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Endoscopic control after retroperitoneal pancreas transplantation with a Roux-en-Y duodenojejunostomy for exocrine drainage

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Abstract

Background. *Simultaneous pancreas and kidney transplantation is a gold standard in the treatment of diabetes mellitus complicated by stage 5 chronic kidney disease as a result of diabetic nephropathy. One of the main problems of clinical pancreas transplantation is the pancreas graft*

exocrine drainage. In order to preserve the advantages of the retroperitoneal graft location and avoid the main disadvantage of duodenal drainage, namely, fatal complications potentially arising in case of necessary graft removal, we have proposed a modified method of retroperitoneal pancreatic transplantation with exocrine drainage via a modified Roux-en-Y duodenojejunostomy. It reduces the number of severe surgical complications and increases the recipient survival rate. When this method was used in previous years, it was not possible to assess the condition of donor duodenum mucosa and interintestinal anastomoses.

Objective. *To demonstrate the possibility of endoscopic assessment of interintestinal anastomoses when performing retroperitoneal pancreas transplantation with small intestine drainage of exocrine secretions.*

Results. *The article presents our initial experience of endoscopic assessment of the interintestinal anastomoses and the mucous membrane of the donor duodenum after retroperitoneal pancreas transplantation with exocrine drainage via a Roux-en-Y duodenojejunostomy.*

Conclusion. *The presented case demonstrates the feasibility of diagnostic endoscopic interventions when performing retroperitoneal pancreas transplantation with small intestine drainage of pancreatic secretions.*

Keywords: simultaneous pancreas and kidney transplantation, retroperitoneal pancreas transplantation, enteric exocrine drainage, endoscopic evaluation of the pancreas graft

Conflict of interest. The authors declare no conflict of interest

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MDP, major duodenal papilla
SPKT, simultaneous pancreas and kidney transplantation
PG pancreas graft

Introduction

According to the Federal Register of Diabetes Mellitus, the total number of patients with diabetes mellitus in the Russian Federation is more than 4.9 million people (3.3% of the population of the Russian Federation); more than 277 thousand people suffer from type 1 diabetes mellitus (5.6%) [1, 2]. Diabetes mellitus is one of the main causes of stage 5 chronic kidney disease, which requires constant renal replacement therapy. This complication significantly worsens the quality of life of patients and shortens life expectancy, placing diabetes in the 7th place among the causes of death in the global ranking [3]. Combined kidney and pancreas transplantation is the gold standard for surgical treatment of type 1 diabetes mellitus complicated by the diabetic nephropathy resulting in stage 5 chronic kidney disease [4, 5]. At the moment, this is the only way to achieve true insulin independence, avoiding exogenous insulin and the need for constant monitoring of blood glucose levels, which would undoubtedly improve the quality and life expectancy of patients [6, 7].

Pancreas transplantation has the highest rate of surgical complications compared to transplantation of other solid organs [8, 9]. One of the main problems in clinical pancreas transplantation is the method of drainage of pancreatic secretions. In the process of developing surgical transplantation techniques, various options were used, such as: the drainage into the free abdominal cavity, stoma diversion into the anterior abdominal wall, ligation and injection of the main pancreatic duct, drainage into the urinary tract [10–13]. By the beginning of the 2000s, the transplant community had recognized that enteric exocrine

drainage is the most optimal and physiological method [14, 15]. Currently, the most common methods of transplantation include transplantation with an intra-abdominal graft location and the formation of a duodenojejunal anastomosis, as well as a retroperitoneal graft transplantation technique with forming a duodenoduodenal anastomosis [16, 17]. The retroperitoneal location has undoubted advantages: a lower incidence of intestine paretic changes, no communication with the free abdominal cavity in the event of complications, which in this case can be treated by minimally invasive techniques [18, 19]. When forming a duodenoduodenal anastomosis to assess the status of the interintestinal anastomosis, perform a biopsy and drainage/stenting of the Wirsung duct, the endoscopic diagnostic and treatment methods are available [20–22]. The defect of native duodenum occurring when the interintestinal anastomosis fails or after the pancreas graft (PG) removal becomes a serious problem under conditions of constant immunosuppressive therapy as the reparative processes are considerably reduced, all of which leads to the formation of “high” duodenal fistulas which treatment becomes a very difficult surgical task. This often contributes to the development of serious infectious complications and significantly reduces recipient survival rates [23]. In order to eliminate the main drawback of duodenal drainage we have developed and implemented in clinical practice a modified method of exocrine drainage via a Roux-en-Y duodenojejunostomy. The use of this technique can reduce the number of severe surgical complications and increase the recipient survival rates. Earlier, in patients operated on using this technique, it was impossible to assess the condition of the donor duodenum mucosa and interintestinal anastomoses, due to the fact that the anastomosis was formed at a distance of 40–60 cm from the ligament of Treitz. In later operations, we formed the anastomosis at a distance of 30 cm from the Treitz ligament,

