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Auxiliary liver transplantation with arterialization of the portal vein for acute hepatic failure

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Abstract Six adult patients suffering from acute hepatic failure and with a high urgent status underwent heterotopic auxiliary liver transplantation. In four of these patients, the portal vein of the liver graft was arterialized in order to leave the native liver and the liver hilum untouched and to be able to place the liver graft wherever space was available in the abdomen. The arterial blood flow via the portal vein was tapered by the width of the anastomosis. Two patients died, one of sepsis on postoperative day 17 (POD), the other after 3 months due to a severe CMV pneumonia. There were no technically related deaths. The native liver showed early regeneration in all cases. In one patient, the auxiliary graft was removed 6 weeks after transplantation. Four weeks later, he had to undergo orthotopic retransplantation due to a recurrent fulminant failure of the recovered native liver. This patient is alive more than 1 year after the operation. We conclude that heterotopic auxiliary liver transplantation with portal vein arterialization is a suitable approach to bridging the recovery of the acute failing native liver.

Keywords Liver transplantation, portal vein arterialization · Auxiliary liver transplantation

Introduction

Orthotopic liver transplantation has improved the prognosis of patients suffering from fulminant hepatitis enormously [18, 19, 21, 24]. Alternative methods to orthotopic liver transplantation, including liver support, heterotopic transplantation, partial orthotopic liver transplantation, and xenografting, are currently being evaluated [4, 10, 13, 17, 21]. The aim of the auxiliary approach is to support the patient's failing liver for a period of time until the native liver has recovered. Once that happens, immunosuppression can be tapered and eventually stopped. The liver graft either atrophies or has to be explanted surgically.

Despite improved long-term prospects, auxiliary liver transplantation has not yet gained general acceptance [16]. The excellent results of orthotopic whole liver transplantation in the treatment of fulminant hepatic failure (FHF), as well as the reported high morbidity rate of the auxiliary method due to technical complications and problems in the early postoperative period, have made transplant surgeons somewhat wary of the latter approach.

Here, we report our experience with heterotopic auxiliary liver transplantation in the treatment of FHF with arterialization of the portal vein of the liver graft. We demonstrate that the latter variation makes it possible to decrease morbidity due to surgical complica-

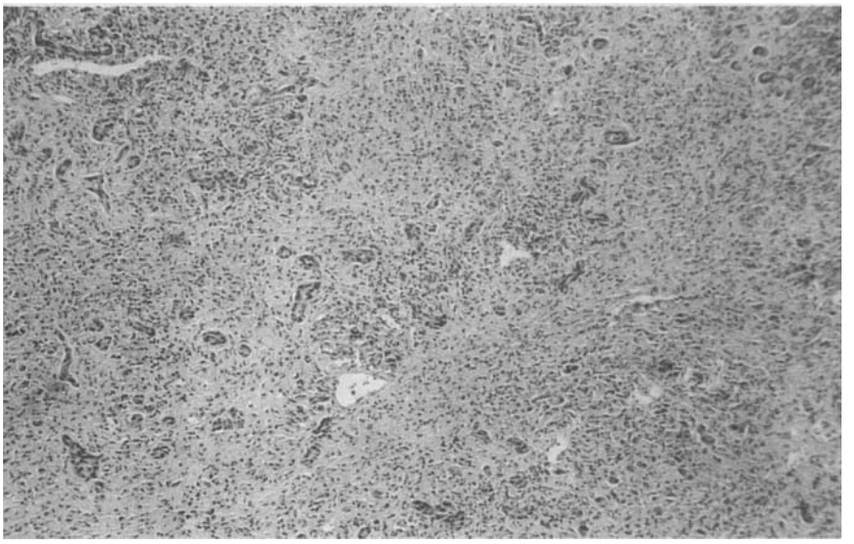


Fig. 1 Specimen of an acute failing recipient liver. About 90% of the hepatocytes are necrotic. There are still some zones of vital hepatocytes (H & E, × 100)

tions. Our reason for arterializing the portal vein is to leave the hilum of the native liver untouched. The necessary amount of liver tissue can be placed wherever there is enough space in the abdomen. Thus, even marginal liver grafts can be accepted for this life-saving procedure.

