Survival from massive intraoperative pulmonary thromboembolism during orthotopic liver transplantation

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Summary
We report a case of massive pulmonary embolism occurring at the time of graft reperfusion in a patient undergoing orthotopic liver transplantation. The clinical diagnosis of pulmonary embolus was aided by on-table echocardiography. Cardiopulmonary bypass and surgical embolectomy prevented her death. We discuss the differential diagnosis, possible aetiology of pulmonary embolism in this context and subsequent management. (Br. J. Anaesth. 1998; 80: 685–687)

Keywords: liver transplantation; monitoring echocardiography; complications pulmonary embolism

Pulmonary embolus is under diagnosed as a cause of death in the perioperative period.1 Orthotopic liver transplantation (OLT) is associated with acute changes in cardiovascular physiology at the time of reperfusion of the donor liver and these may obscure the diagnosis of pulmonary embolism, with consequent delay in treatment. Anaesthetists need to consider the possibility of acute pulmonary embolism as a cause of severe or prolonged hypotension at reperfusion.

Case report
A 31-yr-old woman with Caroli’s syndrome (intrahepatic bile duct dilatation leading to recurrent bile stone formation) was undergoing liver transplantation. All preoperative investigations were normal except for her coagulation profile which was mildly deranged: prothrombin time 16 s (normal 13 s) and partial thromboplastin time 37 s (normal 32 s).

Anaesthesia was induced using standard i.v. induction, followed by neuromuscular block, intubation and ventilation with isoflurane in an air–oxygen mixture. Invasive monitoring included a radial arterial cannula, right internal jugular central cannula and pulmonary artery catheter, derived values from which demonstrated the usual pattern in these patients of increased cardiac output and systemic vasodilatation immediately after induction of anaesthesia (table 1).

Aprotinin was given i.v. throughout the procedure (after a test dose), with an initial loading dose of 2 000 000 u. followed by infusion of 500 000 u. h⁻¹.

After a prolonged dissection (because of the large native liver) veno-venous bypass was established (femoral–portal to axillary) using non-heparin-bonded tubing and a centrifugal pump (Biomedical vortex pump 550, Medtronic). Bypass flow, although continuous, could only be maintained at 1.5 litre min⁻¹, limited by the small size of the axillary vein.

Throughout the anhepatic phase, physiological and coagulation variables remained stable, with coagulation supported by transfusion of fresh frozen plasma. At the end of the anhepatic phase, blood-gas tensions and serum biochemistry were normal.

After blood flushing of the donor liver, declamping of the suprahepatic inferior vena cava (IVC) and portal vein, and reperfusion of the donor liver, there was an anticipated decrease in systemic arterial pressure. This was treated with i.v. volume replacement and increasing doses of norepinephrine, to a maximum of 0.2 µg kg⁻¹ min⁻¹ to maintain mean arterial pressure at 70–75 mm Hg, with systemic vascular resistance index (SVRI) >1600 dyn s cm⁻⁵ m². The transplanted liver appeared normal on inspection.

The coagulation profile was within acceptable limits (prothrombin time 22 s, activated thromboplastin time 48 s) and the surgical field showed no signs of oozing. The thrombelastograph tracing at this point suggested a mild hypercoagulable state. In total, she had received 11 u. of fresh frozen plasma.

Approximately 3 min after reperfusion, the liver was lifted to examine the inferior surface for any anastomotic leak. At this point acute haemodynamic changes occurred. Profound systemic hypotension and pulmonary hypertension were accompanied by a broad complex bradycardia on standard CM5 ECG monitoring, in association with a decrease in end-tidal carbon dioxide P\textsubscript{ETCO\textsubscript{2}} as measured continuously by capnography (4.5 to 0.7 kPa). Airway pressures remained normal. Auscultation of the chest and heart sounds revealed no abnormality. Immediate resuscitation consisted of three doses of epinephrine 1 mg and atropine 3 mg into the central circulation. After a delay of approximately 30–45 s systemic arterial pressure and heart rate responded to the resuscitative measures, but with a marked decrease in cardiac index (CI) (table 1), which could not be improved, even with continuous infusion of high-dose epinephrine.

In an attempt to reduce pulmonary artery pressures, nitric oxide 10 ppm via the inspiratory limb of the ventilator was commenced, together with pulmonary arterial prostacyclin and glyceryl...
The working differential diagnosis was of an excessively severe metabolic response to reperfusion of the donor liver (despite having been routinely blood flushed before reperfusion), air embolus (which seemed unlikely) or massive pulmonary thromboembolism. Reperfusion is usually associated with a period of hypotension, but this generally responds rapidly to i.v. volume, vasoconstrictors and calcium.

At this stage there was evidence of poor tissue perfusion, with anuria and severe metabolic acidosis (pH 7.05, base deficit 15 mEq litre⁻¹, lactate 12 mmol litre⁻¹). Transthoracic two-dimensional echocardiography was performed with the patient on the operating table and the abdominal incision still open. This revealed good left ventricular function and a dilated right ventricle with right to left deviation of the interventricular septum. Doppler signal showed a waveform suggestive of gross tricuspid regurgitation. No thrombus was seen in the right atrium or ventricle.

