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BRIEF REPORT

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Resolution of cirrhosis-related pulmonary shunting in two children with a transplanted liver

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Abstract We treated two children with hypoxemia caused by intrapulmonary shunting associated with cirrhosis secondary to extrahepatic biliary atresia. Following orthotopic liver transplantation, digital clubbing and intrapulmonary shunting were resolved, as demonstrated by normalization of room air arterial blood gases, reduction in shunt fraction, and perfusion lung scanning with ^{99m}Tc-labeled macroaggregates of albumin. We recommend that early liver transplantation be considered for young subjects with a severe hepatopulmonary syndrome.

Key words Pulmonary shunting, liver transplantation · Liver transplantation, pulmonary shunting

Introduction

Mechanisms to explain intrapulmonary shunting in chronic liver disease have been proposed, but the etiology has not been established, and severe shunting can be irreversible [2, 5, 6]. As postoperative changes may worsen hypoxemia, severe hypoxemia due to shunting has been considered a contraindication to orthotopic liver transplantation (OLT) [3, 8]. Two of our patients with hepatopulmonary syndrome were in critical condition due to progressive liver failure or hypoxemia, and so we decided to perform OLT.

We report here that in two children with cirrhosis secondary to extrahepatic biliary atresia, complete resolution of the progressive hypoxemia occurred after OLT.

Case reports

Case 1

A 2-month-old girl underwent the Kasai procedure at Kumamoto University Medical School following the diagnosis of biliary atresia. Progressive cirrhosis with portal hypertension developed, and partial splenic embolization (PSE) was done for hypersplenism when she was 5 years old. At that time, she required esophageal injection sclerotherapy (EIS) and transileocolic vein obliteration (TIO) of gastroesophageal varices had to be done to treat recurrent variceal hemorrhage. At age 8, the patient complained of progressive fatigue and dyspnea on exertion . Physical examination revealed digital clubbing without cyanosis and spider angiomas. Orthodeoxia was nil. At rest, on room air, she was hypoxic [arterial oxygen tension (PaO_2) 60 mm Hg] and hypocapneic [arterial carbon dioxide tension ($PaCO_2$) 28 mm Hg]. After 20 min of breathing pure oxygen, her PaO_2 rose to 129 mm Hg, with an alveoloarterial oxygen gradient ($AaDO_2$) of 553 mm Hg. The right-to-left shunt ratio [0.0031 (PAO_2-PaO_2) / (5 + 0.0031 (PAO_2-PaO_2)] was estimated to be 25 %, with a forced inspiratory oxygen (FiO_2) of 1.0. Perfusion lung scanning was not done before OLT. Chest X-ray, pulmonary function tests, and electrocardiography were normal, and continuous administration of oxygen was not required.

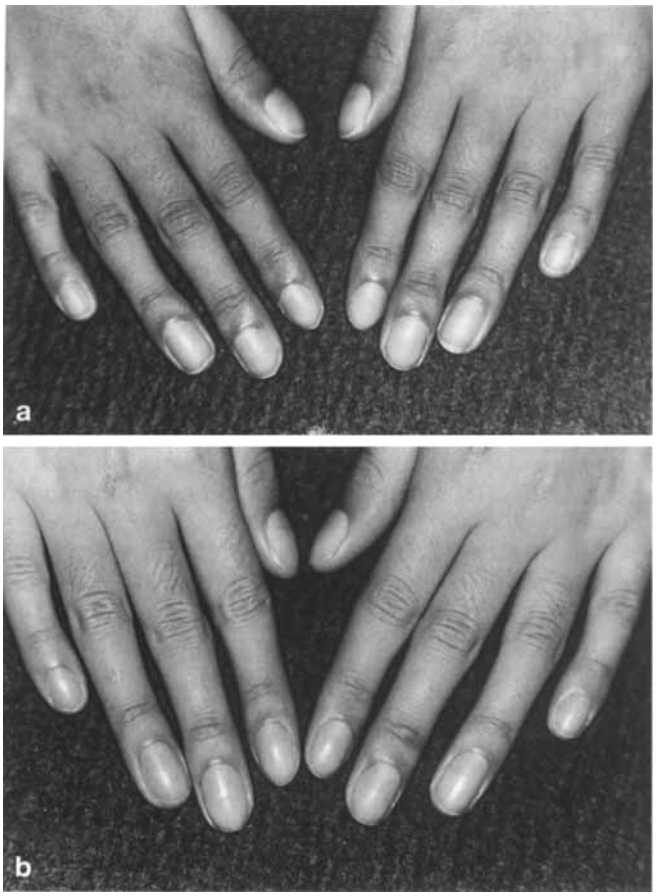

Fig. 1 a,b Progressive resolution of digital clubbing after OLT in case 1: **a** clubbing is apparent prior to OLT; **b** clubbing is no longer apparent 6 months after OLT

