Cardiology in the Young

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Successful living donor liver transplantation after stent implantation in a patient with Alagille syndrome and severe bilateral pulmonary artery stenosis

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Brief Report

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Abstract

Severe pulmonary hypertension is a contraindication for liver transplantation owing to high mortality. However, decision-making regarding the treatment approach for patients with bilateral peripheral pulmonary artery stenosis, typically complicated by elevated main pulmonary artery and right ventricle pressures, can be challenging. Here, we report successful living donor liver transplantation after bilateral pulmonary artery stent implantation in a patient with Alagille syndrome, severe bilateral peripheral pulmonary artery stenosis, and extremely high main pulmonary artery and right ventricle pressures.

Pulmonary hypertension is diagnosed in ~4–8% of patients with liver diseases, and when accompanied by portal hypertension it results in portopulmonary hypertension.[1] The pulmonary hypertension is defined by elevated mean pulmonary artery pressure and pulmonary artery resistance, the severity of which is associated with higher rates of mortality during the perioperative period. Approximately one-third of patients with portopulmonary hypertension die in the early postoperative period following liver transplantation largely owing to acute right ventricular failure.[2,3] Treatment of pulmonary hypertension is, thus, required before liver transplantation. Mean pulmonary artery pressure <35 mmHg is required to ensure that the right ventricle will not fail following engraftment of the donor liver. For patients with peripheral pulmonary artery stenosis, elevated main pulmonary artery and right ventricle pressures are common. For these patients, a reduction in right ventricle pressures, as well as pulmonary artery pressures, is essential before liver transplantation. However, co-morbidities associated with liver diseases often present prohibitive surgical risks. Less invasive interventions to treat peripheral pulmonary artery stenosis and lower right ventricle pressures are needed. To this end, we report a case of successful bilateral stenting of the pulmonary artery and reduction of right ventricle pressure to allow liver transplantation.

Case report

A 3-month-old boy was referred to our hospital for liver transplant evaluation. Jaundice was diagnosed within days of birth, which gradually worsened despite medical therapy. He was diagnosed with Alagille syndrome owing to characteristic facies, peripheral pulmonary artery stenosis, and cholestatic jaundice. A definitive diagnosis was obtained by liver biopsy and genetic analysis, which revealed a 2688G > A heterozygous mutation in exon 23 of the *JAG1* gene. Cardiac catheterisation revealed an elevated main pulmonary artery pressure of 80/10 (38) mmHg, left pulmonary artery pressure of 13/9 (11) mmHg, right pulmonary artery pressure of 17/9 (12) mmHg, right ventricle pressure of 86/9 mmHg, central venous pressure of 7 mmHg, and left ventricle pressure of 65/11 mmHg. The minimum diameters of the right and left pulmonary arteries before the first upper branches were 2.6 and 3.4 mm, respectively, and morphologically hypoplastic and narrow (Fig 1a).

Stent implantation of the bilateral peripheral pulmonary arteries was performed at the age of 4 months using 3.0 × 8.0-mm-length Nobori® stents (Biosensors, Tokyo, Japan) at an outside institution to reduce right ventricle pressure. Unfortunately, when the patient returned to our institution at 6 months of age, right ventricle pressure and left ventricle pressure were increased at 107/8 and 94/8 mmHg, respectively. Additional stent implantation was then performed to treat the residual right pulmonary artery stenosis using 3.5 × 8.0-mm-length Nobori-S® stents, and bilateral pulmonary artery stent re-dilatation was performed using serial inflations of percutaneous transluminal angioplasty balloons to the diameters of 4.0, 5.0, and

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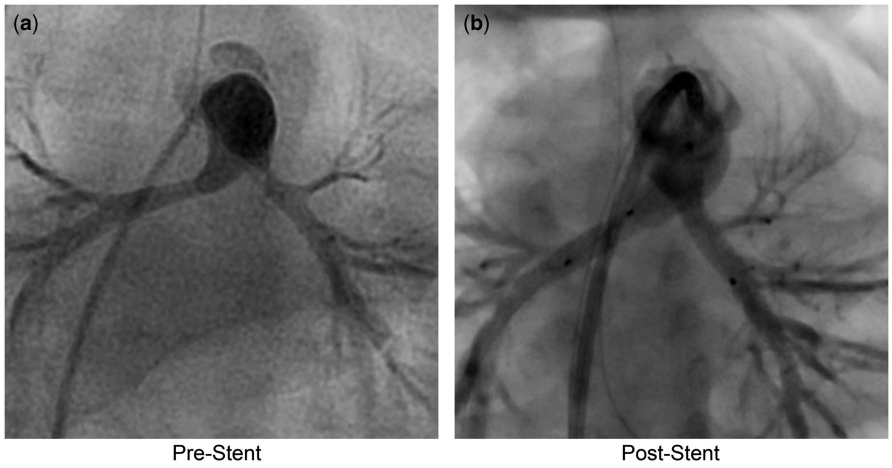

