Anaemia in lung transplant patient caused by parvovirus B19

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Abstract

The case history is presented of a lung transplant patient who developed prolonged parvovirus B19 infection with severe transfusion dependent anaemia. The patient was treated with intravenous immunoglobulin after which the haemoglobin rose, together with a reticulocytosis. The patient then remained transfusion free and the virus cleared more than three months after the initial immunoglobulin treatment. The clinical and social implications for this group of patients are discussed.

Keywords: parvovirus B19; lung transplantation; immunoglobulin therapy

Case history

The patient had undergone lung transplantation for cystic fibrosis and was maintained on FK506, azathioprine, and prednisolone immunosuppression. In addition, she had undergone total lymphoid irradiation for obliterative bronchiolitis. The patient presented (day 1) with severe shortness of breath and dizziness. The haemoglobin level was 3.5 g/dl and she was normocytic with reticulocytopenia and a normal white cell and platelet count. Blood parameters were normal and a bone marrow aspirate confirmed red cell aplasia.

The serum on day 1 was positive for parvovirus B19 DNA by dot blot DNA hybridisation and polymerase chain reaction (PCR). There was, however, an equivocal reaction for parvovirus B19 specific IgG which was probably due to the passive transfer of antibody during the course of blood transfusions.

The patient's haemoglobin again fell from 12.7 g/dl on day 62 to 9.5 g/dl on day 79 after the initial presentation and she was treated with intravenous Sandoglobulin in a total daily dose of 0.4 g/kg. However, because of chronic renal impairment secondary to the previous use of cyclosporin and FK506, we used only one quarter of the total dose on day 79, half the total dose on day 80, and three quarters of the total dose on day 81. The total dose of 0.4 g/kg was given only on day 82 after ensuring that renal function remained stable. The treatment was discontinued after six days because of deteriorating renal function. Serum taken before treatment showed a high viral load and equivocal IgG level. Parvovirus B19 IgM was positive, indicating that the patient was mounting an early response to the virus. An impressive reticulocytosis was seen on the second day of immunoglobulin therapy and a week later was 10.3% (fig 1).

Serum analysed after immunoglobulin therapy on day 84 was negative for parvovirus B19 by DNA dot blot hybridisation but remained PCR positive, indicating a persistent infection.

Table 1. Parvovirus B19 test results

<table>
<thead>
<tr>
<th>Day</th>
<th>IgM</th>
<th>IgG</th>
<th>Dot blot</th>
<th>PCR</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>&lt;1</td>
<td>0.176</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>23</td>
<td>&lt;1</td>
<td>0.275</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>79</td>
<td>3.1</td>
<td>0.309</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>84</td>
<td>7.8</td>
<td>2.513</td>
<td>–ve</td>
<td>+ve</td>
</tr>
<tr>
<td>102</td>
<td>1.4</td>
<td>1.234</td>
<td>–ve</td>
<td>+ve</td>
</tr>
<tr>
<td>140</td>
<td>&lt;1</td>
<td>1.316</td>
<td>+ve</td>
<td>+ve</td>
</tr>
<tr>
<td>192</td>
<td>&lt;1</td>
<td>0.606</td>
<td>–ve</td>
<td>–ve</td>
</tr>
</tbody>
</table>

Sandoglobulin given on days 79, 80, 81, 82, 83, and 84.

IgM: <1 negative; >3 positive; 1–3 equivocal.

IgG: <0.80 negative; >1 positive; 0.8–1 equivocal.
Pneumothorax in adults with cystic fibrosis dependent on nasal intermittent positive pressure ventilation (NIPPV): a management dilemma

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Abstract

The management of pneumothorax in three adult patients with cystic fibrosis dependent on nasal intermittent positive pressure ventilation is described.

Keywords: cystic fibrosis; nasal intermittent positive pressure ventilation (NIPPV); pneumothorax

Transplant listed patients with cystic fibrosis who develop hypercapnic hypoxic (type 2) respiratory failure can be kept alive until donor organs become available with the introduction of nasal intermittent positive pressure ventilation (NIPPV). We describe the management of three transplant listed cystic fibrosis patients who developed pneumothoraces while dependent on NIPPV.

Case reports

A 20 year old man awaiting double lung transplantation was established on NIPPV because of deterioration in his spirometric values and blood gas tensions. He was infected with Burkholderia cepacia, had a forced expiratory...
Pneumothorax in adults with CF dependent on NIPPV

A 28 year old man with an FEV₁ of 0.8 l who had been established on NIPPV for 22 months developed a large (50%) left sided pneumothorax whilst using the ventilator. His NIPPV pressure was set at 19 mm H₂O. The pneumothorax was not associated with a respiratory exacerbation, but he was treated with intravenous antibiotic therapy and intravenous amiphylline to aid sputum expectoration while his NIPPV was discontinued. Capillary blood gas analysis while breathing room air gave a Po₂ of 53 mm Hg (7.1 kPa) and a PCO₂ of 41 mm Hg (5.5 kPa). The pneumothorax was drained using an intercostal tube and the lung re-expanded quickly, following which capillary blood gas analysis on 24% oxygen gave a Po₂ of 61 mm Hg (8.1 kPa) and a PCO₂ of 44.9 mm Hg (6.0 kPa). The patient maintained adequate blood gases for the duration of his admission and only required further NIPPV one month after his pneumothorax. He remains well, but NIPPV dependent, 27 months following his pneumothorax.