which made it possible to use endoscopic methods. We present the initial experience of endoscopic assessment of the status of the enteroenteric, duodenojejunal anastomoses, and donor duodenum mucosa after retroperitoneal pancreas and kidney transplantation with forming a duodenojejunostomy on a Roux-en-Y excluded small intestine loop.

Case Report

Recipient

Patient B. 26 years old had type 1 diabetes mellitus complicated by stage 5 chronic kidney disease resulting in diabetic nephropathy. From patient's medical history it was known that the onset of the disease had been noted at the age of two, and an insulin therapy was immediately prescribed. Secondary diabetic complications gradually progressed: retinopathy, nephropathy. In September 2021, stage 5 chronic kidney disease was diagnosed and the renal replacement therapy with program hemodialysis began. Indications for simultaneous pancreas and kidney transplantation were considered.

Surgery

Considering the irreversible nature of the underlying disease, absent absolute contraindications, and the availability of histocompatible grafts (renal and pancreaticoduodenal), the simultaneous pancreas and kidney transplantation was performed on April 24, 2023. Access was obtained through a midline laparotomy. The first stage was retroperitoneal kidney transplantation into the left iliac region; the neoureterocystoanastomosis was formed using an internal ureteral stent.

Retroperitoneal pancreas transplantation was performed using a modified technique with the drainage of the graft pancreatic secretions into the recipient's jejunum with a Roux-en-Y diversion of a small intestine loop. An arterial anastomosis was formed between the common

arterial anastomosis of the Y-shaped vascular implant of the graft and the recipient common iliac artery; for this, at the stage of pre-transplantation treatment, an anastomoses were formed between the superior mesenteric artery of the graft and the internal iliac artery of the graft, and between the splenic artery of the graft and the external iliac artery of the graft. A venous anastomosis was formed between the portal vein of the graft and a part of the recipient's inferior vena cava. Then a duodenojejunostomy was made, for which purpose, the small intestine was separated at a distance of 30 cm from the ligament of Treitz, followed by forming an antiperistaltic anastomosis between the efferent and afferent loops using a linear stapler. Next, through the stoma formed in the peritoneum, a 10 cm long small intestine loop excluded up to Roux-en -Y was passed into the right retroperitoneal space, fixing it to the peritoneum with separate interrupted sutures. In the retroperitoneal space, a duodenojejunostomy was formed using a double-row hand suture between the duodenal portion of the graft and the Roux-excluded loop of recipient's small intestine. The pancreas graft bed was drained with three drainage tubes (medially, laterally, and to the interintestinal anastomosis), and 2 drainage tubes were additionally placed in the pelvic cavity and in the renal graft bed, one each. The surgery duration was 7 hours, the cold ischemia time for the renal allograft was 6 hours, and the cold ischemia time for it was 8 hours.

Immunosuppressive therapy

The patient received three-component basic immunosuppressive therapy (IST) with the induction; the induction IST included intravenous methylprednisolone 750 mg intraoperatively with its further intravenous drip administration of 250 mg over the next two days, intravenous drip basiliximab 20 mg intraoperatively and on the 4^{th} postoperative day. Maintenance IST consisted of extended release tacrolimus once daily at a

dose to achieve target blood levels of 8–9 ng/mL, mycophenolic acid 720 mg orally twice daily with a dose reduction to 360 mg orally twice daily from the 14th day, methylprednisolone 16 mg orally once a day with a gradual dose tapering by 4 mg on the 14th, 28th, and 56th days.

