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Orthotopic Liver Retransplantation – Case Report

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ABSTRACT

We report a case of orthotopic liver retransplantation (OLRT) in a patient who was suffering from rejection and graft failure after orthotopic liver transplantation (OLT). The patient was a 32-year old female who had diagnosed liver lesion – hepatic cirrhosis. Within two months, with presented condition as a terminal stage of her disease, she underwent the OLT and immunosuppressive postoperative management. Two months after the OLT, in the one-week period, the patient underwent two new operations because of obstructive icterus due to fulminant cholangitis and subhepatic abscess. In spite of this operative and conservative treatment the patient's condition did not improve. Because of graft failure due to bile duct necrosis, she underwent an ORLT operation and her condition is satisfactory, till now. We confirmed that the overall impact of retransplantation persists because patients undergoing elective retransplantation have significantly better prognosis than those requiring an emergency operation.

Key words: liver transplantation, rejection, graft failure, liver retransplantation

Introduction

Orthotopic liver transplantation (OLT) is widely accepted as optimal therapy for acute and chronic progressive debilitating liver disease, as well as for metabolic disease. Results have become excellent, with 1-year patient survival reported to range from 60–80% depending on the sta-

tus of the patient survival and center-related factors¹⁻². Therefore, improved results have enabled surgeons to justify the use of transplantation before patients have end stage liver disease. However, the frequency of rejection after transplantation ranges from 30 to 70%³⁻⁴. The

range of patients who experience acute or chronic graft failure and whose condition requires liver retransplantation is 9–27%⁵.

We report a case of orthotopic liver retransplantation (OLRT) in a patient who was suffering from rejection and graft failure after first OLT.

Case Report

In December 2002, a 32-year-old female was admitted to our hospital with jaundice, pruritus, nausea, vomits and a low-grade fever. The patient had a significant medical history of alcoholism and diagnosed liver lesion. She also suffered from ovarian cyst – operatively treated 4 years earlier, and hospitalized and conservatively treated for Gillian Barre Syndrome.

The diagnostic tests carried out presented us with the following laboratory analysis – increased levels of liver enzymes and total bilirubin, negative serum tests for hepatitis A, B, C, D, E, G and normal amount of α antitripsin, normal iron level and iron binding capacity, negative autoimmune markers; abdominal ultrasound – hepatomegaly, splenomegaly, ascites (microbiology – *Enterococcus faecium*, cytology – mesothelial discharge); gastroscopy – varices esophagi – signs of portal hypertension. She had been treated with metylprednisolone and diuretics. On the tenth day of hospitalization the patient developed radiological confirmed pleural pneumonia, which decreased after cyprofloxacin therapy.

One month after the start of hospitalization the patient underwent liver biopsy with the found of fibroplasy, hepatocytic anisocytosis and anysonucleosys, and extended bile ducts. The laboratory analysis of serum presented leucocytosis, while the cytological analysis of bone marrow presented rich mature granulocytosis. The patient then quickly developed the hepatorenal syndrome, so that

the therapy was supplemented with albumin, dopamine, ursodeoxycholic acid and ryfampin for treatment of pruritus.

At that moment the patient's condition was presented as a terminal stage of her disease, and the OLT was indicated. So, her name was placed on the OLT Waiting List with the status of high urgency.

Two months after the start of her hospitalization the patient underwent OLT (piggy-back technique). The duration of the operative procedure was seven hours. The recipient's blood group was A, Rh negative, while that of the donor was 0, Rh negative. The patho-histological examination of explanted liver was: Hepatic cirrhosis. According to the Postoperative (OLT) Treatment Protocol the patient's immunosuppressive therapy consisted of cyclosporine, metylprednisolone, azatioprin; prophylaxis antibiotic, gancyclovir, antitrombhotic prophylaxis, diuretics, cardio tonics and analgesics. The laboratory analysis of serum presented high levels of total bilirubin, liver enzymes and C reactive protein. CMV DNA was negative, while cyclosporine (C2) drug level was 845. Microbiologic tests of catheter and operative wound swab, bile and abdominal discharge were sterile.