Patients and methods

Over the last 3 years, auxiliary liver transplantation was performed in our department on six patients, aged 18–49 years, suffering from FHF. In all cases, the criteria of O'Grady et al. [14] had been met and the patients placed on the "high urgent" list for transplantation. The decision to use the auxiliary method was made during the operation. One key criterion for this method was the intraoperative appearance of vital hepatocytes and mitoses in the frozen section of the native liver (Fig. 1). The surgical technique depended on the quality of the graft (cold ischemia, percentage of fatty cells) and the space available in the abdominal cavity. The auxiliary partial orthotopic liver transplantation (APOLT) technique [8] with left lateral segment transplantation was used once. The right lobe (segments 5–8) was transplanted heterotopically twice. A full-size graft was transplanted heterotopically three times. The following results will focus on four patients transplanted heterotopically with arterialization of the portal vein (Table 1).

Results

With the exception of one early vascular complication in patient K.L., primary function was observed in all auxiliary grafts (Table 1). Graft function was documented by the patient's clinical course (fading encephalopathy), biochemical parameters, and hepatobiliary scintigraphy.

One patient (Ch.R.) was placed on a triple drug immunosuppressive regimen. The other three patients (K.L., K.N., B.L.) were treated with an induction therapy of ATG for 7 days in addition to triple drug therapy consisting of CyA, imuran, and cortisone.

Table 1 Heterotopic auxiliary liver transplantation with arterialized portal vein in patients suffering from fulminant hepatic failure (*i.p.* immunosuppression, *FHF* fulminant hepatic failure, *p.v.* portal vein, *OLTX* orthotopic liver transplantation)

Patient/Age (years)	Disease	Graft	Technique	Complications	Follow-up
C.R. 49	A hepatitis	Full-size	Heterotopic, p.v. arterialized	Small-bowel perforation, sepsis	Died POD 17
K.L. 18	Ecstasy	Full-size	Heterotopic, p.v. arterialized	Portal vein thrombosis, acute rejection, abscess	i.p. stopped after 4 months graft removed, well
K.N. 25	non A non B non C hepatitis	Full-size	Heterotopic, p.v. arterialized	Acute rejection	i.p. stopped, died 3 months postoperatively from CMV pneumonia
B.L. 20	B hepatitis	Segments 5–8, split	Heterotopic, p.v. arterialized	Acute rejection	Graft removed, recurrence of FHF, OLTX, well

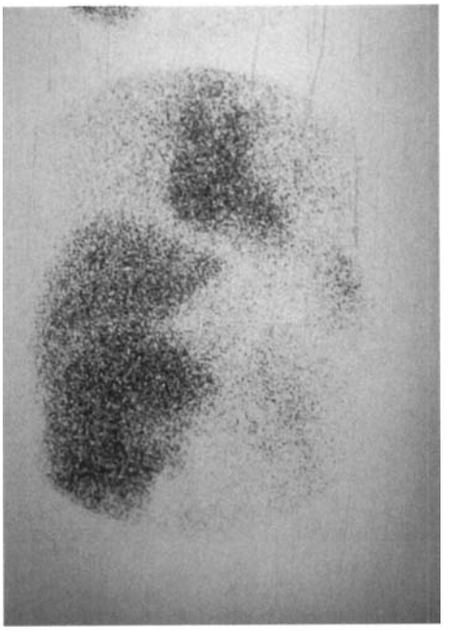
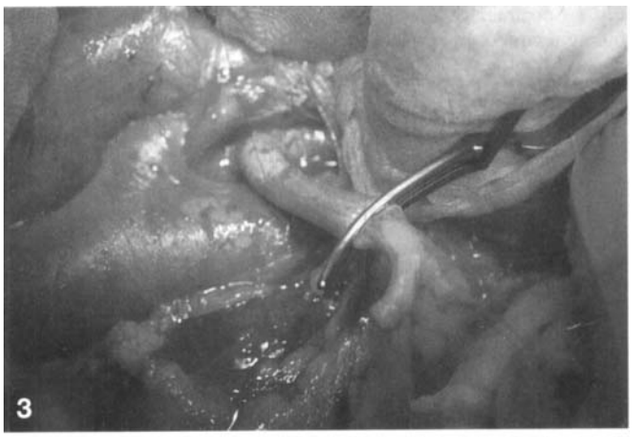