The third NIPPV dependent cystic fibrosis patient to develop a pneumothorax attended clinic with neck discomfort. She was not breathless. A chest radiograph demonstrated surgical emphysema in the neck and air in the pericardial space, but no evidence of a pneumothorax. NIPPV was withheld and she was maintained on 24% oxygen overnight. As she did not deteriorate it was decided to withhold NIPPV until the surgical emphysema had resolved, but two days after presentation she received a double lung transplant.

Discussion

At the Manchester Adult Cystic Fibrosis Unit we have treated 52 of 334 patients (16%) for a pneumothorax over the last 17 years and commenced 23 patients on NIPPV. Only three of our patients have developed a pneumothorax whilst dependent on NIPPV and one of these was iatrogenic. It is surprising that the reporting of pneumothoraces either as a consequence or coincident with NIPPV is not more common. However, our figures and those from another large adult cystic fibrosis unit indicate that this is a rare event. In other respiratory diseases the occurrence of a pneumothorax while patients are being treated with NIPPV is also rare. This probably reflects that, in conditions such as kyphoscoliosis and the neuromuscular disorders, the lungs are relatively normal. In contrast, cystic fibrosis is characterised by progressive pulmonary infection and apical subpleural bronchiectatic cysts that often rupture. In the future the incidence of NIPPV associated pneumothorax may increase as NIPPV is used more widely in patients with cystic fibrosis.
The ventilator described in these cases is pressure preset. The inspiratory and expiratory times are individualised to allow sufficient expiratory time to avoid autopositive end expiratory pressure and breath stacking. The pressure is then set to improve alveolar ventilation. It is important to balance adequate ventilation with peak inspiratory pressure, especially in those patients with low pulmonary compliance, to reduce the risk of barotrauma. Permissive hypercapnia may be acceptable in this situation as long as the patient remains asymptomatic. Pressure support ventilation may be preferable in patients with subpleural cysts who are at risk of barotrauma, as the peak airway pressure (including the swings associated with coughing on the ventilator) and the mean airway pressure may be lower. Conversely, it may be necessary to produce higher pressures in acutely sick patients. Some cystic fibrosis units use machines that generate higher pressures than the ventilator described in this paper. It is important to be aware of the maximum pressures generated and to balance the risk of barotrauma with patient benefit. We are not aware of any reports describing the relative risks of volume and pressure preset nasal ventilators in cystic fibrosis.

The development of a pneumothorax in a patient with cystic fibrosis receiving NIPPV can be a challenging clinical situation. As in the first case described here, pneumothorax may cause an abrupt deterioration in respiratory status and at the same time necessitate withdrawal of NIPPV. However, as demonstrated by the second case, other patients who are not in a respiratory exacerbation may remain relatively stable when NIPPV is withdrawn, reflecting that their “physiology” has been reset by NIPPV. If NIPPV is withheld or the inflation pressure is reduced and the PCO₂ rises, hypercapnia is acceptable in the short term as long as the patient remains asymptomatic. Alternatively, in a patient who requires continuing NIPPV following a pneumothorax, it can be delivered safely providing the pneumothorax is being drained through a patient intercostal tube.

An additional perceived benefit of NIPPV in patients with cystic fibrosis is that it may aid sputum expectoration. However, when NIPPV is withdrawn following pneumothorax without chest intubation, sputum clearance techniques are modified to avoid increases in intrathoracic pressure which may result in sputum trapping. Our experience shows that good hydration, intravenous aminophylline, intravenous antibiotic therapy, DNase, and adequate analgesia may be of benefit. The reintroduction of NIPPV can be associated with further air leaks and the length of time that a patient refrains from NIPPV following a pneumothorax is dictated by clinical circumstance. Reducing ventilator pressures may facilitate the reintroduction of NIPPV. However, it is important to appreciate that the pressure delivered by a non-invasive ventilator is measured from within the mask and is not necessarily the pressure achieved in the trachea and alveoli, as there is usually a significant fall in pressure across the nose and upper airway. This may be especially true in cystic fibrosis patients with rhinitis and nasal polyps. Overnight feeding can precipitate type 2 respiratory failure in patients with cystic fibrosis who have severe lung disease due to splitting of the diaphragm and increased CO₂ production. In NIPPV dependent cystic fibrosis patients with a pneumothorax it may therefore be prudent to discontinue feeding until NIPPV can be reinstalled.

This brief report highlights the dilemma of managing the rare complication of pneumothorax in NIPPV dependent adult patients with cystic fibrosis. Clearly, each patient requires meticulously supervised and individualised management with the risks of mechanical ventilation being balanced against the potential benefits.


Pneumothorax in adults with cystic fibrosis dependent on nasal intermittent positive pressure ventilation (NIPPV): a management dilemma
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