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PROSPECTS AND RISKS OF LIVER TRANSPLANTATION IN THE REPUBLIC OF SAKHA (YAKUTIA)

ABSTRACT

In order to study the condition of patients after liver transplantation the histories of patients who were on inpatient treatment at the RHN№1 - NCM department of therapy, Yakutsk in 2003 – 2017, were analyzed. Transplantation was performed in the stage of decompensation of liver cirrhosis of viral and non-viral etiology. Timely transplantation of the liver prevents fatal outcome and prolongs the life expectancy of patients.

Keywords: liver transplantation, re-transplantation, chronic viral hepatitis, liver cirrhosis, decompensation, immunosuppressive therapy, complications, mortality.

In the course of many diffuse and focal liver diseases there comes a period when traditional therapeutic methods of treatment or surgical interventions become ineffective, and the out-of-control disease continues to progress, leading the patient to imminent death. Such patients until recently were considered to be incurable, i.e. «hopeless.»

There is a large number of patients with terminal liver diseases, as evidenced by our medical practice and published papers of Russian researchers, in whom the conservative management of hepatic insufficiency, portal hypertension syndrome or cholestasis is practiced, including mostly ineffective chemotherapy in inoperable tumors. The majority of specialists recognize the palliative nature of these methods, which, at best, can only temporarily stabilize the patients' condition. A radical way to treat terminal liver disease is liver transplantation [4, 6-8].

The Republic of Sakha (Yakutia) (RS (Ya)) has one of the highest rates of viral hepatitis B, C, D and mixed forms in Russian Federation. In recent years, the number of young patients with liver cirrhosis (LC) due to chronic mixed hepatitis has increased.

At a certain point of LC course, decompensation begins which leads to bleeding from the enlarged veins of the esophagus. Therefore, until 2005, endoscopic sclerotherapy of varicose veins of the esophagus and stomach was performed at the Therapy department of «The Republic Hospital №1– The National Center of Medicine" (RHN№1 - NCM) in cooperation with physicians of the endoscopy department, which allowed to prevent relapses of bleeding and prolong the life of patients [1, 3].

In 2004 the Clinical Center of the RHN№1 - NCM has become an associate of the FGBU "Academician V.I. Shumakov Federal Research Center of Transplantology and Artificial Organs" (FRCTAO). On December 29, 2004, for the first time in the history of Yakutia, Professor Y.G. Moisiuk has successfully transplanted the cadaveric liver to a patient from the Dzhebariki-Khaya village, who had primary biliary cirrhosis (PBC). In 2005, two more transplantations of cadaveric liver were successfully performed by Professor Y.G. Moisiuk to patients from our republic [1, 2, 5].

The main areas of work in the field of clinical transplantology are: identification and selection of potential recipients of donor organs; performing appropriate surgical intervention; conducting adequate immunosuppressive treatment to maximize the life of the graft and recipient [7].

Due to the permanent scarcity of cadaveric organs, the liver transplantation program in the Russian Federation has developed and is currently developing in two directions: transplantation of the cadaveric liver and transplantation of liver fragments from living related donors. It was the latter direction that made it possible to significantly increase the number of performed liver transplantation operations to patients in our republic. Thus, since 2010, we sent 24 patients with LC of various etiologies to FRCTAO and State Research Center Burnasyan Federal Medical Biophysical Center of Federal Medical Biological Agency (SRC-FMBC) (Moscow). All patients underwent transplantation of a liver segment from a living related donor.

The indisputable advantage of transplantation from a living donor is independence from the system of cadaver organs supply, and thus, the possibility of scheduling the operation depending on the condition of the recipient (and not the short "on ice time" period of cadaver liver). The modern level of hepatic surgery allows getting a quality transplant from a living donor with minimal ischemic and mechanical damage. The liver is considered the most convenient organ transplant in terms of immunological compatibility. This is due to the known immunocompetence of the liver, which to some extent suppresses the immune response of the recipient organism. Therefore, the selection of a donor liver to a particular patient is not difficult from the immunological point of view. The use of related transplants greatly simplifies the conduct of drug-induced immunosuppression [4, 8].

