Autotransplantation of pancreatic islets.
A single-center first experience

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Autotransplantation of pancreatic islets. A single-center first experience

INTRODUCTION: *Islets auto-transplantation (IAT) is a well-known procedure that may improve glycemic control after total or completion pancreatectomy compared to insulin therapy alone.*
CASE REPORT: *We herein report our experience in IAT with the case of a sixty years old woman underwent completion pancreatectomy for recurrent pancreatitis. She received IAT by percutaneous trans-hepatic intra-portal injection. The patient recovered well, except for a surgical wound infection that was treated with vacuum therapy. She was discharged on p.o.d. 27th in good general conditions and tolerating a diet.*
DISCUSSION: *Data in literature demonstrate that IAT is cost-effective on the long-run compared to insulin therapy in patients with diabetes. 30-days mortality rate for islets auto-transplantation (IAT) following total pancreatectomy is 5%, which is comparable with previous reports on total pancreatectomy without IAT. Our report may expand the literature on this procedure in order to further develop and improve both technique and outcomes, and clarify the correct indication to surgery.*

KEY WORDS: Auto-transplantation, Chronic pancreatitis, IAT, Pancreatic islets, Total pancreatectomy

Introduction

Islets auto-transplantation (IAT) is a well-known procedure that may reduce insulin dependence incidence after total or completion pancreatectomy. In a recent meta-analysis by Dong and colleagues [1], 15 articles reporting IAT outcomes after total and partial pancreatectomy were analyzed and discussed.

We herein report our experience in IAT. In detail, the case and the follow-up results of a woman that underwent a completion total pancreatectomy for complications of chronic pancreatitis and then treated with IAT at Niguarda Ca' Granda Hospital (Milan, Italy).

Case Report

A sixty years old woman came to our attention complaining of recurrent abdominal pain. Six years before she underwent duodenopancreatectomy at another institution for chronic pancreatitis in a setting of pancreas divisum, complicated by a grade B pancreatic fistula, and perianastomotic gastric ulcerations. Furthermore, she lat-

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er underwent endoscopic stenting of the main pancreatic duct due to persistence of abdominal pain. About her past medical history she reported tonsillectomy, appendectomy, hysteroannessiectomy, glaucoma, melanoma. Preoperative fasting glucose blood level was 62 mg/dl.
Given her past history, the recurrent abdominal pain and relapsing pancreatitis, after multidisciplinary discussion she underwent on March 2014 a completion total pancreatectomy and islet autotransplantation.
According to the literature [2], pancreatic islets isolation consists of six steps: (1) cleaning of the resected pancreas and cannulation of the main duct; (2) organ perfusion; (3) digestion; (4) dilution, tissue collection and rinse; (5) purification through a density gradient; (6) islets number evaluation. The aim is to obtain as much as possible islets combining both enzymatic and mechanic harvesting from the pancreatic tissue. After the perfusion with an enzymatic solution using peristaltic pumps, the tissue is manually centrifuged to obtain small cell clusters that are then diluted with a cold solution. Then the endocrine fraction is harvested through a purification phase, that allows obtaining islets with different grade of purity. To determine the number of islets a known volume of cell suspension is colored with an insulin-specific marker and analyzed under the microscope (10x). The standard range for islets size is 50 mm and purity is then calculated as the proportion of 100 mm islets found in sample. For IAT cell culturing is usually not needed.
Islet infusion is then performed 24 hours after pancreatectomy under ultrasound and fluoroscopic guidance, by intra-portal trans-hepatic percutaneous injection. A color-doppler ultrasound is then performed to rule out bleedings or thrombosis of the portal vein.
The patient recovered well, except for a surgical wound infection that was treated with vacuum therapy. She was discharged on p.o.d. 27th in good general conditions and tolerating a diet. During the follow up after 6 months the patients was doing well, with the need of small doses of insulin (3-5u of fast-acting insulin at mealtime). A glycemic holter test was performed 8 months after surgery demonstrating an average glycemia of 197 mg/dl (range 82-355). Blood exams 12 months after surgery demonstrated fasting blood glucose 113 mg/dl, basal C-Peptide 1.3 ng/ml, postprandial C- Peptide 2.2 ng/ml, glycated hemoglobin (IFCC-HbA1c) 72 mmol/mol.

