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# Situs inversus of donor or recipient in liver transplantation

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**Abstract** Situs inversus is a rare anatomical abnormality that is often associated with multiple, complex malformations. In the past, patients with situs inversus were considered unsuitable candidates for transplantation or organ donation because associated visceral, and especially vascular, anomalies pose special technical difficulties. Recently, several cases of successful liver transplantation in recipients with situs inversus have been published using modified surgical techniques. This report reviews the literature and describes our own experience, including two liver graft recipients with complete and incomplete situs inversus, and one patient who underwent successful transplantation using a liver from a donor with situs inversus.

**Key words** Situs inversus, liver transplantation · Liver transplantation, situs inversus

## Introduction

Situs inversus refers to the mirror image of the viscera, while situs solitus is defined as the normal anatomical situation. Situs inversus is a rare anomaly that was first described in humans almost 400 years ago by Fabricius [3]. Its frequency is reported to be between 1/4000 and 1/20000 live births [3, 24]. Chromosome aberrations such as balanced translocation (12/13) appear to have a significant influence on the development of human situs, symmetry, and heart development [27]. Chromosomes 10, 13, and 18 are thought to be involved in lateralization and situs determination [5]. Recently, a gene was discovered that controls embryogenic turning and visceral left-right polarity in mice [9, 28]. Mirror image orientation of the viscera often appears with other rare congenital malformations, including Kartagener's syndrome [14], optic pit syndrome [10], Ivemark syndrome [13], and polysplenia syndrome [18]. Associations with cardiac and intestinal malformations, absent or interrupted inferior vena cava, preduodenal portal vein, and aberrant hepatic artery have been reported [9]. Until recently, situs inversus was considered an absolute contraindication for liver transplantation [20]. However, the common association of situs inversus and biliary atresia has led to improved technical feasibility of transplanting livers into mirror image viscera. Since 1988, several cases of successful liver transplantation in situs inversus recipients have been reported using modified surgical techniques (Table 1). Moreover, technical vari-

**Table 1** Situs solitus liver transplantation in recipients with situs inversus (*pLTX* partial liver transplantation, *S* segment, *art. thromb.* arterial thrombosis, *cryp.* cryptogenic, *PNF* primary nonfunction)

| Author (year) | Primary disease | Technique | Outcome, follow-up |
|---|---|---|---|
| Kawamotó (1995) Brisbane, AUS [15] | Biliary atresia ($n = 1$) | pLTX (SII, III) | Alive, re-LTX (chronic rejection) |
| Farmer (1995) Los Angeles, USA [8] | Biliary atresia ($n = 6$) | Midline position, piggy-back | 5/6 Alive, 1 death (adenovirus infection) 40.6 ± 25.9 months |
| Watson (1995) Cambridge, UK [26] | Biliary atresia ($n = 7$), Cryp. cirrhosis ($n = 1$) | Piggy-back ($n = 3$) | 8/8 Alive, 2re-LTX (art. thromb., PNF), 28 (0.7–60) months |
| Klintmalm (1993) Dallas, USA [17] | Laennec's cirrhosis ($n = 1$) | 90° Rotation | Alive, 6 months |
| Colomb (1993) New Orleans, USA [6] | Biliary atresia ($n = 2$) | Orthotopic, piggy-back; orthotopic, separate infra- and suprahepatic vena cava anastomoses | 2/2 Alive, 42 and 29 months |
| Barone (1992) Little Rock, USA [2] | Congenital hepatic fibrosis ($n = 1$) | Orthotopic | Alive, 6 months |
| Falchetti (1991) Brussels, Belgium [7] | Biliary atresia and polysplenia ($n = 12$) | pLTX ($n = 4$) | 10/12 Alive |
| Todo (1990) Pittsburgh, USA [24] | Biliary atresia and polysplenia ($n = 2$) | Auxiliary; orthotopic, piggy-back | 1/2 Alive, 1 death at 9 months (re-LTX, infarction), 10 months |
| Hoffmann (1989) Cambridge, UK [12] | Biliary atresia and polysplenia ($n = 2$) | Orthotopic, separate infra- and suprahepatic vena cava anastomoses | 0/2 Alive, 1 death on day 7 (re-LTX for art. thromb.), 1 death at 1 month (liver failure) |
| Raynor (1988) Nebraska, USA [20] | Biliary atresia and polysplenia ($n = 1$) | Orthotopic, separate infra- and suprahepatic vena cava anastomoses | Alive, 7 months |
| Klein (1988) Los Angeles, USA [16] | Biliary atresia and polysplenia ($n = 1$) | Orthotopic, piggy-back | Alive, 5 months |