Materials and methods

The analysis of the disease history of 41 patients (25 women, 16 men), age range 27 to 61 years, who were hospitalized after liver transplantation (LT) in the department of therapy RHN№1 - NCM in the 2004-2017 period. Ethnic composition of patients: 33 Yakuts, 8 patients of other ethnicity (Russians et al.). Age groups: less than 30 years old - 8 patients, 31-40 - 12, 41-50 years - 11, 51-60 - 9, 61 years and older - 1. The average age was 37 years. The primary conditions that led to LT: chronic viral hepatitis B, D, C (CHB, CHD, CHC, respectively); primary biliary cirrhosis (PBC); primary and secondary sclerosing cholangitis, LC of toxic and alimentary origin (i.e. alcohol-related liver disease, non-alcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH)). In two patients with CHB and CHD LC, the transplantation was performed at the stage of hepatocellular carcinoma.

All patients underwent general clinical, laboratory and instrumental methods of diagnosis, as well as consultations of specialists, in accordance with national guidelines and standards of care for patients who underwent LT. A prerequisite was to obtain informed consent from patients to participate in the study and conduct additional diagnostic interventions.

Results and discussion

High incidence of chronic hepatitis and LC in the RS (Ya) procured the

implementation of liver transplantation (LT) in the RHN№1 - NCM.

Since 2013, 14 patients underwent segmental LT from a living related donor in RHN№1 - NCM. In August 2016 for the first time in the history of medicine of our republic, transplantation of cadaveric liver was successfully performed in RHN№1 - NCM.

There is an annual increase in the number of LT in Yakutia (Fig. 1) and surgeries carried out in the RHN№1 - NCM (Fig. 2). LT from a living related donor is preferred in Yakutia due the scarcity of cadaver organs. It is also more feasible for the patient and his or her relatives, because there is no need for the recipient and the donor to travel to Moscow. Moreover, the waiting times for the LT are significantly reduced.

The primary conditions leading to LT in Yakutia: CHD - 24 patients (58.3%), PBC - 6 (14.6%), CHC - 5 (12.1%), secondary sclerosing cholangitis - 2 (4.8%), CHB - 2 (4.8%), primary sclerosing cholangitis - 1 (2.4%), LC of toxic and alimentary origin - 1 (2.4%).

The vast majority of operated patients are females aged 30-50 years of indigenous ethnicity with cirrhosis of the viral etiology. Patients with LC due to CHD (58.53%) were mostly young people under 40 years old, infected in childhood during invasive medical procedures. It should be noted that the number of patients with autoimmune liver diseases has increased in recent years. They are mostly middle-aged women.

It should be emphasized that among patients who underwent LT, three patients successfully underwent liver retransplantation:

1. Patient N., female, born in 1959, the transplantation of cadaveric liver was performed in the Shumakov FRCTAO due to decompensated PBC on December 29, 2004. The postoperative period proceeded smoothly. 3-component protocol of immunosuppression was chosen for this patient, which included tacrolimus (Prograf®), methylprednisolone (Medrol®) and mycophenolic acid (Myfortic™). Later the patient developed PBC in transplanted liver. The only way to improve patient's condition was to perform liver retransplantation. Prior to surgery, several plasmaphereses were performed to lower bilirubin levels. On April 1, 2010, transplantation of cadaveric liver was successfully carried out at the same institute. Currently, the patient continues to receive drug-induced immunosuppression according to protocol. Patient is feeling well and continues to work.

2. Patient I., male, born in 1973, required an orthotopic transplantation of a liver segment from a living related donor (brother) due to CHB LC, which was performed in SRC FMBC on September, 12, 2013. Postoperative period was complicated by cicatricial stricture of end-to-end choledochocholedochostomy, which led to the development of mechanical jaundice and, ultimately, graft dysfunction. Liver retransplantation was the only feasible option. On September 2, 2017 the transplantation of cadaveric liver was successfully performed in the same institute. Currently, the patient is receiving a standard 2-component drug immunosuppression, the overall condition is satisfactory.

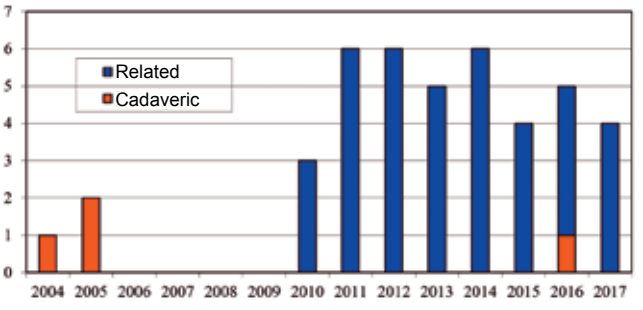

Fig. 1. The number of liver transplantations in the RS (Ya)

