Combined orthotopic liver transplantation and Caesarean section for the Budd–Chiari syndrome

J. M. J. VALENTINE, G. PARKIN, S. G. POLLARD AND M. C. BELLAMY

Summary

Fulminant hepatic failure is a rare complication of pregnancy. We describe a case of Budd—Chiari syndrome that resulted in the need for combined liver transplantation and Caesarean section at 32 weeks’ gestation. The anaesthetic and perioperative management are discussed. (Br. J. Anaesth. 1995; 75: 105–108)

Key words
Anaesthesia, obstetric. Liver, transplantation.

Case report

A 28-yr-old Asian woman presented at 31 weeks’ gestation in her second pregnancy with a 6-week history of right upper quadrant pain, jaundice, vomiting, dysphagia and general malaise. There was no past medical history of note, although she had returned from Pakistan 2 months previously. On examination, she was found to be hypertensive (140/100 mm Hg), with ascites, hepatomegaly and sacral oedema. Uterine size was appropriate to gestation.

Investigations revealed deranged liver function tests, normal antithrombin III (AT III), markedly reduced protein C and protein S concentrations and a negative viral hepatitis screen (table 1). Abdominal ultrasonography confirmed hepatomegaly, intra-abdominal and pelvic ascites but failed to show any dilatation of hepatic ducts or mass lesion. Doppler studies revealed a low velocity waveform and forward flow in the hepatic artery, and normal waveform hepatic veins. Despite this, the radiologist suspected hepatic venous thrombosis and Budd–Chiari syndrome.

Upper gastrointestinal endoscopy showed an isolated oesophageal ulcer with no evidence of varices. Magnetic resonance imaging revealed a swollen oedematous liver, patent vena cava and portal vein. A thrombus was noted in the inferior vena cava at the level of the hepatic veins. A 90–95 % chance of hepatic venous thrombosis was estimated. After reviewing the literature, we decided to deliver the baby by Caesarean section at the time of orthotopic liver transplantation.

PERIOPERATIVE MANAGEMENT

Dexamethasone was commenced to improve fetal lung maturity. Transplantation occurred 72 h later. Premedication consisted of ranitidine, metoclopramide and sodium citrate orally. Non-invasive monitoring was commenced, and 20° of left lateral tilt employed. After preoxygenation, anaesthesia was induced by a modified rapid sequence technique using alfentanil 7.5 mg, midazolam 7.5 mg and atracurium 50 mg. Cricoid pressure was applied and the patient’s trachea intubated without difficulty. A 16-gauge nasogastric tube was inserted and the stomach contents aspirated. The lungs were ventilated with 1.5 % end-tidal isoflurane concentration in oxygen-enriched air. Anaesthesia was supplemented with infusions of alfentanil 3 mg h⁻¹ and atracurium 30 mg h⁻¹. Gelofusine and ephedrine were administered to support arterial pressure during insertion of catheters.

The following catheters were inserted percutaneously for drug and fluid infusion and pressure monitoring: 20-gauge left radial arterial catheter, right subclavian triple lumen central venous catheter, right internal jugular fiberoptic ejection fraction pulmonary artery flotation catheter (Baxter, Edwards Critical Care, Irvine, CA, USA) and a right internal jugular 18-French gauge percutaneous cardiac bypass cannula (Research Medical, Midvale, UT, USA).

Infusions of dopamine 3 μg kg⁻¹ min⁻¹ and 4 % glucose in 0.18 % saline (70 ml h⁻¹) were maintained throughout surgery and into the early postoperative period. A rapid infusion system (Haemonetics, JON M .  J .  VALENTINE, MRCP, FRCA, GILL P ARKIN, MB, BS, FFARCSI, MARK C .  BELLAMY, MA, MB, BS, FRCA (Intensive Care Unit); STEPHEN G. P OLLARD, MA, MS, FRCS (Liver Transplant Unit); St James’s University Hospital, Beckett Street, Leeds LS9 7TF. Accepted for publication: February 2, 1995. Correspondence to M.C.B.

