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Reference

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Single lung transplantation for adult respiratory distress syndrome after paraquat poisoning

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Abstract

Ventilator-dependent patients are considered poor candidates for lung transplantation. A 17 year old boy developed adult respiratory distress syndrome (ARDS) due to paraquat poisoning. A single lung transplantation was carried out with a successful outcome.

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Although ventilator dependence has traditionally been regarded as a relative contraindication for lung transplantation, candidates who deteriorate while on a waiting list and patients who develop acute respiratory failure in the absence of any associated organ dysfunction represent unique situations that merit cautious examination. We report the perioperative management of a patient who developed adult respiratory distress syndrome (ARDS) after paraquat ingestion.

Case history

A 17 year old farmer with a recent history of diarrhoea and abdominal pain was admitted to the hospital because of worsening respiratory distress. The plasma creatinine level was raised (272 µM/l) and bilateral lung infiltrates were seen on the chest radiograph. Renal dysfunction and gastrointestinal signs resolved within one week. However, despite treatment with intravenous antibiotics, corticosteroid, and inhaled nitric oxide (NO), the patient’s respiratory condition progressively deteriorated. A lung biopsy specimen had revealed obliterative bronchiolitis, few inflammatory cells, and extensive fibrosis associated with an intact alveolar framework. Several diagnoses were evoked including farmer’s lung fibrosis, viral infection, and paraquat poisoning. After a multidisciplinary consultation he was accepted as a candidate for an urgent lung transplant since there was no evidence of a septic state or an associated organ failure, and the patient’s relatives denied a suicidal attempt.

Mechanical ventilatory support was continued for five weeks until a suitable lung donor was found. After induction of anaesthesia a left-sided double lumen tracheobronchial tube was inserted. Conventional mechanical ventilation was applied selectively on the right lung with inhaled NO (8–15 ppm). High frequency jet ventilation was applied on the left lung until clamping of the pulmonary artery. Partial cardiopulmonary bypass was instituted and lung transplantation was performed through a standard thoracotomy in the fifth intercostal space. After a cold ischaemia time of 270 minutes the donor lung was reperfused and conventional mechanical ventilation was resumed on both lungs with the application of a PEEP of 5 cm H2O. Weaning from cardiopulmonary bypass was successful with inotropic support (epinephrine 0.1 µg/kg/min). Although respiratory compliance and arterial oxygen tension were markedly improved, the pulmonary artery pressure remained elevated at 37 mm Hg. A trial of inhaled NO (2–20 ppm) was ineffective whereas an incremental infusion of nitroglycerin (1–5 µg/kg/min) induced a progressive fall in pulmonary artery pressure without any deterioration in oxygen exchange or in pulmonary shunting.

Postoperatively, despite signs of anaesthesia emergence and satisfactory chest radiographs and gas exchange, the patient failed to sustain spontaneous breathing as a result of generalised muscular weakness (with normal sensitivity) that was attributed either to prolonged immobilization, administration of corticoid related myorelaxants, or a toxic insult. The diagnosis of paraquat intoxication was confirmed by the patient himself and by immunoassay detection of paraquat in lung and muscle samples (134 µg/g and 328 µg/g, respectively) obtained 59 days after herbicide ingestion. No paraquat had been detected in several plasma samples obtained 4–24 days after the onset of gastrointestinal symptoms. On the 10th day after transplantation a 3 mm right bronchopleural fistula developed that was initially treated by stapling, pleural drainage, and antibiotics. A right pneumonectomy was finally performed 29 days after transplantation because of persistent air leakage and the risk of contralateral bronchopneumonia. Histological sections of the native lung revealed extensive and obliterative intra-alveolar and bronchiolar fibrosis with ectatic subpleural air spaces whereas the arteries and large bronchi were normal. After partial recovery of the neuromyopathy the patient was weaned from the ventilator 17 days after transplantation and he was discharged from the hospital 88 days after transplantation. Presently, he is able to lead an independent life. Thirteen months after the procedure pulmonary function tests showed the following values: FEV1, 2.23 l; FVC, 3.3 l, and TLC, 4.9 l.

Discussion

Paraquat is a water soluble quaternary ammonium derivative, poorly absorbed by the oral route (5–10%) and unbound to plasma proteins. Peak plasma concentrations are reached within 1–4 hours and decrease rapidly thereafter as the compound is taken up by the tissues and cleared by the kidney. In our case paraquat was undetectable in plasma obtained...
four days after the start of gastrointestinal symptoms whereas high levels were found on lung and muscle samples taken as late as nine weeks after herbicide ingestion. Indeed, paraquat is actively concentrated in alveolar pneumocytes and skeletal muscles. The acute pulmonary lesions have been attributed to the formation of oxygen derived free radicals and lipid peroxidation products whereas activation of “resident” macrophages are implicated in lung fibrosis. All pharmacological treatments including free radical scavengers, iron chelators, cochinine or corticoids are of unproven value, but encouraging results have recently been reported with a combination of cyclophosphamide and methylprednisolone.

In the most severe form the early mortality is related to respiratory, cardiac, renal and hepatic failure. In less severe poisoning a progressive bronchiolo-alveolitis develops and, once changes in the lung become apparent radiologically or if ventilatory assistance is required, the condition is invariably fatal. Lung transplantation has been previously reported in five patients after paraquat intoxication, all of whom died (immediately and up to three months after transplantation) in relation to graft failure, infection, or massive haemorrhage. In the present case the possibility of a suicide attempt was refuted by the patient’s family and, after a multidisciplinary consultation, lung transplantation was advocated as the ultimate treatment of a respiratory insufficiency of unclear origin in the absence of sepsis and other organ failure.

At the time of the lung transplant partial cardiopulmonary bypass was instituted in order to improve blood oxygenation, to prevent right ventricular failure, and to maintain cardiac output after clamping of the right pulmonary artery. After reperfusion of the grafted lung a trial of inhaled NO failed to reduce pulmonary hypertension. In fact, rapid interaction of exogenous NO with superoxide generated during early pulmonary reperfusion may liberate far more toxic oxygen species, such as peroxynitrite and hydroxyl radicals, than direct stimulation of the 3′, 5′-cyclic guanosine-monophosphate (cGMP) pathway with a cGMP analogue, or an intravenous NO donor such as nitroglycerin might confer protective vascular effects while avoiding the release of toxic byproducts.

Postoperatively, toxic myopathy and development of a right bronchopulmonary fistula led to difficulty in weaning the patient from the ventilator. The myopathy can severely limit the ultimate recovery and repeated biopsies are advocated to document the extent of injured and regenerated muscle fibres. Since muscles are important body stores for paraquat, progressive release may occur resulting in new injuries in the grafted lung and further destruction of the native lung. Ablation of the “remodeled” right lung contributed to the decrease in the risk of infection and to healing of the bronchopulmonary fistula. Fortunately, gas exchange and functional lung volumes remained good. In addition, the patient recovered sufficient muscle strength to lead an independent life and he was compliant with the post-transplant medical regimen and follow up examinations.

The present case illustrates the successful management of paraquat poisoning by a single lung transplantation and is the longest survival ever reported (more than 20 months). However, given the shortage of donor lungs, the unknown psychological state of some candidates, and the bad outcome of previously reported cases, the question of the desirability of lung transplantation as a treatment for acute lung fibrosis after paraquat intoxication should be raised. Such cases should remain exceptional since rare resources and expensive medical treatment should be utilised for eligible candidates accepted onto a transplant programme.