Preventive antibiotic therapy

In the postoperative period, preventive antibiotic therapy was administered up to the following scheme: intravenous meropenem 1 g 3 times a day for 7 days, intravenous vancomycin 500 mg once a day for 5 days, intravenous ornidazole 500 mg 2 times a day for 10 days. Then, for 5 months, the patient received co-trimoxazole 480 mg orally once daily.

Preventive anticoagulant therapy

As anticoagulant therapy, from the first day, heparin was administered at a dose of 10,000 units per day intravenously via an infusion pump for 4 days. Then, from the 10th day, fraxiparin was prescribed at a dose of 0.3 ml subcutaneously twice daily for 20 days with a switch to prophylactic administration of acetylsalicylic acid at a dose of 100 mg orally once a day.

Antisecretory therapy

From the moment of the pancreas graft reperfusion, 1200 μg of octreotide was administered per day via an infusion pump. From the seventh day, octreotide was administered subcutaneously 3 times a day at a total dose of 1200 μg with a gradual reduction and complete withdrawal of the drug by the 30th day under the control of blood amylase levels.

Postoperative period

The drain from the pelvic cavity of the transplanted renal graft and the lateral drainage from the PG were removed on the first postoperative

day, the drainage from the interintestinal anastomosis and the medial drainage from the PG were removed on the 5th and 8th days of the post-transplantation period, respectively.

The primary initial function of the grafts was noted as the normalization of azotemia from the 2nd day, euglycemia without administering exogenous insulin during the first hours after the PG reperfusion.

On the 4th day after surgery (28.04.2023), a decrease in blood hemoglobin by 15 g/L for 3 hours was noted. Considering the ultrasound results of absent free fluid in the abdominal cavity and retroperitoneal space and the presence of melena, the condition was regarded as gastrointestinal bleeding that required esophagogastroduodenoscopy. At an examination using an OLYMPUS GIF-H190 video gastroscope having a length of 1350 mm, a large amount of fluid mixed with lysed blood was visualized in the gastric lumen; the mucous membrane was evidently hyperemic, erosions up to 0.3 cm in diameter with hydrochloric acid hematin in the bottom were identified in the stomach body along the anterior wall and greater curvature. The condition was regarded as a Forrest 2c bleeding that did not require obtaining hemostasis endoscopically [24]. During the control endoscopic examination after 24 hours, no evidence of recurrent bleeding was seen. In addition, at endoscopic examination, the formed enteroenteric antiperistaltic anastomosis and duodenojejunostomy were visualized (Fig. 1).

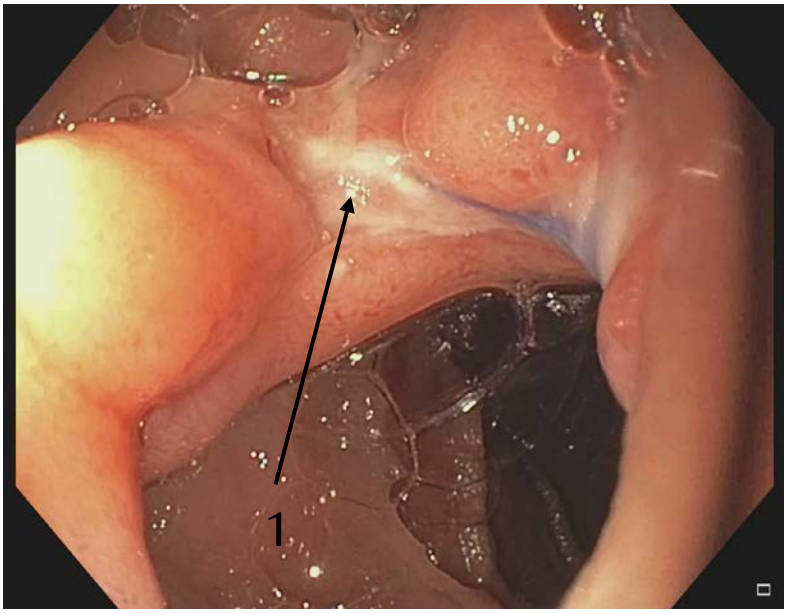

Fig. 1. Endoscopic photo. Duodenojejunal anastomosis. 1, anastomotic line

When assessing the interintestinal anastomoses, no evidence of leakage was obtained; the intestinal walls were without inflammation; neither stenosis nor ulcerative defects were found (Fig. 2).