Table 1 Clinical investigations in the patient (Ag, antigenic; Chromo, chromogenic)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT (s)</td>
<td>16</td>
<td>11–14</td>
</tr>
<tr>
<td>APTT (s)</td>
<td>35</td>
<td>25–40</td>
</tr>
<tr>
<td>Fibrinogen (g litre⁻¹)</td>
<td>4.7</td>
<td>2.0–4.6</td>
</tr>
<tr>
<td>Lupus anticoagulant</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>Anticardiolipin antibodies</td>
<td>Negative</td>
<td></td>
</tr>
<tr>
<td>AT III (u. ml⁻¹)</td>
<td>0.80</td>
<td>0.8–1.2</td>
</tr>
<tr>
<td>Protein C Ag (u. ml⁻¹)</td>
<td>0.49</td>
<td>0.67–1.4</td>
</tr>
<tr>
<td>Protein C Chromo (u. ml⁻¹)</td>
<td>0.61</td>
<td>0.7–1.4</td>
</tr>
<tr>
<td>Protein S Ag (u. ml⁻¹)</td>
<td>0.36</td>
<td>0.75–1.4</td>
</tr>
<tr>
<td>Protein S Chromo (u. ml⁻¹)</td>
<td>0.33</td>
<td>0.6–1.3</td>
</tr>
</tbody>
</table>
Braintree, MA, USA) was connected to the bypass cannula side-arm to facilitate fluid infusion up to a rate of 1500 ml min⁻¹. An 18-French gauge bypass cannula was placed surgically in the right femoral vein and femoroljugular venovenous bypass was commenced at 4 litre min⁻¹ to decompress the inferior vena cava and abdominal wall varices before surgical incision.

A cruciate abdominal incision was made and an argon beam coagulator used for dissection to minimize surgical bleeding. Hysterotomy was performed via a lower segment incision and a live male infant was delivered. Syntocinon 10 u. was followed by an infusion of 40 u. over 2 h. The baby was in good condition with Apgar scores of 8 at 1 and 5 min. Because of respiratory depression his trachea was intubated and lungs ventilated. The infant was transferred to the neonatal unit for observation overnight and his trachea extubated the following morning.

Maternal orthotopic liver transplantation was performed without difficulty. Circulating volume was maintained using packed cells and modified fluid gelatin to maintain a packed cell volume of 0.26–0.32. Coagulopathy was monitored using prothrombin time, activated partial thromboplastin time (APTT), thrombin time, serum fibrinogen concentrations and platelet count. Thrombelastography was also used to assess the clinical clotting profile. Fresh frozen plasma, cryoprecipitate and platelets were transfused as indicated. Potassium chloride and calcium chloride supplements were given to maintain plasma concentrations of potassium at 4.0–5.0 mmol litre⁻¹ and ionized calcium 0.8–1.4 mmol litre⁻¹. At the beginning of the anhepatic phase, a bolus of tranexamic acid 1000 mg was administered and followed by an infusion at 300 mg h⁻¹ to prevent activation of fibrinolysis. Reperfusion was preceded by a bolus of CaCl₂, 10 mmol and was uneventful.

Intraoperative blood and fluid requirements were:
- packed red blood cells 10 u.; fresh frozen plasma 9 u.; cryoprecipitate 8 u.; platelets 8 u.; modified fluid gelatin 3.5 litre.
- After operation the patient was transferred to the intensive care unit where she was sedated with propofol and alfentanil and ventilated for 12 h. Packed cell volume was maintained at 0.26–0.32 with blood and colloid infusion, and the APTT at around 80 s with heparin infusion at 1000 u. h⁻¹. Cyclosporin was commenced i.v. at 50 mg/24 h and insulin was infused to control hyperglycaemia. Azathioprine and hydrocortisone were commenced to complete the immunosuppressant regimen.
- Postoperative recovery was complicated by pyrexia without positive cultures. A chest infection present on chest x-ray was treated with ciprofloxacin and amoxycillin. Thirteen days after operation a CT scan revealed bilateral pleural effusions, right basal consolidation and ascites. No active intervention was required other than a change of antibiotics (teicoplanin and imipenem). *Candida* oesophagitis at 25 days after transplant was treated with fluconazole. Anticoagulation was maintained initially with heparin and then with warfarin. One month after liver transplantation the patient was discharged.

**Pathology**

Two specimens were examined. The first was thrombus from the inferior vena cava. This was organizing thrombus which had formed at least several days before hepatectomy. The second was the explanted liver. This weighed 1760 g. The left lobe was atrophic, the right lobe showed an enhanced nutmeg pattern and the caudate lobe was slightly enlarged. Vessels at the porta hepatis and inferior vena cava were patent, with thrombus in some hepatic venous tributaries.

Histologically there were varying degrees of perivenular venous congestion, liver cell necrosis, extravasation of red blood cells into the space of Disse and hepatocyte regeneration around the portal areas. All changes were compatible with venous outflow obstruction of variable degree in different areas of the liver, The changes in the caudate lobe were only recent, whereas there was established recanalization in some hepatic veins and fibrosis in others.

Overall the changes were of subacute venous outflow obstruction and thrombus in the inferior vena cava with organized thrombus in the hepatic veins confirming Budd–Chiari syndrome.

