Liver transplantation for massive hepatic haemangiomatosis causing restrictive lung disease

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A 34-yr-old man with hepatic haemangiomatosis presented for orthotopic liver transplantation. His massively distended abdomen caused thoracic compression and severe restrictive lung disease. Respiratory failure was the principal indication for transplantation. Increased airway pressures, pulmonary hypertension, systemic hypotension caused by aorto-caval compression, and blood loss, complicated the intra-operative anaesthetic management. Weaning from mechanical ventilation was impaired by acute and chronic metabolic alkalosis, and diaphragmatic laxity.

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Cavernous haemangiomas are the most common benign tumour of the liver and may occur in association with systemic haemangiomatosis. 1–2 Giant haemangiomas (>4 cm in diameter) are rare, but may cause abdominal discomfort and coagulopathy (Kasabach-Merritt syndrome) 3 or can rupture. 4 Orthotopic liver transplantation for haemangiomatosis is unusual, and less than 15 patients have been described. 4–14 We report a patient with massive hepatic haemangiomatosis causing restrictive lung disease who had a liver transplant. To our knowledge, this is the first transplant primarily for the treatment of restrictive lung disease.

Report of patient

A 34-yr-old man presented for liver transplantation because of massive liver haemangiomatosis that affected his respiratory function. He had presented elsewhere 16 yr before with abdominal pain, and laparotomy and biopsy revealed multiple cavernous haemangiomas in the liver. He also had evidence of a systemic haemangiomatosis syndrome, with haemangiomas in the mandible, eye socket, and hands. Attempted hepatic resection via a thoracoabdominal approach was abandoned because of excess bleeding. He underwent hepatic artery embolization and cholecystectomy. Two years later, repeat hepatic artery embolization was carried out in an attempt to limit the growth of the tumour but this was unsuccessful and he was referred to our institution. Further surgical intervention was not felt to be possible. He was treated with alpha-interferon, which has been reported to be of use in infantile hepatic haemangioendotheliomatosis, 15 but without success and the disease progressed.

Over the years, as his liver tumour grew, the patient’s condition gradually worsened. Two months before transplantation, he became weak and lethargic, with dyspnoea on minimal exertion, persistent abdominal discomfort, and peripheral oedema. His abdomen was massively distended, and he had to remain upright at all times because of shortness of breath. Examination showed jugular venous distention and markedly diminished lung air-entry.

The chest radiograph (Fig. 1A) showed bilateral raised hemidiaphragms with small lung fields. Computerized axial tomography (CT) (Fig. 2A) of the thorax showed a compressed pulmonary vascular bed, especially in the lung bases, and abdominal CT (Fig. 2B) showed massive hepatomegaly. Transthoracic echocardiography was normal except for a mildly dilated right atrium, moderately dilated right ventricle, and an elevated pulmonary artery systolic pressure estimated at 56 mm Hg. There was no evidence of right to left shunt.
Arterial blood gas analysis showed hypoxaemia (Pao2 7.6 kPa, Spo2 86% on room air), hypercarbia (Paco2 8.2 kPa), and complete metabolic compensation for the respiratory acidosis (pH 7.4, HCO3− 37 mEq litre−1, base excess +11). Pulmonary function tests (Table 1) were notable for a severe restrictive process with forced expiratory volume in 1 s (FEV1) 1.26 litre (29% of predicted) and a proportional decrease in forced vital capacity (FVC) at 1.73 litre (32% of predicted). His diffusing capacity of the lung for carbon monoxide (DLCO) was 2.87 (41% of predicted). Supplemental, low-flow (1–2 litre min−1) oxygen was required. Liver function tests were abnormal: Aspartate transaminase (AST) at 123 unit litre−1 total bilirubin 41 mmol litre−1 and alkaline phosphatase 1213 unit litre−1, and International normalized ratio (INR) 1.4. Haematological tests showed a decompensated intravascular coagulation, thrombocytopaenia, and fibrinolysis (fibrin split products >40 mg ml−1, ref. <10; fibrinogen 108 mg dl−1, ref. 175–350; activated partial thromboplastin time 36 s, ref. 21–33; platelet count 104×109 litre−1, ref. 150–450). On the day of surgery blood gas deteriorated: Pao2 7.2 kPa, Paco2 12.4 kPa, pH 7.33, HCO3− 49 mEq litre−1, base excess +21.