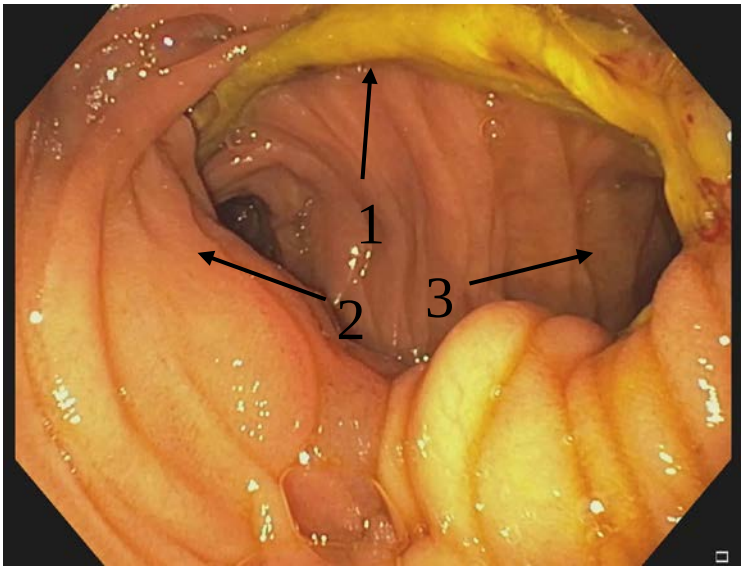

Fig. 2. Endoscopic photo. Antiperistaltic enteroenteric anastomosis. 1, anastomotic line; 2, efferent end of the small intestine, 3, loop of the small intestine directed to the retroperitoneum

The mucous membrane in the anastomotic area was pink and velvety. The sutured stump of the donor duodenum was healthy, without signs of inflammation (Fig. 3).

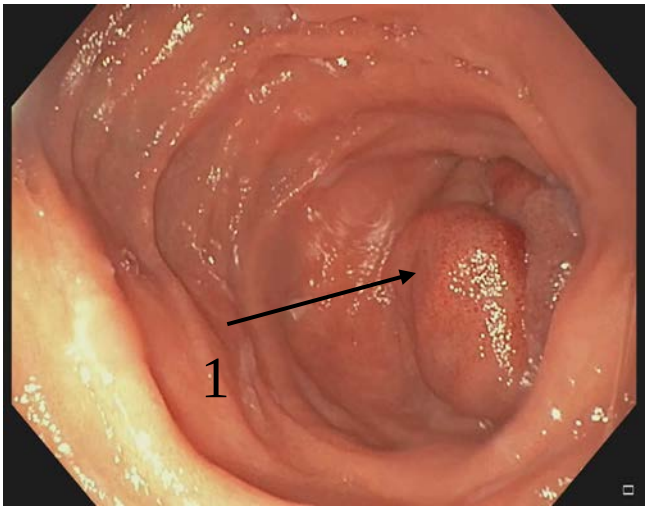

Fig. 3. Endoscopic photo. Donor duodenum. 1, sutured stump of the donor duodenum

Laterally to the anastomotic spurs, the donor major duodenal papilla (MDP) was visualized, hemispherical in shape, up to 0.6 cm in diameter, with an orifice of 0.2 cm (Fig. 4).

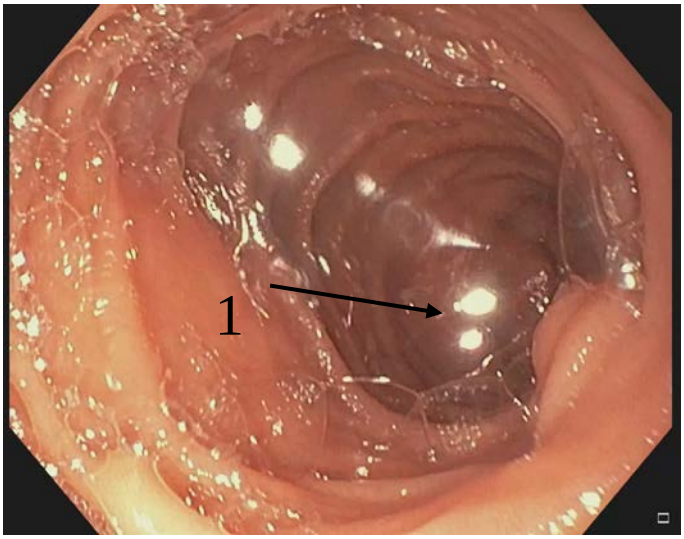

Fig. 4. Endoscopic photo. Donor duodenum with major duodenal papilla. 1, donor major duodenal papilla