Figure 1. Pulmonary artery angiography before and after stent implantation. (a) Long segmental stenosis was seen in the bilateral pulmonary arteries by angiography. Average pulmonary artery diameter was 3.0 mm. (b) Implanted stents were dilated by percutaneous transluminal angioplasty balloon to a maximum of 6.0 mm diameter.

6.0 mm (Fig 1b). After these interventions, main pulmonary artery pressure, right ventricle pressure, and central venous pressure decreased to 77/7 (33), 87/10, and 3 mmHg, respectively. Given mean pulmonary artery pressure <35 mmHg, the patient was felt to be a possible candidate for liver transplantation. To further evaluate candidacy, acute volume challenge test was performed to assess right ventricular function.[4] Right ventricular function is defined as appropriate for liver transplantation if right ventricle end-diastolic pressure and central venous pressure are normal at <12 and <10 mmHg, respectively. The patient's right ventricle end-diastolic pressure and central venous pressure were found to be acceptable at 11 and 5 mmHg, respectively. Immediately after this examination, the patient's liver function rapidly deteriorated and living donor liver transplantation was performed at the age of 13 months. Apart from transient intraperitoneal bleeding during the perioperative period, the transplant was otherwise uncomplicated and deemed a success with normalisation of liver function.

Discussion

Pulmonary hypertension is a common complication of liver failure, and liver transplantation is essential in the definitive management of both conditions. However, the degree of pulmonary hypertension greatly affects perioperative mortality, and severe pulmonary hypertension is a contraindication to liver transplantation[2,3] owing to right ventricular dysfunction and inability to tolerate the acute volume challenge upon anastomosis of the donor liver to the patient's circulation.[4] Therefore, assessment of liver transplantation candidacy in patients with pulmonary hypertension requires careful evaluation by invasive assessment of pulmonary artery pressure and resistance. If pulmonary hypertension is present, treatments to reduce pulmonary artery pressure and improve right ventricular function are critically important before liver transplantation. However, these criteria do not apply to patients with peripheral pulmonary artery stenosis because main pulmonary artery and right ventricle pressures do not reflect peripheral pulmonary pressures and resistance. For these patients, surgical pulmonary artery plasty is recommended to effectively and durably reduce right ventricle pressure by as much as 55%.[5] In contrast, although stent implantation is an effective treatment option, durability is low and rates of repeat intervention are high.[6,7] In addition, rates of in-stent restenosis are high at 24% overall and up to 60% in patients with Alagille syndrome.[7] Although surgical pulmonary artery plasty may be the most appropriate option for long-term efficacy, co-morbidities associated with liver disease and high risk of perioperative bleeding preclude surgical pulmonary artery plasty, and percutaneous stenting is often safer and more appropriate to reduce right ventricle pressure before liver transplantation. Considering the higher rate of repeat intervention and in-stent restenosis rates in patients with Alagille syndrome, drug-eluting stents were selected. In our patient, a percutaneous approach to reduce right ventricle pressure enabled us to offer successful liver transplantation at a significantly lower risk.

A recent study reported that the pathology of elevated right ventricle pressures in pulmonary hypertension or portopulmonary hypertension differs from that of elevated right ventricle pressures in peripheral pulmonary artery stenosis. Therefore, in patients with Alagille syndrome, severe peripheral pulmonary artery stenosis may be less detrimental than pulmonary hypertension and therefore less risky for liver transplantation if they do not have right ventricular dysfunction.[8,9] Nevertheless, mortality and morbidity of liver transplantation in patients with Alagille syndrome patients remain higher than the general population with possibly cardiovascular complications.[10] Given the ability to reduce right ventricle pressure safely by percutaneous stenting in patients with Alagille syndrome and severe peripheral pulmonary artery stenosis, further investigation is warranted to optimise liver transplantation outcomes and develop an appropriate protocol for safer liver transplantation for this vulnerable patient population.

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Conflicts of interest. None.

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