ations and creativity are needed when the donor viscera appear as a mirror image. We report on one liver transplant recipient with complete situs inversus, one with incomplete situs inversus, and one successful donor situs inversus liver transplantation.

## Case reports

Case 1

A 3-year-old girl (13.5 kg, 85 cm) pretreated by hepatoportoduodenostomy 2 months after birth underwent liver transplantation for extrahepatic biliary atresia. A preduodenal portal vein was known to exist from the previous operation. Systemic hypoxia due to intrapulmonary shunts was an additional complicating factor.

Intraoperatively, the situs appeared with a symmetric midline liver, splenomegaly, polysplenia, aplasia of the infra- and retrohepatic vena cava, and an absent portal vein. The presenting complex malformation syndrome seemed practically inoperable, but in the absence of any alternative, the decision was made to proceed with transplantation. Hemodynamic instability supervened and the recipient liver was quickly removed. A much smaller graft was donated from a 3-year-old child (17 kg, 100 cm). The inferior vena cava was anastomosed end-to-end and the hepatic artery end-to-end to the coeliac trunk. The liver showed insufficient reperfusion in the absence of a portal venous blood supply. An attempt to revascularize the liver, including arterialization of the portal vein, was made but was not sufficient. Multiple bleedings complicated the operation, especially from the adhesiolysis of the small intestine. Tamponade was required and biliary reconstruction was provisionally performed with a choledochostomy. Notable bradycardia occurred in the early postoperative phase. The patient died of cardiopulmonary failure related to hemorrhagic shock 2 days after transplantation.

Case 2

A 6-year-old boy (22 kg, 118 cm) underwent liver transplantation for extrahepatic biliary atresia associated with complete situs inversus, polysplenia syndrome, aplasia of the vena cava, and aberrant continuity of the vena hemiazygos. Extrahepatic biliary atresia had previously been treated by a Kasai operation at the age of 8 weeks. This patient received a graft from a 6-year-old donor (25 kg). On operation, the patient's situs presented with the liver on the left side, multiple spleens on the right, and a complete intestinal malrotation. After removal of the Kasai loop and preparation of the recipient liver, the inferior vena cava was found to be absent and the liver veins inserted directly into the right atrium. Transplantation was performed orthotopically. The mirror image donor portal vein was kept long in order to prevent tension on it. The liver veins, portal vein, and hepatic artery were anastomosed using an end-to-end-technique. The infrahepatic vena cava of the donor liver was oversewn. Reperfusion was excellent with initial bile production. Biliary reconstruction was performed with an end-to-side choledochojejunostomy. The patient presented in excellent condition at his last follow up, 42 months post-transplantation.

**Table 2** Situs inversus donor liver transplantation in patients with situs solitus

| Author (year) | Primary disease | Technique | Outcome, follow-up |
|---|---|---|---|
| Asfar (1995) Ontario, Canada [1] | Postalcoholic cirrhosis ($n = 1$) | Heterotopic, counterclockwise 90° rotation | Died on POD 20 (ARDS, bile leak, sepsis) |
| Herrera (1996) Cantabria, Spain [11] | Cirrhosis ($n = 1$), no etiology reported | Orthotopic, piggy-back | Alive, 30 months |