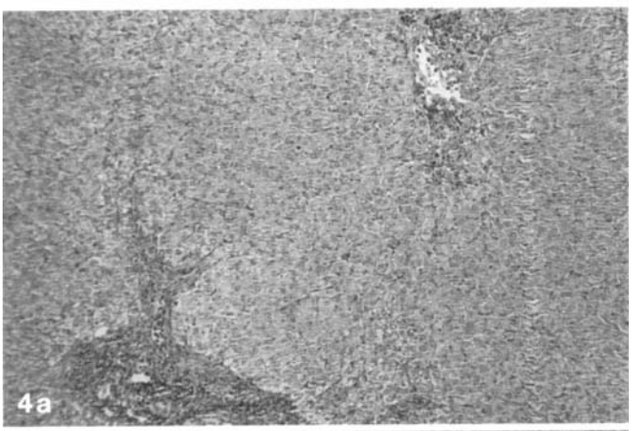
Fig. 2 Radioisotope scanning (99^{m}TcIDA-tracer) of native and transplanted liver of patient K.L. 6 weeks after successful heterotopic auxiliary segmental liver transplantation. The auxiliary transplant in the lower right abdomen is still more active than the recipient-regenerating liver

Patient Ch.R. recovered well at first. The ongoing regeneration of his native liver was documented by biopsy. Fourteen days after transplantation, he became septic. He was reoperated on postoperative day (POD) 15 due to an acute abdomen. A small bowel perforation with an accompanying peritonitis was found. The patient died on POD 17 of septic shock.

Patient K.L., admitted for "ecstasy" poisoning, was found to have a thrombosed portal vein 12 h after undergoing urgent transplantation. An urgent reoperation was performed. The portal vein was thrombectomized and anastomosed to the internal iliac stump of the interposed vessel to the aorta. The further clinical course was complicated by an intra-abdominal abscess 3 weeks after surgery. This could be drained by a percutaneously inserted catheter. A biopsy of the graft confirmed the diagnosis of cholangitis. The native liver showed excellent regeneration 3 months after auxiliary transplantation (the regeneration was checked clinically and by radioisotope scanning (Fig. 2). Immunosuppression was reduced (only CyA continued) and then stopped after 4 months. Due to persisting cholangitis, the graft was removed 4 months post-transplantation. The patient recovered well. Liver function is excellent more than 1 year after admission.

The 25-year-old patient K.N. had an uneventful postoperative course at first. Two weeks later he was treated





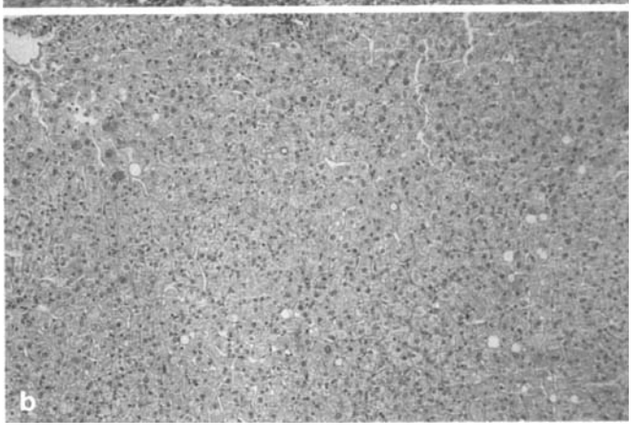


Fig. 3 Intraoperative scene in patient B.L. The iliac artery bifurcation of the donor is anastomosed to the infrarenal aorta of the recipient. Both stumps of the iliac arteries are anastomosed to the hepatic artery and the portal vein of the graft