The combination of the echocardiographic findings and the clinical picture indicated a diagnosis of massive pulmonary embolism. Hence it was decided to proceed to sternotomy with full cardiopulmonary bypass, and surgical exploration of the main pulmonary trunk.

At sternotomy the right ventricle was seen to be grossly dilated. Cardiopulmonary bypass was instituted immediately and mean perfusion pressure was maintained at 70 mm Hg. Two clots measuring approximately 5 × 3 cm each were removed from the main pulmonary trunk (fig. 1).

Discussion

There are only two reports in the literature describing acute pulmonary embolism during OLT, both of which were fatal.2,3 Echocardiographic studies have shown that pulmonary embolization of air and thrombi is common during graft reperfusion4 and post-mortem studies have confirmed massive platelet thromboembolism as a cause of sudden death in patients undergoing OLT.5,6

Thrombotic episodes are rarely considered in patients undergoing OLT as coagulopathy is the norm. They have impaired synthesis of clotting factors, are exposed to citrate toxicity, haemodilution and clotting factor consumption, and demonstrate increased fibrinolysis, increased concentrations of tissue plasminogen activator (TPA) and decreased concentrations of TPA-specific inhibitor.7

The aetiology of intraoperative pulmonary thromboembolism is multifactorial. In our patient there were several potential contributory factors: first, the large size of the native liver (2485 g) may have caused partial obstruction to the free flow of blood in the IVC; second, fresh frozen plasma may have rendered the patient hypercoagulable during veno-venous bypass, although no clots were seen in the circuit or on the cannulae subsequently; and third, aprotinin together with fresh frozen plasma and a relatively normal prothrombin time may have enhanced the size of an existing clot or even formation of a clot de novo. Aprotinin is used during OLT because of its antiplasmin activity and has been described previously as a causative factor in thrombus formation.8,9

Finally, an acquired deficiency of antithrombin III, proteins C or S may also accompany liver disease causing a hypercoagulable state.

The appearance of the embolus at embolectomy suggested that the source was from the IVC, perhaps a saddle thrombus, although subsequent venographic examination performed 36 h after operation did not confirm this.

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**Table 1** Cardiovascular variables for the patient during the transplant procedure

<table>
<thead>
<tr>
<th></th>
<th>After induction</th>
<th>Anhepatic phase</th>
<th>2 min after reperfusion</th>
<th>5 min after reperfusion</th>
<th>After CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mm Hg)</td>
<td>70</td>
<td>65</td>
<td>75</td>
<td>65</td>
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</tr>
<tr>
<td>CVP (mm Hg)</td>
<td>5</td>
<td>8</td>
<td>10</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>CI (litre min⁻¹ m⁻²)</td>
<td>4.2</td>
<td>5.0</td>
<td>6.6</td>
<td>1.8</td>
<td>3.5</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>14</td>
<td>13</td>
<td>19</td>
<td>46</td>
<td>24</td>
</tr>
<tr>
<td>SVRI (dyn s cm⁻⁵ m²)</td>
<td>1238</td>
<td>912</td>
<td>788</td>
<td>2000</td>
<td>1189</td>
</tr>
<tr>
<td>PCWP (mm Hg)</td>
<td>7</td>
<td>9</td>
<td>12</td>
<td>—</td>
<td>14</td>
</tr>
</tbody>
</table>

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**Figure 1** One of the two clots (approximately 5 × 3 cm) removed from the main pulmonary trunk.
Reperfusion of the donor liver usually causes characteristic changes in cardiovascular physiology, which include pulmonary hypertension in association with severe hypotension, a low SVRI and a high cardiac output. Systemic vasoconstriction is rare and the changes generally respond rapidly to volume expansion. In this case, the correct diagnosis was suggested by systemic vasoconstriction, a low cardiac output, reduced $P_{CO_2}$ and ECG signs of bundle branch block. The absence of response to pulmonary arterial vasodilators and evidence of acute right heart failure on echocardiography added weight to the diagnosis of massive thromboembolism, and precipitated the subsequent correct management.

The accuracy of echocardiography in the diagnosis of acute pulmonary embolism is uncertain. However, in some clinical situations two-dimensional and Doppler echocardiography may have an important role. In our patient they showed right to left deviation of the interventricular septum, right ventricular dilatation, tricuspid regurgitation and a hyperkinetic left ventricle. The pulmonary trunk was not seen.

The decision to proceed to surgical embolectomy was taken as the patient was deteriorating rapidly and the necessary expert staff and services were on site. While medical therapy with thrombolytic agents is the intervention of choice in uncomplicated massive pulmonary embolism this would have been inappropriate given the ongoing major surgery.

The successful management of massive pulmonary thromboembolism requires a high index of suspicion, supportive clinical findings and readily available cardiothoracic surgical services. Prompt diagnosis is essential, and is made more difficult when the condition occurs in circumstances where it is least expected, and when it mimics expected changes in physiology.

References