**Discussion**

Liver disease in pregnancy is rare, complicating only 0.1 % of cases [1]. Forty percent of cases can be accounted for by viral hepatitis. Liver disease unique to pregnancy comprises intrahepatic cholestasis of pregnancy (increased fetal risk), acute fatty liver of pregnancy and HELLP syndrome, both the latter two carrying high maternal and fetal risk when untreated. Acute fatty liver and HELLP syndrome are diseases of the third trimester and show similar clinical signs of jaundice, coagulopathy and increased liver enzyme concentrations. The immediate termination of pregnancy by Caesarean section has been shown to improve both maternal and fetal outcome [1]. The greatest experience of surgical intervention in liver disease of pregnancy seems to be related to acute spontaneous hepatic rupture in HELLP [2–4]. Treatment options have included orthotopic liver transplantation [5].

The Budd–Chiari syndrome remains one of the rarer causes of liver disease of pregnancy. It has recently been well reviewed [6–8] and is characterized by structural and functional abnormalities of the liver caused by obstruction to the outflow of hepatic venous blood. This obstruction may be at any site in the hepatic venous system, inferior vena cava or right atrium.

Many aetiologies have been described: myeloproliferative disorders, the oral contraceptive pill and inferior vena cava membranes are perhaps the most common [6]. Pregnancy-related Budd–Chiari syndrome is well recognized and is usually caused by the hypercoagulable state [7]. Concentrations of protein C and protein S have been shown to be reduced in pregnancy to approximately 85 % of those of normal controls [9]. The concentrations in our patient were low compared with this, which is...
likely to have been a major predisposing factor. We are aware of several Asian families in our area with congenital protein C and protein S deficiencies.

Presentation may be fulminant, subacute or chronic. Pregnancy-associated Budd–Chiari syndrome generally presents as an acute or fulminant illness, often in the early puerperium [7]. Abdominal pain, abdominal distension and jaundice are the most common presenting features, with hepatomegaly, ascites and sometimes encephalopathy being found on examination. Biochemical investigations often reveal impaired hepatic synthetic function. The prognosis is uniformly poor without surgical intervention as medical therapy has not been shown to be of any benefit.

There is currently considerable debate as to whether of not optimal management of the Budd–Chiari syndrome is portasystemic shunting or liver transplantation [10–12]. In the chronic form of the condition, where synthetic function is preserved, shunt surgery offers good long-term survival with relatively few patients progressing to orthotopic liver transplantation [11, 13]. However, orthotopic liver transplantation offers good survival rates in Budd–Chiari syndrome and is the treatment of choice in the fulminant variant of the syndrome and in those patients with end-stage liver disease [14–18]. The clinical presentation in our patient more closely resembled the latter; moreover, the Budd–Chiari syndrome in pregnancy in Asian patients generally follows this course [7]. We therefore elected for early orthotopic liver transplantation.

Fulminant liver failure compromising pregnancy and requiring post-partum orthotopic liver transplantation is well described [19–21]. However, we are aware of only two cases of intrapartum orthotopic liver transplantation with successful fetal outcome [22, 23].

The options available for this patient were Caesarean section followed by orthotopic liver transplantation, orthotopic liver transplantation followed by Caesarean section, or combined Caesarean section and orthotopic liver transplantation. We felt that Caesarean section before orthotopic liver transplantation was unsafe because of the risk of severe haemorrhage from abdominal wall varices and coagulopathy. Additionally, anaesthesia and surgery could lead to hepatic decompensation. In view of the fetal maturity, a combined approach was considered the optimal management for a successful outcome for both mother and baby. Because of the risk of fibrinolysis and caval hypertension resulting in massive obstetric haemorrhage, we considered simultaneous hysterectomy. However, as pregnancy following orthotopic liver transplantation is now well described [24–26], a conservative approach was adopted.

Anaesthesia was induced with a high-dose opioid technique. Suxamethonium was avoided as both pregnancy and hepatic failure are associated with pseudocholinesterase deficiency and an unpredictable duration of neuromuscular block [27]. Our standard anaesthetic technique with high-dose alfentanil and isoflurane in oxygen-enriched air was used as this has been shown previously to provide excellent haemodynamic stability [28]. Variants to the technique included left lateral tilt until delivery to minimize aortocaval compression. We used venovenous bypass before skin incision in order to decompress the cava and improve uteroplacental blood flow. Venovenous bypass has been shown to improve haemodynamic stability and reduce the need for volume loading by approximately 3 litre [29]. This was considered an advantage because fluid retention with a hyperdynamic circulation is a feature of third trimester pregnancy, with a risk of fluid overload, particularly in patients given steroids.

Despite the “hypercoagulable” state of pregnancy, there is still a theoretical risk of fibrinolysis resulting from liver failure and the anhepatic state, and ischaemia–reperfusion injury. This can be prevented with tranexamic acid [30] or aprotinin [31–36]. We used tranexamic acid because there is little evidence of procoagulant side effects. Postoperative anticoagulation was commenced immediately as there is a procoagulant state after liver transplantation secondary to reduced levels of protein C–protein S complex [37], independently of any underlying aetiological factors for Budd–Chiari syndrome.

References