Case 3

A 56-year-old woman (53.8 kg, 157 cm) underwent liver transplantation for decompensated postalcoholic liver cirrhosis (Child C). The donor was a 19-year-old woman (45 kg, 174 cm) with a history of dextrocardia who had died of a spontaneous subarachnoidal hemorrhage. Situs inversus was present after donor laparotomy, including a mirror image liver with arterial blood supply from the left gastric artery, preduodenal portal vein, completely mobile retrohepatic vena cava, and cecum mobile. The donor liver weighed 1150 g and was perfused with 10 l of HTK solution (Custodiol, Köhler Chemie, Alzbach-Hähnlein, Germany). Liver transplantation was performed with preservation of the recipient inferior vena cava in the upper right quadrant. The donor hepatic vein confluence and the recipient vena cava were cut longitudinally to allow a wide end-to-side anastomosis. The distal donor vena cava was oversewn. An intraoperatively found partial portal vein thrombosis was removed and thereafter both portal veins were anastomosed using an end-to-end technique. The donor left gastric trunk was anastomosed with the recipient hepatic and gastroduodenal arteries as a branch patch. Biliary reconstruction was performed with an oblique choledochocholedochostomy with t-tube insertion. The liver showed excellent homogenous reperfusion and initial bile production. Initial immunosuppression consisted of cyclosporin-based triple induction therapy including antithymocyte globulin and prednisolone. Seventeen months after transplantation, the patient is in excellent condition with normal blood chemistry.

## Discussion

To date, experience with liver transplantation in recipients with situs inversus, and especially the use of situs inversus liver grafts, is still very limited. The association of biliary atresia with situs inversus in children has led to attempts to treat these patients by liver transplantation. Several cases of successful liver transplantation for biliary atresia have now been reported using different transplant techniques. including orthotopic transplantation, partial transplantation, preservation of the inferior vena cava, 90° rotation, and auxiliary liver transplantation. Table 1 summarizes the reported cases and techniques of liver transplantation in recipients with situs inversus.

Because of the limited cavity for the right lobe of the liver graft, a donor-recipient liver ratio below 1 is helpful for transplantation of a situs inversus recipient with a situs solitus liver. The pretransplant vascular hepatic blood supply should be evaluated carefully. Our first case report illustrates a fatal outcome because of the intraoperatively discovered malformation syndrome that made vascular reconstruction virtually impossible. In retrospect, separation of the portal vein areas with divided portal-venous and arterialized caval-venous liver perfusion might have been an operative alternative in such a case of low portal vein flow [19]. New examination techniques like angiography magnetic resonance with peripheral application of contrast medium may allow visualization of the vascular supply, especially in small patients suffering from biliary atresia. Depending on the individual vascular anomalies, donor-derived or artificial vascular grafts may have to be interposed to ensure adequate anastomoses. Additional vascular grafts of the donor should always be preserved for reconstruction.

To date, only two cases of donor situs inversus liver transplantation have been reported, including one heterotopic [1] and one orthotopic technique [11] (Table 2). Herrera and colleagues described the use of a modified technique including preservation of the vena cava [4, 25] and anastomosis of the donor superior vena cava to the recipient right suprahepatic vein. They recommend, that liver transplantation always be performed with preservation of the inferior cava [4]. In contrast to Herrera, Asfar et al. favor a counterclockwise 90° rotation of the graft in order to bring the donor portal structure into alignment with the portal structure of the recipient for end-to-end anastomosis [1]. The technique, including a 90° rotation of the liver graft with end-to-side anastomosis of the donor inferior vena cava with the recipient infrahepatic vena cava, might cause kinking and obstruction.

The major arguments for transplantation with preservation of the inferior vena cava, which is not the routine procedure at our institution, were to ensure optimal liver vein outflow and because of the smaller size of the situs inversus donor liver compared to the recipient liver. An oversized situs inversus donor liver might compress the vena cava in a situs solitus recipient. In such cases, split or segmental liver transplantation might be an alternative technique [21, 22]. In order to guarantee maximum flexibility in vascular and bile duct reconstruction, it is extremely important to maintain maximum length of all hilar vessels, liver veins, and the bile duct of the donor organ on explantation.

Based on our experience, we recommend that situs inversus donor livers no longer be rejected for transplantation, especially when donor organs are so scarce.

Furthermore, we think that recipients with situs inversus should not be excluded as candidates for transplantation if they stand a fair chance of being treated successfully and if the above mentioned prerequisites are met. In particular, the vascular anomalies should be completely evaluated preoperatively.

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