The patient was brought to the operating room, standard monitors applied and a left radial arterial catheter placed. While in the sitting position, the patient was sedated with midazolam 1 mg and scopolamine 0.8 mg i.v. and the abdomen was prepared for surgery. Oropharyngeal and transtracheal local anaesthesia was administered and endotracheal intubation was carried out with fibreoptic

Fig 1 Chest radiographs before and after surgery showing compression of the patient’s lungs by liver haemangiomatosis, and the improvement after its removal.

Fig 2 Contrast-enhanced computerized axial tomography scans of the abdomen before and after surgery. There is enlargement of the liver to almost completely fill the abdominal cavity. The image after surgery includes a fluid collection and is of a different anatomical level, but the new liver clearly takes up less space in the abdomen.
The surgical dissection was complicated by adhesions from the previous cholecystectomy. The liver was densely adherent to the abdominal wall in the areas near the previous incisions. Near the site of the previous thoracoabdominal incision, the distal portions of the ribs were embedded within the hepatic parenchyma and haemangioma. The abdominal wall was excised bilaterally in a wedge-shaped fashion between the umbilical area and the flank. While removing the liver from its attachment to the abdominal wall, significant bleeding was encountered, and thus the portal vein was ligated, starting the anhepatic phase. (The abdominal wall was excised bilaterally in a wedge-shaped incision, the distal portions of the ribs were embedded adherent to the abdominal wall in the areas near the previous cholecystectomy. The liver was densely adherent to the abdominal wall in the areas near the previous incisions. Near the site of the previous thoracoabdominal incision, the distal portions of the ribs were embedded within the hepatic parenchyma and haemangioma. The abdominal wall was excised bilaterally in a wedge-shaped fashion between the umbilical area and the flank. While removing the liver from its attachment to the abdominal wall, significant bleeding was encountered, and thus the portal vein was ligated, starting the anhepatic phase. (The abdominal wall was excised bilaterally in a wedge-shaped incision, the distal portions of the ribs were embedded

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The patient was transferred to the intensive care unit (ICU). Continued intra-abdominal bleeding caused haemodynamic instability. Haemostasis was secured after repeat laparotomy, with subsequent haemodynamic stability.

On the second post-operative day the patient was alert and co-operative and a trial of weaning from intermittent mandatory ventilation was attempted. While on continuous positive airway pressure (CPAP) of 5 cm H₂O and pressure support of 10 cm H₂O, his CO₂ increased to greater than 13 kPa. Bedside pulmonary mechanics were obtained and these showed maximal inspiratory and expiratory pressures of −18 and +2 cm H₂O, respectively. Over 8 days in the ICU, the patients’ maximal inspiratory and expiratory pressures improved to −20 and +40 cm H₂O, respectively. His spontaneous vital capacity improved from 500 to 1450 ml during the same period of time. The patient was weaned to spontaneous ventilation with 5 cm H₂O CPAP and pressure support of 10 cm H₂O. He mobilized in the ICU while attached to a portable ventilator and improved sufficiently to allow extubation of his trachea 8 days post-operatively. Post-extubation blood gases (FiO₂ 0.21) were PaO₂ 9.2 kPa, PaCO₂ 6.6 kPa, pH 7.39 and serum bicarbonate concentration 30 mEq litre⁻¹. He left hospital 2 weeks after transplantation.

Pulmonary function tests 1 month after surgery, showed marked improvement in his restrictive lung pattern (Table 1) with FEV₁ increased to 1.93 litre (45% predicted). Subsequently, lung function and overall quality of life have continued to improve. One year later, his chest x-ray (Fig. 1) showed improvement in lung volumes and a rounded contour to the diaphragm. Arterial blood gases (room air) showed a Po₂ of 12.1 kPa, PacO₂ 6.1 kPa, HCO₃⁻ 28 kPa and pH 7.4. His transplanted liver continues to function satisfactorily.