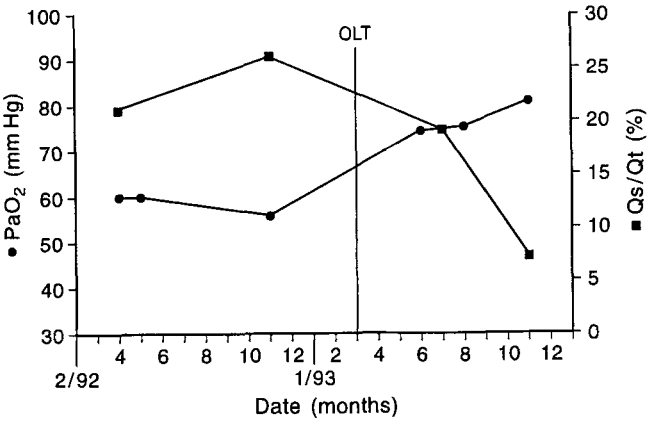

Fig. 2 Evolution of arterial oxygen tension (PaO_2) and shunt fraction (Qs/Qt) before and after OLT in case 1. *OLT*, Orthotopic liver transplantation; *PaO_2*, arterial oxygen tension; *Qs/Qt*, shunt fraction

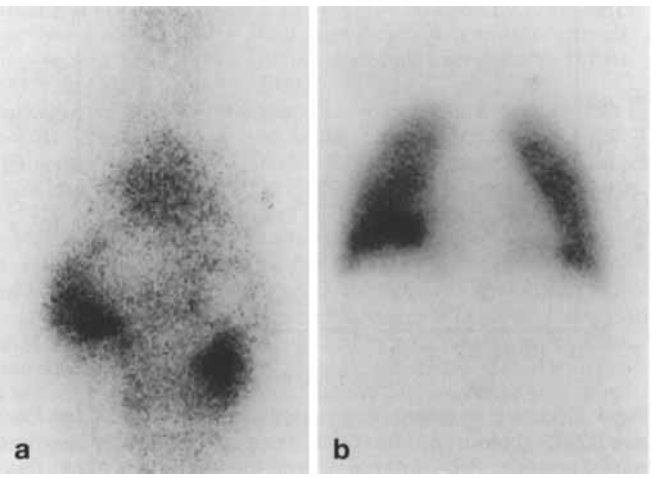

Fig. 3 a Intense renal and abdominal activity on the perfusion lung scan, indicative of right-to-left shunting in case 2. The projection is anterior. **b** Three months after OLT, no systemic activity is demonstrated. The projection is anterior

The patient was placed on the Queensland Liver Transplant Service (QLTS) in Australia waiting list for liver transplantation because of progressive liver failure and progressive hypoxemia. As there was a partial response to pure oxygen, the hypoxemia was not considered a contraindication to OLT. Liver function tests were as follows: total bilirubin 20.0 mg/dl, serum albumin 2.4 mg/dl and alkaline phosphatase 285 IU/l. When the patient was 9 years of age, she underwent OLT. The arterial pulmonary pressure was normal before OLT; it was not measured during or after the transplantation. She extubated herself on postoperative day 5 with no undue consequences.

The patient was discharged 4 weeks after OLT. Rapid clinical improvement was followed by disappearance of the digital clubbing (Fig. 1). After OLT, her PaO_2 on room air improved to 76 mm Hg at 3 months and then to 84 mm Hg at 8 months (Fig. 2). The shunt ratio and liver function tests also returned to near-normal levels (Fig. 2). She has remained well for the past 2 years and attends school on a regular basis.

Case 2

A second child diagnosed as having biliary atresia soon after birth underwent the Kasai procedure. The early postoperative course was unremarkable, with return of liver function tests to normal. However, cirrhosis became progressive, in association with portal hypertension and hypersplenism. EIS and TIO were repeatedly done for recurrent gastric and esophageal variceal hemorrhage . At age 7, she began to complain of generalized fatigue, dyspnea, and poor scholastic performance . She was admitted for evaluation, at which time a physical examination revealed digital clubbing but without spider angiomas and orthodeoxia. Chest X-ray was normal. Arterial blood gases on room air showed a PaO_2 of 62 mm Hg, which increased to 494 mm Hg while on 100% oxygen, with an $AaDO_2$ of 195 mm Hg. The right-to-left shunt ratio was estimated to be 11%. This was confirmed by perfusion lung scanning with ^{99m}Tc-MAA (Fig. 3a).

