

Paraquat intoxication induced sick sinus syndrome

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Abstract

Introduction: Paraquat (1,1'-dimethyl-4, 4'-dipyridylum) intoxication is a major medical problem in developing countries. The ingestion of paraquat is fatal in humans and its mortality rate is as high as 50%. Paraquat intoxication has a systemic effect on the lung, kidney, gastrointestinal tract, central nervous system, and even on the heart.

Case report: A female patient visited our emergency room after suicidal ingestion of paraquat herbicide. The patient received a conventional treatment, including gastric lavage with large amounts of normal saline and charcoal, steroids and antioxidant therapy. Hemoperfusion was consecutively done twice within 12 hours. During the conventional treatment, her heart rate abruptly dropped to below 50 beats per minute and she complained of associated symptoms like dizziness and weakness. At that time her systolic blood pressure was below 80 mmHg. A sinus bradycardia was shown on her electrocardiogram (ECG) and the 24 hours ambulatory ECG monitoring showed a severe sinus bradycardia, sometimes junctional escape rhythms, and non-conducted atrial premature complexes. We administered dopamine as an inotropic agent for two days. After the prompt treatment, her heart rhythm returned back to normal sinus rhythm and the blood pressure was stabilized.

Discussion: The heart is one of the most severely affected organs in paraquat intoxication. After paraquat intoxication, cardiac complications like arrhythmia or myocardial necrosis aggravate the general condition of the patients. Consequently, the early detection of multi-organ dysfunctions and the prompt initiation of proper management for specific organ injuries are very important for the prognosis of a patient intoxicated with paraquat, especially in case of cardiac involvement such as arrhythmia, myocardial necrosis or others.

Keywords: Paraquat; Sick sinus syndrome

Introduction

Paraquat (1,1'-dimethyl-4, 4'-dipyridylum) intoxication is a major medical problem in developing countries, especially in agricultural countries. Most cases of intoxication in adults result from suicidal attempts rather than homicidal or accidental exposure [1,2]. According to several previous literatures, the lethal toxicity of paraquat leads to a high mortality rate with over 50%~60% [3-5]. The exact mechanism of the severe toxicity of paraquat is not understood well yet, however, paraquat can generate free oxygen radicals near mucosal membranes resulting in mucosal damages in several organs such as the lung, kidney, gastrointestinal tract and even in the heart [1,6]. The main acute systemic effects of paraquat intoxication are pulmonary edema and inflammation, convulsion, cardiac injury, renal failure, hepatic failure and others. Finally, those effects can appear with multiple organ failure, including progressive pulmonary fibrosis, acute tubular necrosis of kidney, centrilobular hepatic necrosis, focal cerebral hemorrhage and rarely, with an extensive myocardial necrosis [2,7]. Herein we report an interesting case presenting with sick sinus syndrome after paraquat intoxication.

Case Report

A 48 year-old-female with a depressive disorder visited our emergency room. She was rushed to the hospital by her relatives,

approximately 90 minutes after ingestion of paraquat in a suicidal attempt. She was noted by her relatives as having ingested the toxin with alcohol. The patient had a depressive disorder without medical treatment. Her total consumption of paraquat was about three mouthfuls, which means approximately 60 ml of the commercial 20% concentrate form. When she arrived at the emergency room, her vital signs were stable; especially her heart rate was 76 beats per minute. She had several episodes of vomiting before arriving at the emergency room and complained of epigastric pain, nausea and sore throat. On physical examination, she presented with severe tenderness on the epigastrium and severe excoriation of her mouth and lips. Her initial laboratory data showed a leukocytosis and a well-compensated high anion gap metabolic acidosis without any abnormal findings. Chest radiograph and electrocardiogram (ECG) were normal. The result of sodium dithionite urine test for paraquat was positive with 3+. After she arrived at the emergency room, the patient was immediately treated by gastric lavage with large amounts of normal saline, followed by an infusion of 1 g/kg activated charcoal via a nasogastric tube. The patient got hemoperfusion twice within 12 hours after arriving at the emergency room and simultaneously intravenous injections of dexamethasone (20 mg/day) for 7 days. We also used acetylcysteine, lipoic acid and vitamin C as antioxidant agents. On the 4th hospital day, she complained of exertional dyspnea and fever. At this time, a chest radiograph was conducted and a pulmonary fibrotic change was visible. On the 7th hospital day, the blood pressure abruptly fell to 80/50 mmHg with a heart rate below 50 beats per minute and a sinus bradycardia was visible on the ECG (Figure 1).