Abdominal ultrasounds taken on the occasion of many check-ups during the period of the first postoperative month presented the following founds: liver with slide hyperechogenic structure; normal look, flow and diameter (d) of intrahepatic ducts, hepatic vein, portal vein (d = 13 mm), distal cava vein (d = 14 mm), hepatic artery (d = 6 mm), with no signs of thrombosis, normal spleen, very small amount of intra-abdominal liquid around the liver, and bilateral minimal pleural effusions.

Therapy consisted of neural, decortin, imuran, sinersul, controloc, diltiazem, lupocet, oxazepam. The patient was dis-

charged one month after the OLT operation.

Two weeks later the patient was admitted to hospital with the symptoms of abdominal pain and jaundice. The laboratory analysis of serum presented high levels of total bilirubin and liver enzymes. Therapy consisted of infusions of crystalloids, bolus of steroids, imuran, meronem, acyclovir, trimetoprim+sulfamethoxazol, diltiazem and induction therapy of intravenous administration of tacrolimus with drug level in serum 21.0 mcg/L. Abdominal ultrasound presented the following finds: hyperechogenic structure of liver, wider diameters of intrahepatic bile ducts in the left liver segments, great amount of ascites in septas, normal look, flow and diameter of vascular structures, and bilateral renal lesions. The patient underwent percutaneous puncture of ascites. Microbiological examinations presented positive hemoculture – *Enterococcus*, so that therapy was supplemented with vancomycin.

Control abdominal ultrasounds five and ten days later presented the same finds, but with a much wider intrahepatic bile ducts in the left liver segment. Vascular structures were normal, and bilateral pleural effusions were found. Liver biopsy presented cholestasis without elements of rejection. Computer tomography of liver confirmed that find.

Two months after the OLT surgery the patient underwent a new operation with symptoms of obstructive icterus because of a fulminant cholangitis. The intraoperative find was normal vascular structure without signs of thrombosis; wider all intrahepatic ducts – pathohistological examination presented the parts of epithelium with necrotic changes. The reconstruction of hepaticojejunal anastomosis by Roux, cholangiodrainage with Wutzl catheters and intra-operative cholangiography were performed. On the fifth postoperative day abdominal ultra-

sound showed ascites, dilated intrahepatic bile ducts and other as the earlier finds. The laboratory analysis of CMV DNA was 35,100 kop/ml.

On the seventh postoperative day the patient presented the symptoms of peritonitis with abdominal ultrasound found of subhepatic abscess. The third surgical treatment was performed with laparotomy, evacuation and drainage of intra-abdominal abscess. Microbiological examinations of abdominal liquid were positive – *Enterococcus* and *Candida albicans*, so the therapy was once again supplemented with vancomycin. Control abdominal ultrasound presented a minimal amount of ascites, anechogenic region in the portal zone with necrosis and dilatation of intrahepatic bile ducts and the other, as it was the case in the earlier finds.

At this moment the orthotopic liver retransplantation (OLRT) was indicated. The patient's name was placed on the OLT Waiting List with the status of high urgency again.

Six months after her first presentation in hospital and three months after her first OLT the patient underwent an OLRT operation (piggy-back technique). The donor's blood group was 0, Rh negative. One month after performing OLRT and the same postoperative management the patient's health condition is satisfactory.

Discussion

Liver transplantation evolved rapidly in the 1980s. Today, OLT is the therapy of choice for many patients with chronic, advanced, irreversible liver disease. Indication for liver transplantation due to alcoholic cirrhosis is 21.6% of all OLT in adults⁶. The important consideration is that carefully selected alcoholic patients would have a higher risk on the basis of medical complications due to alcoholism, such as cardiomyopathy, miopathy, pan-

creatitis, infections, hepatoma, encephalopathy and malnutrition. Despite some early conclusions, more recent studies have documented equivalent survival rates in alcoholic and nonalcoholic transplant recipients⁷.

Our patient had a significant medical history of alcoholism and diagnosed liver lesion without any other medical complications, which will give the higher risk for a successful OLT. We performed the classical OLT procedure (piggy-back technique) and postoperative management.

