect (14). However, because diquat does not cause damage to type II pneumocytes and there is no evidence that diquat can cause pulmonary fibrosis, whether treatment with glucocorticoids or immunosuppressive agents can improve the prognosis of patients with acute diquat poisoning needs further investigation.

The patient in this case had tachycardia and his electrocardiogram suggested myocardial ischemia. Later, he developed hypotension and his blood tests showed increased levels of markers for myocardial injury. These findings support that acute diquat poisoning causes myocardial damage at an early stage. Currently, no relevant experimental data is available on the correlation between diquat ingesting dose and the degree of myocardial injury. Therefore, for patients with high-dose diquat poisoning, prompt evaluation of the degree of myocardial injury and corresponding treatments are recommended.

Diquat has toxic effects on central nerve cells and can cause a variety of central nervous system symptoms, including cerebral edema, cerebral infarction, brainstem hemorrhage, and central pontinemyelinolysis (8, 13). In this case, the patient presented delirium, positive neck resistance and limb tendon reflex, which might be associated with abnormal nervous system function. However, due to the rapid progression of the patient's condition and the decision of the family to abandon treatments, there is a lack of intracranial imaging results to confirm the presence of central nervous system changes in the patient.

So far, there is no specific effective treatment for diquat poisoning. Current treatment strategies include prompt termination of absorption (gastric lavage, catharsis, *etc.*) and promotion of elimination (enhanced diuretic, hemoperfusion, and hemodialysis). Although there is a lack of evidence that hemoperfusion or hemodialysis can improve the prognosis of patients, its clearance effect is definite. Therefore, early blood purification treatment is still a preferred choice for patients with moderate to severe conditions (3, 15). In addition, because antioxidants can eliminate and prevent the generation of reactive oxygen species caused by diquat, the use of antioxidants, such as N-acetylcysteine (NAC), Glutathione (G-SH), melatonin, and vitamin C (16, 17), is also considered as one of the treatment methods for diquat poisoning patients. However, its efficacy requires further investigation.

In summary, this rare case report supports the rapid progression of multiple organ dysfunction caused by high-dose diquat poisoning and highlights the need for developing preventive measures and effective treatments.

Conflict of Interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author Contributions

First author: Formal analysis, Writing – original draft; Second author: Conceptualization, Writing – review & editing; Corresponding author: Data curation, Methodology,

Writing – review & editing, Supervision.

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Data Availability Statement

All relevant data are within the manuscript.

Ethics Statement

This case study was reviewed and approved by The Ethics Committee of The Seventh Hospital of Sun Yat-sen University. The patients' relative provided the written informed consent to participate in this study.

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