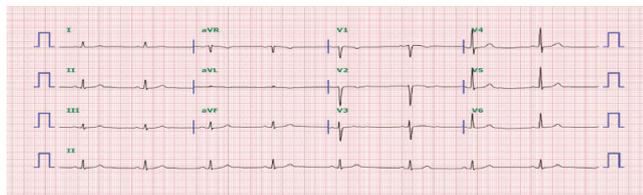


Figure 1: An electrocardiogram shows sinus bradycardia (heart rate 50 beats per minute). At that time, the systolic blood pressure was below 80 mmHg and the patient felt mild dizziness and weakness.

At that time, the patient felt a mild dizziness and general weakness. A 24 hours ambulatory ECG monitoring was conducted and severe sinus bradycardia, sometimes junctional escape rhythms and non-conducted atrial premature complexes were seen (Figure 2).

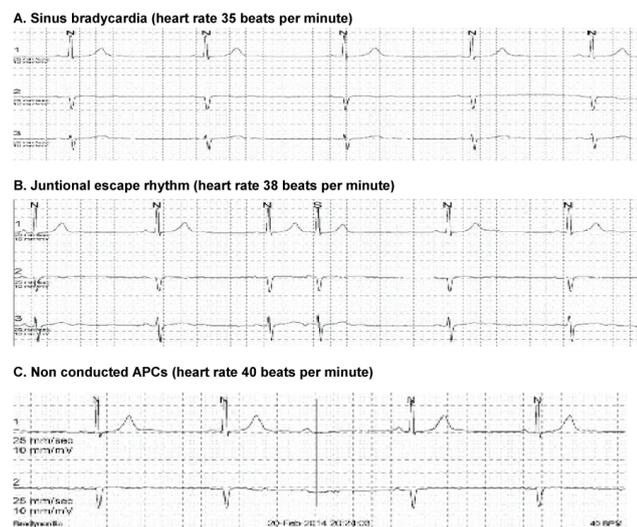


Figure 2: The 24 hours ambulatory electrocardiogram monitoring (Holter test) shows severe sinus bradycardia (A) and junctional escape rhythm (B) and non-conducted atrial premature complexes (APCs) (C). The patient had associated symptoms and signs, such as dizziness, weakness and hypotension.

Even if there was no sinus pause with duration over 3 seconds, we could conclude that she had a sick sinus syndrome because there were associated symptoms and signs like dizziness, weakness and hypotension combined with the ECG abnormalities mentioned above. There was no evidence for causes of a sick sinus syndrome such as pharmacologic agents, electrolytes imbalance, hypoxia or an intrinsic cause like ischemic heart disease [13]. There was no any change on her laboratory data except for the aggravation of leukocytosis and a slight decline of the estimated glomerular filtration rate (GFR). Dopamine was used as inotropic agent for two days. After that, her vital signs recovered and her heart rhythm returned to a normal sinus rhythm (Figure 3), but the pulmonary fibrosis was progressively aggravated (Figure 4).

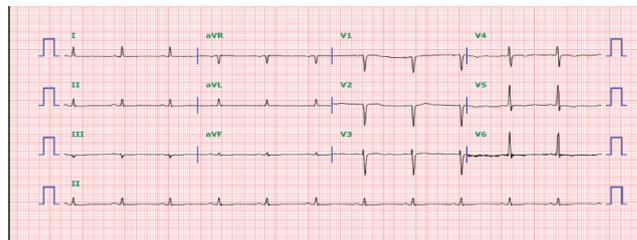


Figure 3: The cardiac rhythm returned to normal sinus rhythm after inotropic agent administration.

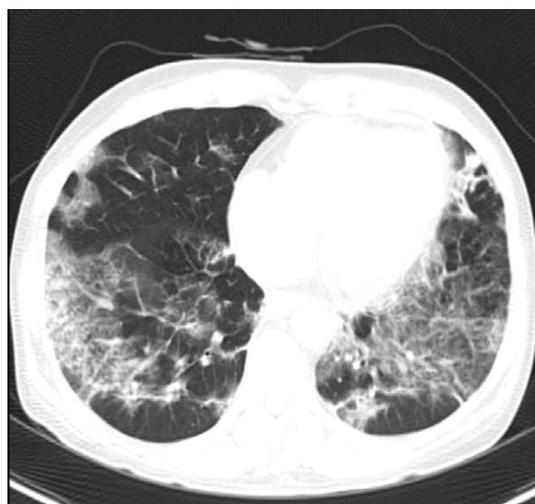


Figure 4: The patient complained of exertional dyspnea. The high resolution computerized tomography shows progressive pulmonary fibrosis.

