Clinical Toxicology

Acute renal failure in a case of paraquat poisoning with relative absence of pulmonary toxicity

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Summary: A 37 year old male presented after the ingestion of paraquat (‘Gramoxone’, 20% w/v). Plasma paraquat concentrations indicated that he had a greater than 50% probability of death. The patient survived following a period of acute oliguric renal failure and with only mild pulmonary toxicity.

Introduction

Paraquat (1,1′-dimethyl-4,4′-bipyridylium dichloride) is widely used as a herbicide, and is usually marketed either as a 20% (w/v) solution (‘Gramoxone’) or in a granular form (25–80 g/kg, for example ‘Weedol’, ‘Pathclear’). Toxicity is usually seen following ingestion, and may range from mild (ingestion of <20 mg paraquat ion/kg body weight) to fulminant (>40 mg paraquat ion/kg body weight),¹ with the latter commonly proving fatal. In addition to intense local irritation of the mouth, oropharynx and oesophagus, multiple organ (cardiac, respiratory, hepatic and renal) failure may occur, although pulmonary features predominate and are the usual cause of death.

We describe a case of severe paraquat poisoning complicated by the development of oliguric renal failure, and in which there was only mild pulmonary toxicity. The patient made a complete recovery.

Case report

A 37 year old male with a previous history of depression and alcoholism presented to a peripheral hospital following the ingestion of several mouthfuls (at least 50 ml) of ‘Gramoxone’. He was initially given 20 ml syrup of ipecacuahana and subsequently 50 g activated charcoal, prior to transfer to the West Midlands Poisons Unit.

Plasma paraquat concentrations were assayed by polarized fluorescence immunoassay (Abbott TDX, Abbott Diagnostics, Maidenhead, UK), using reagents kindly supplied by Professor J. Landon, St Bartholomew’s Hospital, London. On admission to this unit, plasma concentrations of paraquat were 1720 µg/l and 590 µg/l at 3.5 and 7.5 hours, respectively, from the time of ingestion. These levels indicated that there was a greater than 50% risk of a fatal outcome.² He progressively developed oropharyngeal inflammation of sufficient severity that he was unable both to eat or drink.

Despite intravenous fluid replacement therapy his urine output fell progressively over the 12 hours following his admission. Despite the infusion of dopamine and bolus doses of frusemide, he remained oliguric and his serum creatinine rose from a concentration of 128 µmol/l on admission to 527 µmol/l over a period of 4 days. Peritoneal dialysis was begun at this stage and continued for a period of 13 days until there was evidence of recovery of renal function. Enteral nutrition by a fine-bore nasogastric tube proved intolerable to the patient, and hence total parenteral nutrition was given by way of a Hickman line for a total period of 7 days.

On initial and subsequent clinical examination his lung fields were clear to auscultation. Formal pulmonary function tests, however, showed a combined pattern of restrictive and obstructive ventilatory defects over the initial period of his admission. The ratio of forced expiratory volume in 1 second to forced vital capacity reached a nadir of 50% on day 15, in comparison to a normal value of 81% (S.D. 10%). Values on admission and at

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discharge from hospital were 65% and 64%, respectively. This could, in part at least, be attributed to difficulty in co-operation with the test, since the oropharyngeal inflammation caused discomfort when accommodating the mouthpiece of the apparatus. However the alveolar gas transfer factor corrected for lung volume varied between 1.79 and 1.98 mmol/min/kPa/l (n = 5) and hence remained within the reference range (mean 1.76, S.D. 0.27), and this finding is in contrast to the typical pulmonary abnormality of paraquat toxicity.\textsuperscript{3} Serial arterial blood gas estimations, moreover, showed no indication of hypoxaemia. Chest radiographs taken on admission and regular intervals thereafter (daily for the first week and twice weekly until discharge) showed ill-defined shadowing at the base of the left lung field, although this neither progressed nor resolved.

There was no evidence of hepatic toxicity at any stage. Biochemical liver function tests were at all times normal.

Clinically the patient remains well, with no symptoms of exertional dyspnoea and a good effort tolerance. On recovery the patient also interestingly exhibits a transverse band of white discolouration of the nail plate, a recognized feature of paraquat poisoning.\textsuperscript{4}

Discussion

The patient described was extremely fortunate to survive the ingestion of what would normally be considered to be a fatal dose of paraquat, and moreover unusual that he had so little evidence of pulmonary toxicity. The most conservative estimate of the amount he ingested is 50 mg paraquat ion/kg body weight: ingestions of greater than 40 mg/kg usually follow an acute fulminant course with 100% mortality, and always with pulmonary damage.\textsuperscript{1} The reason this patient survived is not clear. Ragoucy-Sengler et al.\textsuperscript{5} recently reported a series of paraquat ingestions in which three patients unexpectedly survived despite having apparently fatal plasma paraquat concentrations. All three survivors were, as was our patient, heavy consumers of alcohol. Ragoucy-Sengler et al. suggest that a former history of alcohol abuse may protect against paraquat toxicity, and speculate that changes in antioxidant levels may be important.

Paraquat is eliminated mainly by the kidney and acute renal failure is a recognized complication of paraquat poisoning, with reports of both oliguric\textsuperscript{6,7} and non-oliguric\textsuperscript{8,9} cases. Beebejaun et al. found proximal renal tubular necrosis by histopathological examination of a fatal case of paraquat poisoning,\textsuperscript{10} consistent with the observations of Ecker et al.,\textsuperscript{11} who observed that functional paraquat renal toxicity was restricted to the proximal nephron in mice. Paraquat poisoning may lead to a Fanconi syndrome with a variety of proximal tubular abnormalities, including glycosuria, phosphaturia and aminoaciduria, as shown in the series of three cases reported by Vaziri et al.\textsuperscript{12} In two of these cases, glomerular filtration improved, so illustrating the reversible nature of paraquat-induced renal failure. All three cases, however, ultimately succumbed to respiratory failure. Transient oliguria has been described in other cases of paraquat poisoning,\textsuperscript{6} and in one case was attributed to glomerular and tubular haemorrhage.\textsuperscript{7}

One case of non-oliguric renal failure has been reported which resolved following haemodialysis, and as with the present case, occurred without respiratory insufficiency.\textsuperscript{8} Renal biopsy showed features of acute tubulo-interstitial nephritis, and on recovery there was no evidence of proximal tubular dysfunction. Our case therefore represents a second example of acute renal failure due to paraquat in which there was little evidence of pulmonary toxicity. The renal elimination of paraquat occurs in a biphasic fashion with an early, rapid and a late, slow elimination phase, due possibly to the development of renal tubular damage caused by the paraquat itself. It is possible that this is aggravated by dehydration, hence reinforcing the necessity of fluid replacement as an immediate clinical priority. This was promptly addressed in the current case, facilitated by central venous pressure monitoring. The other priorities of clinical management including the relief of oropharyngeal inflammation, avoidance of oxygen therapy and referral to a specialist centre have been reviewed previously.\textsuperscript{1}

References

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