Fig. 4a Specimen of the auxiliary liver graft of patient B.L. 4 weeks after transplantation. The specimen shows slight sinusoidal infiltration with lymphocytes. The parenchyma is in rather good shape (H & E, × 100). **b** Specimen of the regenerating native liver of patient B.L. 2 months after acute liver failure. The specimen demonstrates vital hepatocytes and no signs of fibrosis. The zonal architecture is rather normal. Some fatty changes can still be seen (H & E, × 100)

with a high dosage of cortisone due to a biopsy-proven acute rejection. Ten weeks after the successful transplantation, the patient was discharged and went home. Yet, 10 days later, he was readmitted suffering from fever, headache, and enteritis. We found an extremely high CMV-IgM titer and detected the virus in the serum, urine, and liver tissue. The patient, who was still under immunosuppression consisting of cortisone and CyA, was treated with virostatic drugs and immunoglobulins. He developed a CMV pneumonia and died shortly after. The postmortem showed an inconspicuous abdominal cavity with a well-regenerated native liver.

Patient B.L. also had an uneventful course initially. An acute rejection was successfully treated with cortisone. Because of an excellent regeneration of the native liver and an abdominal wound infection, the decision was made to remove the graft 6 weeks after the procedure. Only cortisone, 10 mg/day, was continued as immunosuppression. The surgical procedure, including anastomosis, is shown in Fig. 3. Artery and portal vein were connected to the iliac bifurcation of the donor used as an interposition graft. The other end of the graft was anastomosed to the infrarenal aorta. The histopathological specimen of the graft and the regenerated liver are shown in Fig. 4. Four weeks after the auxiliary transplantation, the native liver seemed to be fully regenerated. However, some periportal infiltration was still visible (Fig. 4b). Unfortunately, the patient developed acute liver failure again. The underlying cause remained quite unclear although the negative HBsAg status turned positive in spite of active and passive vaccination. The patient had to undergo orthotopic transplantation in a high urgent state. The fully recovered native liver was entirely necrotic 4 weeks later. The postoperative course was uneventful, but the patient is still HBsAg-positive and is being treated with virostatic drugs. He is still in our outpatient aftercare 10 months after discharge.

Discussion

Auxiliary liver transplantation is a method that has been quite well known since the early days of liver transplantation. Welch [23] was the first to describe the successful use of a heterotopically placed auxiliary graft in a canine experiment. He concluded that a short period of viability could be observed after heterotopic auxiliary transplantation. The clinical use of auxiliary liver transplantation for fulminant liver failure is rather new. The aim is to use auxiliary transplanted liver tissue to support the failing native liver until it has had time to recover. Once that happens, immunosuppression can be stopped. In 1980 Bismuth et al. performed the first clinical auxiliary heterotopic transplantation using a reduzed-size liver graft [1].

A key to success with the auxiliary approach is the indication. Sufficient information must be available showing that the native liver has not suffered previous diseases and, therefore, that it has a chance to regenerate [5]. Interestingly, in all four of our cases, from a biochemical and/or histomorphological point of view, a regeneration of the failing liver tissue did occur from 10 days to 4 weeks after the procedure, i.e., a period of time that exceeds the capabilities of currently available liver support systems [10] but that is certainly short enough to justify a temporary approach.

There appears to be some skepticism about using the auxiliary approach to treat hepatitis B for fear of chronic liver failure in the long term after FHF [24]. Then again, even in fulminant courses, clearance of the virus has been proven and was also seen in two of our patients.

To what extent the age of the patient should be taken into account with the auxiliary approach has not yet been established. In Europe, advanced age has been found to be an important factor that impedes native liver recovery [5]. In our experience, however, age (up to 49 years) was not of importance as far as tissue regeneration was concerned.

In all of our cases, the decision to use the auxiliary approach was made intraoperatively. To the experienced liver surgeon, the appearance of the frozen section of the native liver tissue ultimately determines the approach to be used. The importance of other biochemical parameters have not yet been established [3–5].

