Paraquat Poisoning: First Case Report in Australia

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Citation

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Abstract

Paraquat poisoning is almost universally fatal even if ingested in small quantity. Multiple accidental exposures have been reported in Australia but in this case report, we shall discuss about the first case of intentional paraquat poisoning in Australia found in the medical literature. The patient was intubated as soon as she arrived at the emergency department and was treated in intensive care unit for 23 days but unfortunately passed away due to respiratory failure. This case report serves to explore the complications associated with paraquat poisoning and current recommended treatment.

CASE

A 47-year-old female presented to emergency department with ongoing nausea, vomiting and small volume haematemesis following ingestion of one large drink of Paraquat (Sprayseed 250) 3 hours prior to presentation. The actual amount of Paraquat ingested was unknown. There were no history of abdominal pain, diarrhoea, seizure or fever.

Past medical history included depression. Four months prior to current presentation, she was admitted with attempted suicides through wrist cutting, strangling with cords and jumping out of a truck secondary to depression and anxiety related to family breakdown. During this previous admission, she underwent six sessions of electroconvulsive therapy (ECT). Her medications at this current presentation included olanzapine 10mg daily and mirtazapine 45mg daily. There were no family history of mental illnesses. She lived with her two teenage children in suburban Melbourne.

On examination, the patient was alert and orientated and had a respiratory rate of 20 per minute, heart rate of 80 per minute, blood pressure of 138/72 mmHg and oxygen saturation of 99 percent on room air. Physical examination was unremarkable apart from tenderness in the epigastric area. Initial blood test results were mostly normal apart from a white cell count of 20.3 x 109/L with neutrophil count of 18.38 x 109/L, hypokalaemia of 3.1 mmol/L and lactate level of 3.7 mmol/L (normal 0.5-2.2 mmol/L). Liver function test was within normal ranges. Urine test revealed a high level of Paraquat. Initial chest X-ray showed no acute abnormality. The patient was admitted to intensive care unit due to high risk of multi-organ failures and commenced on intravenous pantoprazole infusion. She was also intubated and treated with charcoal and haemofiltration as per discussion with Poisons Information Centre. Fuller's Earth was not available at our service. The treating team was advised against administration of excessive oxygen due to further formation of free radicals. Gastric lavage was deemed inappropriate due to the late presentation and underlying haematemesis.

The patient's admission was complicated by multiple medical issues.

- Haemodynamic instability needing inotropic support
- Anaemia requiring multiple blood transfusions
- Acute renal failure treated with haemofiltration
- Acute liver failure with coagulopathy necessitating transfusion of fresh frozen plasma and cryoprecipitate
- Right lower lobe pneumonia due to methicillin resistant Staphylococcus aureus (MRSA)
- Progressive diffuse pulmonary fibrosis requiring high dose of intravenous dexamethasone
- Respiratory failure
- Persistent fever despite ongoing Infectious Disease team input

The patient received ceftriaxone 2g daily and metronidazole twice daily for 4 days, varying dose of vancomycin for 14 days, piperacillin/tazobactam 4.5g twice daily for 9 days, meropenem 500mg thrice daily for 8 days and dexamethasone 8mg thrice daily for 6 days and 8mg twice

daily for 3 days. CT chest performed on day 9 of admission revealed bilateral diffuse ground glass opacity involving upper and lower lobes consistent with acute respiratory distress syndrome. The patient was ex-tubated on day 10 but had to be re-intubated nine hours later due to respiratory distress. A percutaneous tracheostomy was performed on day 12. Her fraction of inspired oxygen (FiO2) requirement was worsening despite appropriate management. Following a family meeting, full palliative care was commenced on day 23 and the patient was pronounced dead on the same day. Coroners Court of Victoria was contacted because it was a reportable death involving suicide and poisoning.