The conventional treatment including steroids and antioxidants was continued. Her general condition improved and the patient could be discharged. In addition, she had no further episodes of cardiac arrhythmia such as sick sinus syndrome noted in her follow up.

Discussion

Paraquat is a very toxic bipyridil herbicide unless it is appropriately and carefully used [1]. The extremely high fatality of paraquat intoxication results from an inherent severe toxicity of paraquat and the lack of effective management [6]. The annual mortality of patients intoxicated with paraquat was reported to be over 50% in several previous studies. And most cases of paraquat intoxication in adults are due to suicidal attempts rather than accidental exposure [2,3,6]. Symptoms of paraquat intoxication are dose-dependent. Mild symptoms of paraquat intoxication can appear with doses up to 20 mg/kg, which usually produce gastrointestinal problems like vomiting, diarrhea and an excoriation of the oropharyngeal mucosa. Moderate symptoms of paraquat intoxication can occur with doses between 20 mg/kg and 50 mg/kg of paraquat. These doses of paraquat may produce a lung injury like pulmonary fibrosis, acute renal failure, acute hepatic injury and even a heart injury. A fulminant intoxication with at least 50 mg/kg paraquat may lead to multiple organ failure and

death within 3 days [2]. According to several previous studies, the mortality rate of patients intoxicated with paraquat was over 50%. In addition, the lung involvement was over 90% and a cardiac involvement especially appeared in about 40% of the patients intoxicated with paraquat [7]. Although the lung is a major target organ in paraquat intoxication and acute respiratory failure resulting from pulmonary fibrosis is the most common cause of death in patients intoxicated with paraquat, cardiac manifestations can frequently appear. However, the underlying mechanism of cardiac damage is not known yet [8,9].

The clinical picture of cardiac involvement shows a broad spectrum with varying degrees of severity; ranging from minimal ECG changes to extensive myocardial necrosis [7,10]. We reported one case with cardiac involvement, which showed a delayed atrial fibrillation induced by paraquat intoxication. However, until now, we were not able to find any literature showing arrhythmia other than atrial fibrillation due to paraquat intoxication. The heart is one of the most seriously affected organs in paraquat intoxication and cardiac disturbances may lead to fatal complications [11]. As known, a sick sinus syndrome is a generalized abnormality of cardiac impulse formation that may be caused by intrinsic diseases of the sinus node or by extrinsic causes. The diagnosis of sick sinus syndrome may be difficult because of the slow and variable course of the syndrome. And some of its symptoms (e.g. fatigue, confusion, dizziness, palpitations, syncope etc.) are mild and nonspecific, so it may often be misdiagnosed as another disease [12]. The electrocardiographic evidence of sick sinus syndrome includes inappropriate sinus bradycardia, sinus exit block, sinus pause or arrest. A sick sinus syndrome has a protean presentation with variable degrees of clinical severity. Also, a sick sinus syndrome may often lead to sudden death if it remains untreated with appropriate managements [14,15]. Therefore, a symptomatic bradycardia should be treated with proper methods regardless of its cause. In general, the conventional treatment of paraquat intoxication includes gastric lavage with large amounts of normal saline, gastric lavage with charcoal, treatment with antioxidants, cyclophosphamide, dexamethasone, hemoperfusion and so on [2]. But, until now, there have been no definite guideline for the treatment of paraquat intoxication and it varies from conservative care only to conventional treatment [6]. Consequently, the early detection of multi-organ dysfunctions and the prompt initiation of proper management for specific organ injuries are very important for the prognosis of a patient intoxicated with paraquat, especially in case of cardiac involvement such as arrhythmia, myocardial necrosis or others. In the presented case, the paraquat-induced bradycardia produced associated symptoms and signs such as dizziness, general weakness and hypotension. These symptoms and signs also aggravated the patient's general condition. However the vital signs and general condition of this patient were normalized by the immediate and proper management with an inotropic agent. Although there is no known mechanism of cardiac injury after paraquat intoxication [8], we

may carefully say that the early detection and immediate management of cardiac manifestations are very important in patients intoxicated after paraquat ingestion.

Conclusion

Paraquat intoxication can cause an injury in several organs, including the lung, kidney, gastrointestinal tract, central nervous system and the heart. Cardiac manifestations after paraquat intoxication can frequently appear with a broad spectrum, ranging from minimal ECG changes to myocardial necrosis. Herein we reported an interesting case with paraquat induced sick sinus syndrome.

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