Discussion

Since the first case of IAT performed in 1977 in Minnesota [1], there are now strong evidences of cost-effectiveness of pancreatic islet transplantation. About islets allograft, the Collaborative islets transplant registry reported the experience from 1999 to 2008, demonstrating that of 198 recipients expected at 3-years post-first infusion, 23% were insulin independent, 29% were insulin dependent with detectable C-peptide, 26% had no detectable C-peptide (including those known to have lost islet function), and 22% had missing data [3]. IAT overcomes some disadvantages related to allotransplantation, like organ availability and rejection [4].
On the other hand, Dong and colleagues reported that 30-days mortality rate for islets auto-transplantation (IAT) following total pancreatectomy was 5%, which is comparable with previous reports on total pancreatectomy without IAT, and a borderline significant association was observed between insulin independence rate and Islets equivalents transplanted per body weight [1].
As reported by Beckwith and colleagues, the outcome of IAT in terms of full or partial graft function or graft failure shows a large variation that can be related to multiple factors, for example patient selection, quality of donor organ, quality of islet manufacturing, and immunosuppressive protocol. Graft survival rates in the multicenter Edmonton trial were lower than the values used in the present model, i.e., full graft function was 44% after one yr and 14% after two yr, and partial graft function was 10% after one yr and 44% after two yr.[5] However, even for these outcomes, islet transplantation is cost-saving and cost-effective in the long term after transplantation when compared with standard insulin treatment [5]. In particular, effectiveness measured in quality-adjusted life years (QALY) is reported better for islet transplantation than for standard insulin treatment already from the first post-transplant year. Moreover, cumulative cost becomes lower starting at the 11th yr after transplantation; hence, islet transplantation is better than standard insulin treatment starting the ninth yr after transplantation [5].
One of the major interests in pancreatic surgery is to reduce the rate of pancreatic fistula after duodenopancreatectomy, a frequent and harmful complication with an average incidence rate of 20% [6]. Given the results reported in literature, we hypothesized that total pancreatectomy followed by IAT may be a safe and effective procedure, instead of duodenopancreatectomy, in patients with pancreatic head or biliary duct neoplasms at high risk to develop pancreatic fistula. Therefore, we decided to set up a protocol for total pancreatectomy and IAT in our Institution for the above-described cohort of patients. The transplantation procedure is the one previously described. Fasting glucose blood level, glicate hemoglobin, C-Peptide (both basal and after glucagon administration) anti-GAD antibodies, PCR and D-Dimer will be tested perioperatively and during the follow up at 3, 6, 12, 24, 36 months. Moreover, during the follow up a quality of life questionnaire will be administered to evaluate patients' satisfaction.

Conclusions

Pancreatic islets auto-transplantation is a safe and effective procedure and good outcomes have been reported after total pancreatectomy for chronic pancreatitis. We reported our experience of a successful treatment for a

completion pancreatectomy for chronic pancreatitis. Considering the acceptable metabolic control attainable by IAT after total pancreatectomy, this approach might be a suitable alternative to standard duodenopancreatectomy for patients affected by neoplasms of the head of the pancreas at high risk to develop a postoperative fistula.

Riassunto

L'autotrapianto d'isole pancreatiche (IAT) è una procedura ben nota che consente di migliorare il controllo glicemico dopo una pancreasectomia totale (o completamento di pancreasectomia dopo duodenocefalopancreasectomia) rispetto alla sola terapia insulinica.
In questo lavoro presentiamo la nostra esperienza nel campo dell' IAT riportando il caso clinico di una donna di sessanta anni, sottoposta a completamento di pancreasectomia per episodi ricorrenti di acuzie in un quadro di pancreatite cronica. Il trattamento IAT è stato somministrato mediante iniezione trans-epatica intra-portale. Il recupero post-procedurale è stato ottimale, fatta eccezione per un'infezione di ferita che ha richiesto un trattamento con tecnologia a pressione negativa. La paziente è stata dimessa in ventisettesima giornata post-operatoria, in buone condizioni generali, dopo regolare ripresa dell'alimentazione e della canalizzazione.
I dati presenti in letteratura dimostrano che la IAT è una procedura sicura, garantendo nel lungo periodo un vantaggio rispetto alla terapia insulinica in termini di rapporto costo-beneficio. Riguardo alla procedura chirurgica, è qui utile ricordare che la mortalità a 30 giorni dopo pancreasectomia totale associata a IAT è del 5%, ed è pertanto sovrapponibile ai risultati della pancreasectomia totale senza IAT. Riportando questa esperienza intendiamo contribuire alla crescita della casistica chirurgica attuale in questo campo, proponendo nel futuro un più ampio sviluppo e una più estesa applicazione di tale approccio.

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