This patient was accepted as a QLTS candidate for OLT because of her progressive hypoxemia. This decision was made de-

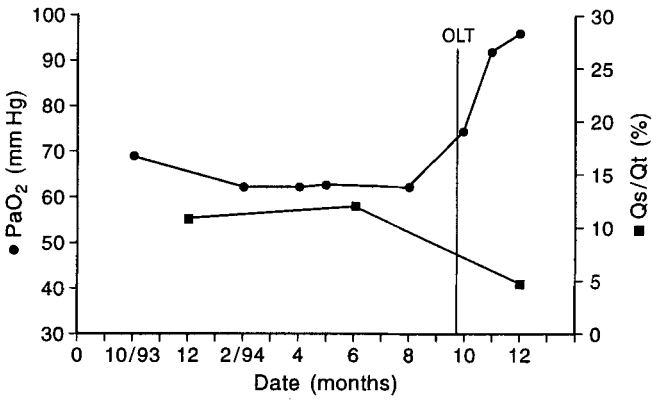

Fig. 4 Evolution of arterial oxygen tension (PaO_2) and shunt fraction (Qs/Qt) before and after OLT in case 2. *OLT*, Orthotopic liver transplantation; *PaO_2*, arterial oxygen tension; *Qs/Qt*, shunt fraction

spite near-normal liver function tests (total bilirubin 1.0 mg/dl, serum albumin 3.9 mg/dl, and alkaline phosphatase 852 IU/l). She underwent OLT 6 months after her initial admission. The postoperative course was uncomplicated, with extubation feasible on the 1st postoperative day. Two weeks after OLT, her PaO_2 was 67 mm Hg on room air and she was discharged without the need for supplemental oxygen. One month following OLT, her PaO_2 was 74 mm Hg, and 2 months later it was 92 mmHg on room air. The shunt ratio reverted to normal levels (Fig. 4), but digital clubbing remained. Systemic activity was not evident on a lung scan done 3 months post-transplant (Fig. 3b). At the 3-month follow-up , she remains well and is very active.

Discussion

Hypoxemia in chronic liver disease was apparently first reported by Snell [12]. In these patients, hypoxemia occurs following intrapulmonary arteriovenous shunting and ventilation-perfusion mismatching [10, 11, 14]. Hypoxemia occurs in approximately one-third of cirrhotic adults, but in children with cirrhosis there seems to be no relationship between intrapulmonary arteriovenous shunting and the degree of liver failure [1]. The pathogenesis of these pulmonary changes remains obscure and the potential for reversibility unknown. A reduction in liver-associated intrapulmonary shunting and resolution of digital clubbing have been observed after recovery from severe liver disease [11, 13]. Starzl et al. [14] have reported improved oxygenation in three children after liver transplantation. However, subsequent experience with hypoxemic cirrhotic patients who have undergone liver transplantation has been disappointing. Thus, severe hypoxemia (room air $PaO_2 < 50$ mm Hg) has remained a contraindication to orthotopic liver transplantation [2].

Table 1 Frequency of resolution of hypoxemia after liver transplantation in children

References	Resolution/Total [%]
Barbe et al. [1]	7/11 (64)
Obbergh et al. [9]	3/3 (100)
Hobeika et al. [4]	5/9 (56)
Laberge et al. [7]	2/2 (100)
Total	17/25 (68)

Recently, two different groups [7, 15] reported successful liver transplantation in patients with hypoxemia due to hepatopulmonary syndrome. Stroller et al. [15] described resolution of intrapulmonary shunting and digital clubbing associated with primary biliary cirrhosis after liver transplantation, and Raberge et al. [7] reported results for two children with cirrhosis secondary to extrahepatic biliary atresia in whom severe progressive hypoxemia completely resolved after OLT. Table 1 summarizes recent data concering resolution or absence of resolution of hypoxemia after OLT [1, 4, 7, 9]. OLT resulted in resolution of hypoxemia in 17 patients whose median PaO_2 was above 60 mm Hg; the remaining 8 patients with PaO_2 below 60 mm Hg all died. These results suggest that patients with a PaO_2 above 60 mm Hg can qualify for liver transplantation if they can be readily oxygenated. The profound hypoxemia in our two patients was completely overcome after OLT. Thus, hypoxemia should not always be considered a contraindication to OLT; indeed, hypoxemia may be an indication for early transplantation, even in patients with a relatively stable liver disease. This should be considered for children only, as such related success has only been noted in children . We propose that children with progressive dyspnea, and (moderate) hypoxemia ($PaO_2 >$ 60 mm Hg), and liver failure undergo prompt transplantation in order to achieve a successful outcome.

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