Figure 1

Chest X-ray on day 1: nil abnormality

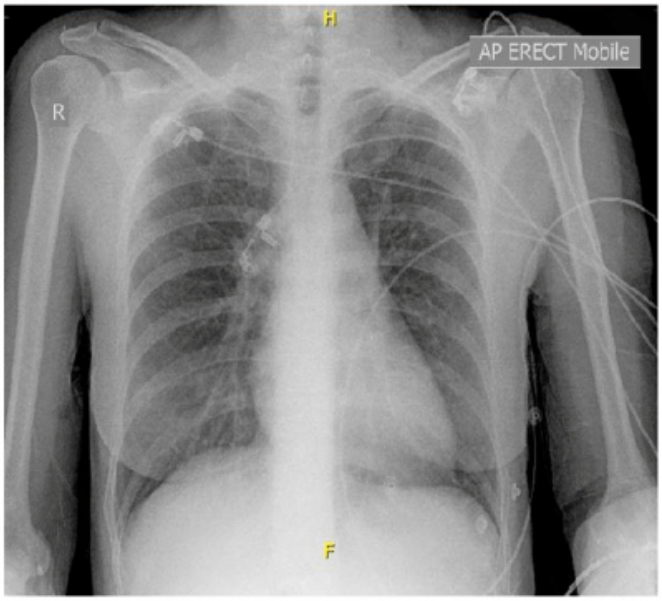


Figure 2

Chest X-ray on day 22: bilateral diffuse mixed infiltrate

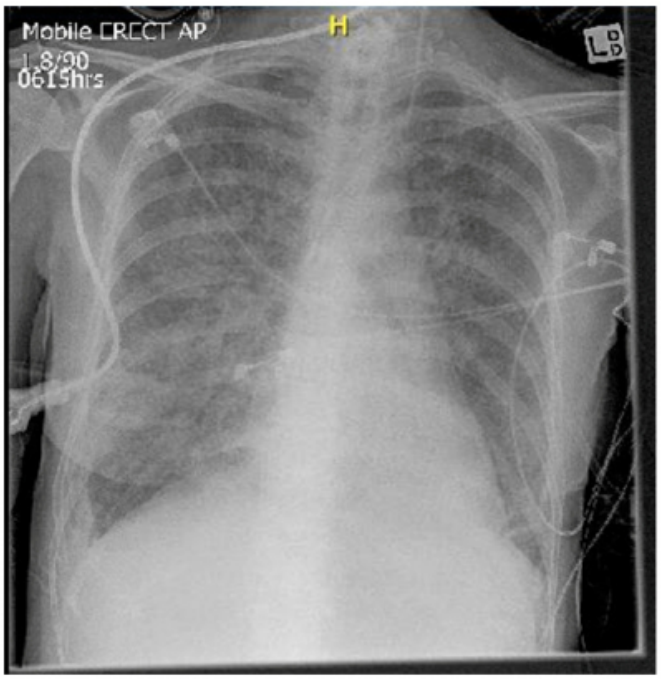


Figure 3

High resolution CT chest on day 9: Ground glass opacity involving upper lobes

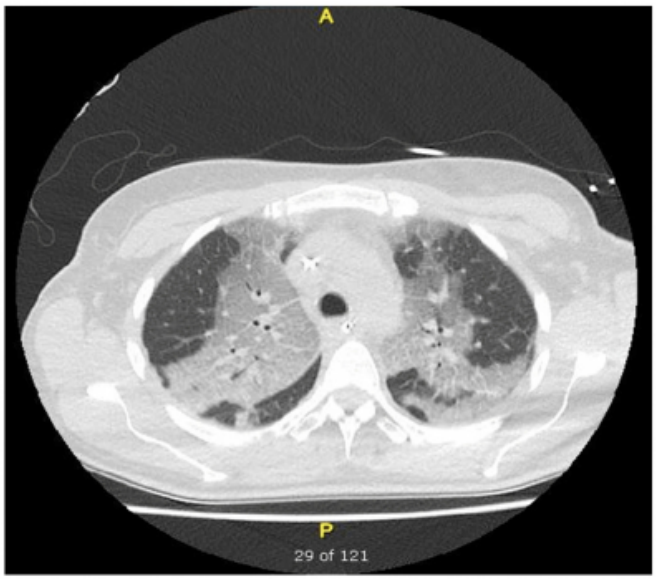
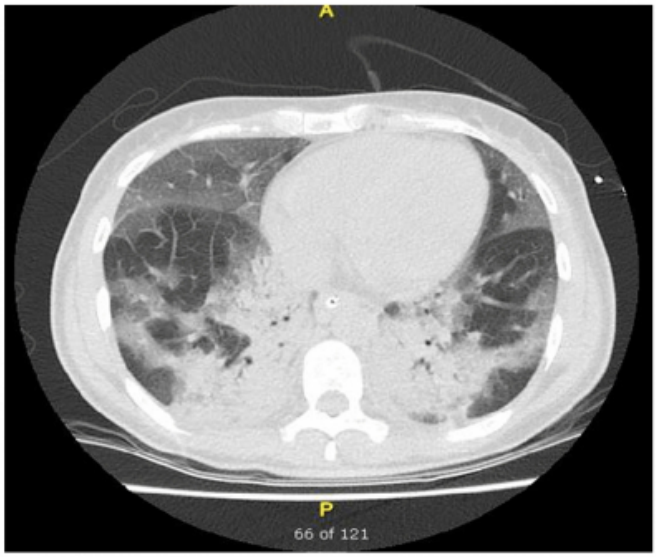


Figure 4

High resolution CT chest on day 9: Ground glass opacity involving lower lobes



DISCUSSION

Paraquat was first produced for commercial purposes in 1961 and is widely used as a herbicide.1 Paraquat exposure can be acquired through ingestion, inhalation and breached skin surfaces.2 The severity of toxicity depends on the amount, duration and strength of contacted paraquat. Paraquat is distributed throughout the body post-exposure and can lead to multi-organ failures. It is the leading cause of lethal poisoning in many parts of the world, especially in Asia. It is universally fatal if ingested in large quantity. According to the data from Monash Injury Research Institute, there are 41 cases of paraquat exposure over a period of 14 years from 2000 to 2013 and majority of these cases occurred in the farms.3 However there are only two cases of intentional ingestion in the state of Victoria, Australia since 2000 and both resulted in death.4 The patient described in this case report is one of them and is the first case report on paraquat poisoning in Australia found in the medical literature.