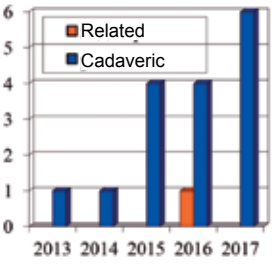

Fig. 2. The dynamics of liver transplantations' growth in the GAU RS (Ya) "RH №1- NCM"

3. Patient T., male, born in 1989, required the orthotopic transplantation of a liver segment from a living related donor due to CHD LC, which was performed by surgeon from FRCTAO who is also a graduate of the Medical Institute of Medical Institute, Yakut State University (currently North-Eastern Federal University named after M.K. Ammosov). An operation was performed on June 28, 2013 at the RHN№1 - NCM for the first time in Yakutia. The postoperative period was complicated by thrombosis of the anastomosis of the hepatic artery and urgent life-saving operation was performed on July 8, 2013: relaparotomy, retransplantation of a liver segment from a second related donor. Following postoperative period proceeded smoothly. Drug immunosuppression was carried out with 2-component protocol - Prograf® and Myfortic™. At present, the patient's condition is satisfactory.

During the period from 2004 to 2017, 7 (17%) of the 41 patients who underwent liver transplantation died: 5 in early postoperative period, 2 patients died within one year after the transplantation due to the infection caused by immunosuppressive therapy (Table).

Survived patients receive immunosuppressive therapy with Prograf® (one patient receives cyclosporine (Sandimmune®) due to adverse reaction to Prograf®). Tacrolimus concentration in the blood serum is continuously monitored. All patients who underwent liver transplantation are followed-up at the polyclinics, in the Clinical-Consultatory Department of RB1 NCM and in the Department of Therapy of the RHN№1 - NCM, periodically undergoing in-patient examination and treatment once or twice a year, depending on the severity of the condition, the timing of the operation and the presence of complications.

Currently, 34 patients who underwent LT are monitored in Therapy Department of the RHN№1 - NCM. In addition, there are 30 patients with chronic diseases of liver at the stage of cirrhosis, 22 of whom are included in the waiting list for the transplantation of the cadaveric liver.

Conclusions. 1. Considering the large number of patients with severe liver diseases in the RS (Ya), good survival after LT, it is necessary to develop state program for the development of transplantology in the RS (Ya).

2. Further development of transplantation (both the transplantation of the liver segment from the living related donor and cadaveric liver) is necessary, because it is one of the most accessible and effective ways of management of patients with terminal liver diseases.

3. Special attention should be given to the quality of HBV vaccination with a 100% coverage of the child population.

4. Foundation of Hepatology Center in RS (Ya) may potentially improve early diagnosis of patients with chronic liver diseases and quality follow-up of patients with chronic liver diseases and patients who underwent LT.

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Patient P., 1966, LC Outcome chronic viral hepatitis B, D	15.12.11 Transplantation of a fragment of a liver from the daughter (Shumakov FNTST and IO)	In the early postoperative period	Accession of infection against IT
Patient S., 1954, PBC	28.10.10 Transplantation of a fragment of a liver from the daughter (Shumakov FNTST and IO)	04.2011	Accession of infection against IT
Patient S., 1989 , LC Outcome chronic viral hepatitis B, D	10.07.11. Transplantation of a fragment of a liver from brother (Shumakov FNTST and IO)	In the early postoperative period	Graft dysfunction
Patient B., 1982, secondary sclerosing cholangitis	10.06.2014г. Transplantation of a fragment of a liver from brother (Burnazjan FMBA)	In the early postoperative period (July)	Aspergillosis
Patient P., 1982, LC Outcome chronic viral hepatitis B, D	04.07.2015 Transplantation of a fragment of a liver from brother (GAU RH№1-NCM	In the early postoperative period	Bleeding from the splenic vein
Patient B., 1961, secondary sclerosing cholangitis	25.06.16 Transplantation of a fragment of a liver outcome SSC from brother (GAU RH№1-NCM) Complication: portal vein thrombosis	In the early postoperative period	Portal vein thrombosis, acute graft rejection
Patient L., 1980, LC of toxic and alimentary origin	28.02.17 Transplantation of a fragment of a liver from son LC of toxic and alimentary origin (GAU RH№1-NCM). Complication: hemoperitoneum. Relaparotomy 28.02.17	In the early postoperative period	Graft dysfunction Acute liver failur

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