Rejection is a common complication that usually occurs 7 to 14 days after transplantation. The patient in our case has common symptoms of rejection that consists of elevated LFTs, fever, lethargy, irritability, abdominal pain, nausea and vomiting, diarrhea, and decreased appetite. To investigate rejection after OLT two new studies of noninvasive methods persist: 1) study of cells and cell patterns within serum and bile, and 2) study of cytokines within serum, bile, or urine of transplant recipients; with the use of the biopsy, still as the »gold standard«⁸.

In our case a liver biopsy provides the definitive diagnosis. According to the literature, treatment of our patient consisted of intravenous steroid bolus and symptomatic therapy. A third immunosuppressive agent may be added to baseline therapy.

Acute graft failure is caused most frequently by primary nonfunctioning or hepatic artery thrombosis, whereas chronic rejection may result in progressive deterioration of liver function with delayed liver failure. Less frequent indications include portal vein thrombosis or acute rejection, and bile duct necrosis, hepatitis or other viral infections in rare cases.

The cause of graft failure, in our case, was a bile duct necrosis. The flow through all hepatic and extra-hepatic anatomical

vascular structure was normal, without any sign of thrombosis.

Therapeutic strategies, including highly potent immunosuppressants like OKT3 or FK506, revascularization techniques, and prostaglandin therapy, have been developed to salvage failing grafts. In the absence of effective methods of extracorporeal support, for the majority of patients OLRT remains the only alternative to death. This consideration was the method of treatment in our case. There are several technical considerations in OLRT that may vary from primary liver transplantation. The importance of procuring vascular grafts is particularly emphasized because vascular thrombosis is one of the frequent causes of graft failure, requiring an alternative method of arterial or portal vein reconstruction. The recipient hepatectomy may vary significantly, so that extra care must be taken in the dissection of the liver and blood vessels. Finally, the viability of the recipient's bile duct should be carefully assessed before biliary reconstruction⁹.

The OLRT that we performed in our case still presents itself as a sufficient treatment and the patient has satisfactory condition of her health.

Analyses of organ transplantation programs are often focused on expenses and the allocation of resources. Liver transplantation encompasses crucial anatomical and technical lessons for a general surgeon, and represents an important component of surgical training in the era of minimally invasive surgery and has provided a profound stimulus to technical and scientific innovation among related surgery of liver disease¹⁰.

Not only does liver retransplantation pose a clinical challenge, but also because of increased costs and a finite number of available donors, serious financial and ethical issues are brought up regarding this procedure. The overall impact of re-

transplantation persists because that patients undergoing elective retransplantation have significantly better prognosis than those requiring an emergency operation. This consideration gives a strongly encourage to the application of patient se-

lection criteria on the basis of proven prognostic factors that will result in the best overall rate of patient survival in both cases, the first as well as the second transplantation^{11–13}.

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ORTOTOPNA RETRANSPLATACIJA JETRE – PRIKAZ SLUČAJA

SAŽETAK

Prikazan je slučaj ortotopne retransplantacije jetre (OLRT) u bolesnice koja je bolovala od reakcije odbacivanja transplantata nakon ortotopne transplantacije jetre (OLT). Bolesnica, 32 godine starosti, je imala dijagnosticiranu leziju jetre – hepatičnu cirozu. Unutar dva mjeseca, s kliničkom slikom terminalnog stadija njene bolesti, ona je liječena operacijski – OLT, te poslijeoperacijskim tretmanom imunosupresije. Dva mjeseca nakon OLT, u razdoblju od jednog tjedna, bolesnica je tretirana dvjema novim operacijama, radi simptoma opstruktivnog ikterusa zbog fulminantnog kolangitisa i subhepatičkog apscesa. Unatoč tom operacijskom i konzervativnom tretmanu stanje bolesnice se pogoršalo. Zbog reakcije odbacivanja transplantata, uslijed nekroze žučnih kanala, bolesnica je operacijski tretirana – OLRT i njezino je stanje do sada uredno. Potvrdili smo da pacijenti tretirani elektivnom retransplantacijom imaju značajno bolju prognozu od onih koji su bili tretirani hitnom operacijom.