The underlying mechanism of paraquat toxicity is due to inhibition of superoxide dismutase, leading to release of hydrogen and superoxide anions, resulting in lipid peroxidation, generation of highly reactive oxygen and nitrate species, and NADPH depletion.5, 6 Exposure through ingestion is followed by gastrointestinal disturbance, including oropharyngeal ulcerations, nausea, vomiting, abdominal pain and diarrhoea. The mucosal ulcerations may result in bleeding, perforation and pneumomediastinum.6 Paraquat toxicity mainly targets the lungs and kidneys. Type I and II pneumocytes actively accumulate paraquat against concentration gradient, thus the lung is particularly prone to the toxic effects of paraquat.5 These patients may present with dyspnoea and haemoptysis. Pulmonary oedema and haemorrhage usually present within 24 hours, followed by progressive pulmonary fibrosis in the next 1 to 2 weeks. In fact, pulmonary fibrosis and respiratory failure are the most common causes of death in paraquat poisoning. Ingestion in large quantity can result in fulminant pulmonary, renal, hepatic and cardiac failures and seizures due to involvement of the central nervous system.6

The subsequent prognosis of paraquat poisoning is mainly determined by the quantity of exposure and paraquat concentration in the plasma7 and urine. The Proudfoot's Curve that was developed in 1979 is the most widely accepted logarithm used for deciding the eventual outcome based on the plasma concentration between 4 and 24 hours post-exposure.8, 9 Based on this curve, accurate prognosis can only be decided at least 4 hours after ingestion because the level of paraquat peaks at 2 hours and declines rapidly afterwards. This data was further extrapolated to 15 days by Scherrmann in 1987. The level of toxicity can also be measured using the urinary sodium dithionate test. The reactions can be graded as colourless, light blue, navy blue and dark blue, with the latter two signifying significant toxicity.5 A recent study by Wunnapuk et al at the University of Queensland revealed that certain renal injury biomarkers may be better at detecting early renal damage associated with paraquat poisoning compared to creatinine. However the study has only been undertaken in rats hitherto.10

Paraquat toxicity is highly fatal even in small quantity. On presentation, resuscitation should be performed as per standard guidelines. These patients may be in respiratory distress due to aspiration, metabolic acidosis or underlying acute alveolitis. It is important to note that excessive administration of oxygen should be avoided because it increases the oxidative stress.6, 11 Clothings exposed to paraquat should be removed. Contact precaution should be undertaken and this was practised during the care of our patient described above. Paraquat is excreted through the kidneys and it is important to treat the patients with intravenous fluids, especially if they are hypotensive, and to establish strict fluid balance.

In line with the Proudfoot's Curve, the most effective modality in managing these patients is to remove paraquat from their system, in addition to supportive measures. If the

patients present early, gastric content should be aspirated followed by the administration of activated charcoal or Fuller's Earth to reduce intestinal adsorption. Gastric lavage has not been recommended by Gawarammana and Buckley due to the corrosive nature of the chemical.6 The mucosal injury associated with paraquat ingestion may necessitate analgesia and nasogastric feeding. Even though 90 percent of paraquat is rapidly excreted through the kidneys within the first 12 to 24 hours,12 subsequent renal failure and shifting of residual paraquat into deeper compartments make clearance difficult. This, together with rapid acquisition of paraquat into the lungs, warrant immediate intervention with haemodialysis or haemofiltration (if haemoperfusion is not available) particularly in those with acute renal failure but it also mean that minimal amount of paraquat is removed through these interventions. It is essential to have ongoing monitoring of renal function, electrolytes and blood lactate concentration.13

Maturation of mononuclear profibroblasts into fibroblasts in the lung results in pulmonary fibrosis. Immunosuppressive agents such as cyclophosphamide, methylprednisolone and dexamethasone have been proposed to be effective in counteracting these inflammatory changes. Apart from that, antioxidants such as vitamin C, vitamin E, N-acetylcysteine, desferrioxamine and salicylic acid have been suggested to improve the outcomes in paraquat poisoning.6 Nonetheless, most of these medications have only been tested in animal studies with minimal human data.

In conclusion, this is no single antidote that is effective against paraquat poisoning at this stage. Supportive measures are vital in managing these patients. Immunosuppression and antioxidants may provide promising results in the future with further large-scale studies.

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