Case Study

Paraquat Poisoning Presenting as Sinus Bradycardia; A Rare Clinical Manifestation

Indranil Sen[1], Spandan Bhadury[2], Dilip Roy[3]

[1]Assistant Professor, department of General Medicine, North Bengal Medical College & Hospital, [2]Professor, department of General Medicine, North Bengal Medical College & Hospital, [3]Junior Resident, department of General Medicine, North Bengal Medical College & Hospital

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Abstract

Paraquat poisoning is a common yet fatal consequence in rural India. Usually it presents with local corrosive effects and early multi organ dysfunction involving lungs, liver and kidney. Here we present a case of a 25 years old man who presented with paraquat poisoning and developed asymptomatic bradycardia after admission. He was treated conservatively with isoprenaline drip, N-acetyl cysteine, steroids and other supportive therapy. The bradycardia recovered spontaneously and patient was discharged.

Keywords: paraquat, bradycardia, isoprenaline

Background

Paraquat is a chemical herbicide which is used quite extensively in India. But it is a highly toxic compound to human subjects and accidental exposure or suicidal attempts are often fatal even in low doses and there are delayed detrimental effects too. The mortality rate of acute paraquat poisoning has a wide variation ranging from 33% to 91% from different studies. [1]the in hospital mortality ranges from 46-55% from different studies.[2] The severity of paraquat poisoning is classified into three categories: mild, moderate-to-severe, and fulminant according to organ system involved and prognosis. Mild poisoning is characterized by local corrosive effects and minor gastrointestinal tract effects like vomiting and pain abdomen. Moderate-to-severe poisoning often leads to acute renal failure, acute hepatitis, acute lung injury, and progressive pulmonary fibrosis. Fulminant poisoning results in multiple organ failure and death within a few days.[3] Still there are gaps in medical literature regarding clinical and pathological features and under reporting of poisoning cases particularly from rural areas is a problem. We report a rare cardiac manifestation following paraquat poisoning in a medical college in north Bengal, India.

Case Report

A 25 year old male presented to the emergency department of our hospital with history of ingestion of about 30 ml of herbicide containing paraquat in

Corresponding Author: Indranil Sen, Assistant Professor, department of General Medicine, North Bengal Medical College & Hospital.

E-mail: docindranilsen@gmail.com

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30% concentration in a suicidal bid about 6 hours ago. He presented with shortness of breath and pain over throat, chest and abdomen. There was no history of any co-morbidity, any serious illness requiring prolonged treatment or hospitalization, psychiatric illness or recurrent self harm. On examination he was in obvious physical discomfort with oral ulcers. Vital parameters were regular pulse with rate 90/min, blood pressure 110/70 mm of Hg in both upper limbs in supine posture, temperature was normal with oxygen saturation 93% in room air. On systemic examination significantly there was epigastric tenderness, rest of the examination was within normal limits. Diagnosis was based on history and patient relatives also had a snapshot of the bottle from which the poison was consumed. Although confirmation can be done by toxicological analysis of gastric lavage it was not done in this case because of risk of further injury and perforation of the visible oral ulcers. Routine blood examination showed haemoglobin 14.1 g/dL, WBC 5700, platelet 1.2 lakh/cc, urea 10 mg/dL, creatinine 0.7 mg/dl, Na 141 mmol/l, k 4.3 mmol/l, total bilirubin 0.6 mg/dl, AST 12U/L, ALT 10 U/L. Chest x ray and ECG done during admission was normal. The following day patient developed bradycardia and hypotension. ECG showed sinus bradycardia. He was put on inotropes and 2 mg atropine was given intravenously but there was no alteration in pulse rate. The hypotension responded adequately to medication and he was put off inotropes after 24 hours. He was put on isoprenaline drip and transvenous temporary pacing was planned if patient becomes symptomatic. On further investigations echocardiography showed good biventricular systolic function and normal diastolic filling. Thyroid profile and coagulation profile was normal, NT-proBNP 163 pg/mL, CPK-MB 2.50 ng/ml. Patient was put on pulse dose of methy prednisolone 1 gram intravenously for 3 days followed by oral methyl prednisolone 16 mg for 7 days. Other supportive therapy included N-acetyl Cysteine 400 mg intravenously thrice daily, proton pump inhibitors, sucralfate, antibiotic ceftriaxone and local chlorhexidine and triamcilone application. Holter monitor was done which showed infrequent supra ventricular ectopics without any sinus pause or arrhythmia. Patient was followed up for 3 more days and gradually his pulse rate normalized and clinical and biochemical parameters were stable. So he was discharged after 5 days of hospital stay in a haemodynamically stable condition.