**Discussion**

Haemangiomas are the only common vascular tumour of the liver and are the most common benign liver tumour. The incidence is reported as being between 0.4 and 20% in autopsy series. Most haemangiomas remain small and asymptomatic and are identified at post-mortem or incidentally as a result of investigation for other conditions. Haemangiomas are mostly solitary, but 10% have multiple locations and may occur as part of a systemic haemangiomatosis syndrome. Those with a diameter of greater than 4 cm are defined as giant haemangiomas.

Giant haemangiomas may be managed expectantly especially if surgical resection is thought to be technically difficult or if the patient has minimal or no symptoms. When patients become symptomatic the options for therapy include hepatic artery embolization and surgical resection. There have also been reports of the use of corticosteroids and radiotherapy in the management of the lesions. Orthotopic liver transplantation (OLT) has been used for giant liver haemangiomas, the principal indications being

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### Table 1 Pulmonary function tests performed 1 month before transplantation and 1 month after transplant, demonstrating the improvement in the restrictive pulmonary physiology. The FVC after surgery may not be complete

<table>
<thead>
<tr>
<th>Test</th>
<th>Pre-transplant</th>
<th>1 Month post-transplant</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC</td>
<td>1.73 litre</td>
<td>2.06 litre</td>
</tr>
<tr>
<td>FEV₁</td>
<td>1.26 litre</td>
<td>1.93 litre</td>
</tr>
<tr>
<td>FEV₁/FVC</td>
<td>72.6%</td>
<td>94%</td>
</tr>
<tr>
<td>FEF 25–75</td>
<td>0.9</td>
<td>2.6</td>
</tr>
<tr>
<td>FEFMAX</td>
<td>3.8</td>
<td>5.0</td>
</tr>
<tr>
<td>MVV</td>
<td>41 litre</td>
<td>71 litre</td>
</tr>
</tbody>
</table>

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pain, functional debility, and risk of rupture. There are less than 15 such patients reported in the literature. In our patient, the principal reason for transplantation was the severe restrictive lung disease.

The anaesthetic management of OLT is challenging and in this patient the difficulties were compounded by several unusual features. First, despite the fact that his airway looked favourable, there was concern that, haemodynamically, because of aorto caval compression, the patient would not tolerate a rapid sequence induction. In addition, the patient could not lie flat because of dyspnoea. Awake fibreoptic endotracheal intubation was performed, and inhalation induction of anaesthesia using sevoflurane followed. In spite of a slow change to the supine position the patient did become hypotensive, but this was responsive to fluid and vasopressor administration. Left lateral tilt could also have been used to decrease aorto caval compression, in a fashion analogous to the use of left uterine displacement in pregnancy.

Second, his pulmonary hypertension (PA systolic pressure 56 mm Hg on pre-operative testing) was a concern. It was felt that, in the current patient, this was almost entirely because of mechanical factors caused by his massive liver lesion and would be reversible post-transplant. Pulmonary artery pressures did decrease (mean pulmonary artery pressure 33–20 mm Hg) after the patient’s liver was removed.

Finally, for a number of reasons, the patient was likely to breathe poorly after surgery. His already elevated bicarbonate concentration (49 mEq litre−1, ref. 22–28) and the massive blood transfusion requirements containing citrate, caused severe metabolic alkalosis and central hypoventilation. The stretching of the diaphragm by the large liver conferred some mechanical advantage pre-operatively but once the liver was removed the diaphragm became lax. In addition, his malnourished state (as a result of pre-operative early satiety from gastric compression and consequent decreased caloric intake) and compressed lungs from tumour mass impaired respiratory function. Each of these factors could prolong mechanical ventilation, but extubation of the trachea was possible 1 week after the transplantation.

In summary, we present a patient with massive hepatic haemangiomatosis, which caused a restrictive-type of respiratory failure. Transplantation was successful in spite of concerns of elevated airway pressures, pulmonary hypertension, severe metabolic alkalosis, inherent surgical difficulties and possible aorto-caval compression. Transplantation improved the patient’s respiratory status and overall quality of life.

References

19 Duchenne GB. Physiology of Motion. Philadelphia: JB Lippincott, 1949; 452–60