The early postoperative period (from 11.05.2023 – the 18th post-transplant day) was complicated by the development of the renal graft acute rejection crisis. The clinical presentation included an acute unexplainable decrease in daily diuresis, a progressive increase in creatinine and blood urea, the level of anti-HLA antibodies, and an increase in the transverse size of the renal graft at ultrasound examination. A combination anti-crisis therapy was pursued, including pulse therapy with methylprednisolone in a total dose of 1250 mg, infusion of polyclonal anti-thymocyte antibodies (anti-thymocyte rabbit immunoglobulin) in a total dose of 400 mg. A favorable clinical effect was noted as the normalized clinical, laboratory parameters and instrumental test results characterizing the renal graft condition.

On the 43rd postoperative day, the patient was discharged from the hospital in satisfactory condition with adequately functioning grafts. Laboratory parameters at discharge were as follows: creatinine 99 μmol/L, urea 6 mol/L, glomerular filtration rate 90 ml/min/1.73 m^2, alpha-amylase 98 U/L, glucose level was within reference range of values.

Discussion

To date, pancreas transplantation remains the only definitive surgical treatment for type 1 diabetes. In most cases, it is performed as a simultaneous pancreas and kidney transplantation in patients with type 1 diabetes mellitus complicated by stage 5 chronic kidney disease resulting in diabetic nephropathy [25–27]. Pancreas transplantation is performed to replace the lost insulin-producing function of the native pancreas. The “cornerstone” of pancreas transplantation remains the problem of pancreatic graft secretions drainage. During the development of surgical techniques for pancreas transplantation, various methods of exocrine secretion drainage were used [28]. In the late 1990s and early 2000s, the

scientific community came to a consensus that the best and more physiological way to drain the pancreatic secretions was the enteral one. However, questions as to which part of the small intestine it should be drained have remained controversial to this day. The most commonly used methods have remained the formation of duodenojejunostomy with the graft positioning in the abdominal cavity and the duodenoduodenal anastomosis with the retroperitoneal graft location. On the one hand, the PG retroperitoneal location has an undoubted advantage, as the pathological focus in the event of complications is located retroperitoneally, which allows an active use of minimally invasive treatment methods. Most often, with this arrangement, the duodenal drainage is used, which increases the risk of developing severe surgical complications. Thus, according to some researchers, the rates of intestinal anastomosis failure can reach 20%, and mortality can amount to 78% [23, 29]. On the other hand, drainage into a small intestine is a technically simpler and safer method for forming an anastomosis, but the intra-abdominal graft positioning contributes to a longer recovery of intestinal motility in the early postoperative period and the development of adhesive disease in the long term. In addition, if complications occur, the pathological focus is located in the free abdominal cavity. In this regard, we have developed and introduced into clinical practice the technique of retroperitoneal pancreas transplantation with pancreatic secretion drainage into a Roux-en-Y excluded loop of the small intestine, and proved the feasibility of successfully performing such transplantation. This technique made it possible to maintain the advantages of the retroperitoneal location of the graft and eliminate the main disadvantage of the pancreatic secretion drainage into duodenum [30]. The level of the interintestinal anastomosis formation (40–60 cm from the ligament of Treitz) chosen for the initially performed transplantations made it

impossible to endoscopically assess the condition of interintestinal anastomoses and the donor duodenal mucosa. At later experience, we made anastomosis at a “higher” level (30 cm from the ligament of Treitz). That made it possible to perform an endoscopic examination to assess the status of the formed anastomosis and duodenum of the graft, as well as made potentially feasible the therapeutic manipulations (endoscopic hemostasis, the main pancreatic duct stenting) or biopsy.

Conclusion

Thus, retroperitoneal pancreas transplantation with the drainage of pancreatic secretions into a Roux-excluded loop of the small intestine is an effective and safe technique ensuring the possibility to endoscopically assess the status of interintestinal anastomoses and to perform therapeutic and diagnostic manipulations on the donor duodenum.

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