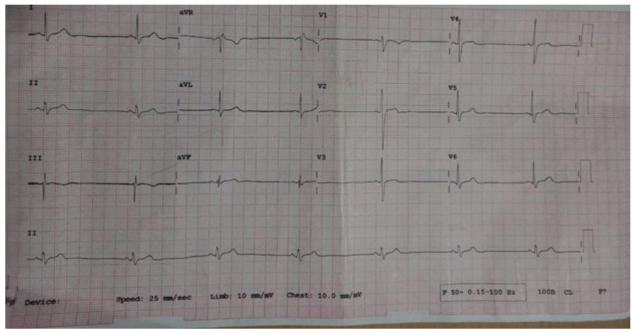

Figure 1: ECG showing sinus bradycardia

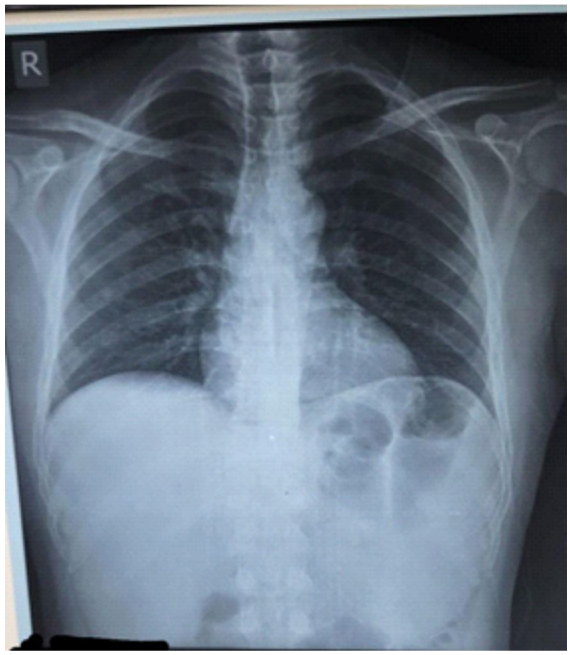

Figure 2: chest x ray on day 1 of admission

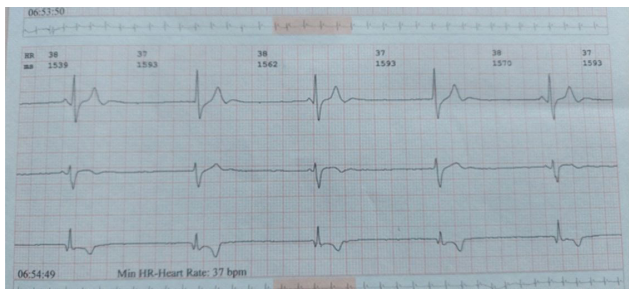

Figure 3: Holter strip showing bradycadia

Discussion

Paraquat $C_{12}H_{14}N_2C_{12}$ is a potent herbicide belonging to the dipyridyl family which is very