An advantage of the APOLT technique may be the stimulation of liver regeneration by the trauma of necessary liver resection. Shiota et al. [18] measured hepatic growth factor (HGF) as a parameter for liver regeneration in FHF and in acute hepatitis. Highly elevated HGF levels were found in the patients with FHF but no significant increase was found in the patients with acute hepatitis. Similar data regarding the APOLT technique are not yet available. Blumgart et al. [2] were able to show that major liver resection led to a significantly measurable growth of the remaining liver compared to minor liver surgery.

From our point of view, possible disadvantages of the APOLT method include the liver resection in a critically ill patient with severe coagulopathy, the resulting danger of postoperative bleeding, and the restricted mass of transplantable tissue. The reported solution, i.e., to resect the right lobe, as done by Boudjema et al. [4], seems to be rather difficult and only suitable for a very select group of stable patients.

Arguments against the technique of heterotopic auxiliary transplantation are given by Terpstra et al. [22]. They feel that the additionally needed portal vein anastomosis in the liver hilum with the requisite dissection of the native liver hilum should be avoided since this can lead to vascular spasm, steal phenomenon, and for

portal vein thrombosis due to graft swelling or competition between the native liver and the auxiliary graft [8, 17].

Our approach to the four cases was the complete arterialization of the portal vein of the graft. Schilling et al. [15] had reported on an experimental technique of portal vein arterialization by anastomosing it to the external iliac artery in heterotopic transplantation. They were unable to establish whether portal blood inflow is necessary for satisfactory liver function or liver regeneration. Van der Heyde and Schalm [9] did not find a decisive role for portal blood inflow but they did observe a functional competition between native and auxiliary liver. Starzl et al. [20] and Marchioro et al. [12] suggested that portal inflow and qualitiy of portal blood (so-called hepatotrophic factors) are necessary for long-term survival of the auxiliary graft.

Our experimental work provided us with detailed data on portal vein flow and resistance. Also, in the long run, we saw no complications related to the arterialization [11]. Our recent results on the clinical use of portal vein arterialization in liver transplantation successfully showed the impact of this approach for a very select indication [6]. This method is also supported by the work of Fisher et al. [7]. They stated that liver regeneration depends on the total hepatic blood flow and that it increases in a high-flow situation. Since we only expected to fulfill a short-term need for sufficient graft functioning, we did not fear any long-term complications of portal vein arterialization.

In all four cases, the portal flow was reduced by intraoperative electromagnetic measurement to about 1.5 l/min of the width of the anastomosis. We observed no procedure-related complications. With the exeption of the patient who died on POD 17, all of the arterialized grafts were removed 6 weeks to 6 months after transplantation. Organ function was excellent and no circulatory problems occurred. Interestingly, we did not find any sign of portal hypertension in these patients. This might have been due to the low resistance of the portal trunk and the sufficient outflow of the heterotopically positioned grafts.

In auxiliary transplantation with the need for acute liver support and the prospect of removing the graft at a foreseeable point in time, this technique provides the opportunity to place sufficient liver tissue anywhere in the abdomen or even in the retroperitoneal space. Drawbacks such as venous outflow gradient [12] or steal phenomenon into the native liver due to constriction of the portal vein of the native liver [13] were not evident in our patients.

In our opinion, when FHF is diagnosed and there is clinical indication for liver transplantation, the auxiliary approach should be seriously considered, particularly when the patient is young and has no history of previous liver disease. The decision should be made intraoperatively and supported by frozen section. When a liver graft is of exceptionally good quality, a split procedure should be done to reduce the space necessary for the liver tissue in the abdomen and also to obtain a second graft for elective transplantation in another patient on the waiting list. In the case of a marginal liver graft, a full-size auxiliary transplantation should be considered. The regeneration of the native liver should be assessed very carefully on a daily basis in order to reduce the risk of secondary complications, to define the exactly time to taper and eventually stop immunosuppression and, possibly to remove the graft. When auxiliary heterotopic liver transplantation is indicated for FHF, arterialization of the portal vein is sufficient and can be performly safely. Only this technique allows one to place the liver tissue anywhere in the abdominal cavity. It serves as a life saving measure that provides temporary liver support for a select group of patients.

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