much in vogue in the rural agricultural set up. The pure inorganic salt is crystalline, white and odorless and commonly procured aqueous solutions which the patient ingested is red in color. It has a caustic action on biological tissues and harmful in all forms of exposure as contact poison to skin and mucous membranes, droplet inhalation along with the common mode of ingestion. [4]Ingestion is the commonest and most fatal mode with a minimum lethal dose of 35 mg/Kg. [5] Absorption occurs in the small intestine with a facilitated, saturable diffusion. In a study done on isolated stripped rat intestinal mucosa three phases of paraquat absorption were identified:- (i) a rate which was faster than diffusion (2-20 mg/ml paraquat); (ii) a rate which was slower than diffusion and obeyed saturation kinetics, with an apparent Km = 116 mM and Vmax = 11.3 mumol/g/hr, at paraquat concentrations up to 150 mg/ml: and (iii) a rate similar to that of diffusion at 200 mg/ml paraquat. Paraquat absorption at 200 mg/ml was also associated with an increase in mucosal permeability and reduction in potential difference. [6]Different hospitals have protocols to administer adsorbents like Fuller's earth, activated charcoal, bentonite to prevent this absorption. The effects are deterministic :-(1) up to 2 g of paraquat ingestion has a bimodal effect, with initial local oro-labial mucosal effects which regress after 2-3 days & simultaneous pulmonary edema or ARDS. (2) about 2-6 g of paraquat ingestion lead to mucosal lesions and within 24 hours there is ulceration and involvement of gastrointestinal tract further complicated by perforation, mediastinitis, peritonitis. Death may occur within 3-5 days due to renal dysfunction or ARDS. (3) Ingestion of >6g of paraquat leads to early multi organ dysfunction with cardiovascular collapse and a grave outcome. [7] Mechanism of cell death is due to generation of superoxide radical induced oxidative stress, depletion of protective NADPH radicals leading to lipid peroxidation, mitochondrial dysfunction and membrane degeneration.[8] Cell death may also occur through necrosis or apoptosis. Generally organs with high metabolic activity, high oxygen tension and energy requirement like lung, heart, kidney and liver are affected first with minimal cerebral involvement as paraquat doesn't cross the blood brain barrier. The deleterious effects in the lungs range from an early destructive phase i followed by a proliferative phase characterized by edema, infiltration by inflammatory cells, fibroblast deposition leading to early fibrosis. Histological evidence of multi organ dysfunction is found from acute tubular necrosis, hemorrhagic cystitis, hepatocyte, esophagogastric necrosis and frank cardiac hemorrhage. [9, 10, 11] The clinical manifestations depend on the organ system involved and mode of entry. In the commonest mode of ingestion there is local pain and swelling of the mouth. There may be serious gastrointestinal effects like nausea, vomiting, pain abdomen, diarrhea often bloody, haematemesis and melena. Respiratory manifestations are shortness of breath and cough which may progress to respiratory failure in form of ARDS and pulmonary fibrosis. Renal involvement leads to acute kidney injury in form of oliguria, haematuria and heavy proteinuria. There may be acute liver failure in form of coagulopathy, jaundice and hepatic encephalopathy. Central nervous system involvement in form of headache, encephalopathy in form of seizures and mental confusion is common. In addition, autopsy studies of patients who died of acute paraquat poisoning showed diffuse cerebral edema and deep white matter lesions, which are mainly located around the lateral ventricles and the third ventricle; and electron microscopy showed obvious brain edema, myelin damaging, microglia or astrocytes proliferation and meningitis. It is uncertain, however, whether these lesions are secondary changes of multiple organ failure or simply reflect the process of brain death. [12] So almost all systems may be involved in paraquat poisoning.

In our patient there was some local gastrointestinal tract involvement which responded to conservative measures but quite strikingly asymptomatic bradycardia which didn't respond adequately to cholinergic medications. Mechanism may be due to toxic myocarditis or sinus node dysfunction. Incidences of Paraquat poisoning presenting with sinus bradycardia are rare as per literature. The first reported case was by Song et al but the patient was later found to have hypothyroidism which was excluded in our patient [13] Myocarditis was ruled out by normal echo and normal levels of NTproBNP. Another two cases were reported in Southern India but there also patients had retroviral and hepatitis B virus infection respectively which could be a confounding factor. [14 and 15] The exact mechanism of transient sinus bradycardia in our patient couldn't be determined but as he didn't respond adequately to anticholinergic drug atropine so probably there was no shortening of atrial refractory periods which

heralds sinus node dysfunction. Now he is kept under follow up in OPD basis to see whether there is any cardiac long term effect.

The prognosis following poisoning is dismal. A previous study had determined the following factors: young age, percutaneous or inhalational route, exposure to less paraquat, and lesser degrees of leukocytosis, acidosis, and renal, hepatic, and pancreatic failures on admission as good prognostic factors of survival after acute paraquat poisoning. [16] Further studies are needed to comprehensively detect the effects and prognosis following paraquat poisoning.

Conclusion

Paraquat poisoning has a myriad of clinical presentations although the initial presentation is similar to any corrosive ingestion. Bradycardia is a rare phenomenon for this poison as tachycardia is the norm. The exact mechanism could not be understood but the conclusions were it was transient and self-limiting so caution to be exercised before proceeding with dual chamber transvenous pacing. An electrophysiology study could have been helpful to detect sinus cycle length, sinus node recovery time and atrial refractoriness but the facility is not available in our cath lab. If the patient presents with bradycardia again or similar cases are encountered EPS can be done.

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Conflict of interest: There was no conflict of interest.

Consent: Patient and relatives had given consent for publication of the case.

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