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Agnieszka Tuszyńska¹, *Edward Franek^{1,2}

Qualification for pancreas transplantation in patient with type 1 diabetes – case report

Kwalifikacja pacjentki z cukrzycą typu 1 do przeszczepienia trzustki – opis przypadku

¹Department of Internal Diseases, Endocrinology and Diabetology, Central Clinical Hospital of the Ministry of the Interior and Administration in Warsaw

Head of Department: Professor Edward Franek, MD, PhD

²Department of Human Epigenetics, Mossakowski Clinical Research Centre, Polish Academy of Sciences, Warsaw

Head of Department: Professor Monika Puzianowska-Kuźnicka, MD, PhD

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Address/adres:

*Edward Franek

Department of Internal Diseases,
Endocrinology and Diabetology
Central Clinical Hospital of the Ministry
of the Interior and Administration in Warsaw
ul. Wołoska 137, 02-507 Warszawa
tel. +48 (22) 508-14-05
edward.franek@cskmswia.pl

Summary

Diabetes is a chronic disease affecting (according to International Diabetes Federation) over 400 million people worldwide and these numbers are going to increase. This is mostly caused by unhealthy lifestyle. It is possible to reduce the risk of type 2 diabetes by improving diet and increasing physical activity, whereas type 1 diabetes, that accounts for 7-12% of cases, is not currently preventable.

Regardless of a type, diabetes is associated with a number of micro and macrovascular complications that affect life expectancy, and which may be prevented by good metabolic control of the disease. In order to maintain normoglycemia and consequently avoid complications novel therapeutic strategies are pursued. Among all available treatment options only pancreas transplantation enables insulin independency, eliminates acute complications and stabilizes long-term renal and neural complications, thereby improving quality of life. Vast majority of recipients are patients with type 1 diabetes and end-stage renal disease in whom glucose control is difficult to achieve resulting in frequent, acute and severe complications (hypoglycaemia, marked hyperglycaemia, ketoacidosis) that require medical attention.

Unfortunately pancreas transplantation is associated with potential risk such as immediate complications (rejection, thrombosis, surgical techniques failure) and necessity for lifelong immunosuppression. Thus, it is essential to evaluate the patient properly in terms of potential contraindications before deciding to perform pancreas transplantation. This paper is a case report showing some issues connected with a proper qualification for the pancreas transplantation.

Streszczenie

Cukrzyca jest chorobą przewlekłą, która (wg Międzynarodowej Federacji Diabetologicznej) dotyka ponad 400 milionów ludzi na całym świecie, a z uwagi na niezdrowy styl życia ten odsetek będzie ulegał zwiększeniu. W przypadku cukrzycy typu 2 możliwa jest redukcja ryzyka zachorowania poprzez poprawę diety i zwiększenie wysiłku fizycznego, podczas gdy cukrzyca typu 1, odpowiadającej 7-12% przypadków, nie można obecnie zapobiec.

Bez względu na rodzaj cukrzycy, niesie ona ze sobą ryzyko powikłań mikro- i makronaczyniowych, które wpływają na długość życia, a którym można zapobiec dzięki dobrej kontroli metabolicznej choroby. W celu utrzymania normoglikemii oraz w konsekwencji uniknięcia powikłań wprowadzane są nowe metody terapeutyczne. Spośród wszystkich dostępnych opcji leczenia jedynie przeszczepienie trzustki pozwala na niezależność od insuliny, eliminuje ostre komplikacje i zapobiega postępowi przewlekłych nefrologicznych i neurologicznych powikłań, polepszając tym samym jakość życia. Zdecydowaną większość biorców przeszczepów stanowią pacjenci z cukrzycą typu 1 powikłaną nefropatią, u których trudno jest uzyskać prawidłową kontrolę glikemii, co skutkuje częstymi i poważnymi powikłaniami (hipoglikemia, istotna hiperglikemia, kwasica ketonowa) wymagającymi interwencji medycznej.

Niestety przeszczepienie trzustki wiąże się z potencjalnym ryzykiem, takim jak ostre komplikacje (odrzucanie, zakrzepica, błędy chirurgiczne), i potrzebą stosowania immunosupresji przez całe życie. W związku z powyższym istotne jest, aby odpowiednio ocenić pacjenta przed podjęciem decyzji o przeszczepieniu trzustki. Niniejsza praca jest opisem przypadku mającym zilustrować niektóre problemy związane z właściwą kwalifikacją chorego do przeszczepienia trzustki.

INTRODUCTION

Diabetes is a chronic disease affecting (according to International Diabetes Federation) over 400 million people worldwide. It is possible to reduce the risk of this type of disease by improving lifestyle. Type 1 diabetes, that accounts for 7-12% of cases, is not currently preventable (1). Regardless of type, diabetes is associated with a number of micro and macrovascular complications that affect life expectancy. In order to maintain normoglycemia and consequently avoid complications novel therapeutic strategies are pursued. Unfortunately type 1 diabetes can only be managed with the delivery of insulin either by subcutaneous injections or by insulin pump. Among all available treatment options only pancreas transplantation enables insulin independency, eliminates acute complications and stabilizes long-term renal and neural complications, thereby improving quality of life. It should be considered in patients with type 1 diabetes in whom glucose control is difficult to achieve resulting in frequent, acute and severe complications (hypoglycaemia, marked hyperglycaemia, ketoacidosis) that require medical attention. Clinical and emotional problems associated with exogenous insulin administration may also be significant indication for a transplantation (2). Patients with type 2 diabetes account for about 7% of the recipients with similar indications as mentioned before (3). It should be emphasized that this treatment option involves contraindications such as severe uncorrectable cardiac disease, malignant neoplasm, ongoing or recurrent infections, high insulin resistance, preserved insulin secretion, persistent substance abuse, unresolvable psychological problems and inability to adhere to post-transplant immunosuppressive regimen (4).

However, the procedure of transplantation itself is connected with possible complications (acute rejection, thrombosis, pancreatitis, infections, intra-abdominal haemorrhage, exocrine pancreatic duct leaks), additionally the patients require lifelong immunosuppression, which often involves many side effects. Therefore, patients qualified for pancreas transplantation should undergo objective multidisciplinary evaluation including psychological assessment. We present below a case of a young woman with type 1 diabetes qualified for pancreas transplantation.

CLINICAL PRESENTATION

A 24-year-old woman (psychology student) with an 8-year history of type 1 diabetes was admitted to the department of diabetology because of poor control of the disease. The main problem included frequent episodes of hyperglycaemia over 400 mg/dl and severe hypoglycaemia (even 20 mg/dl with loss of conscious-

ness) irrespective of maintenance of appropriate diet. In addition she presented with dysuria. Because of neuropathy the patient was receiving oxycodone and lidocaine through an intravenous catheter. She was also treated for hypertension with candesartan, hydrochlorothiazide, amlodipine, clonidine and metoprolol achieving good blood pressure control. The other comorbidities included neurogenic bladder, recurrent urinary tract infections, urolithiasis, celiac disease, peptic ulcer disease, iron-deficiency anaemia, polycystic ovary syndrome, simple breast cyst, vitamin D deficiency.

She was treated with insulin pump, receiving over 100 U/day. She was hospitalized in our department 5 times in one year in order to optimize the treatment and, because of failure to do that, a process of a qualification for pancreas transplantation was eventually started.

On admission physical examination was unremarkable (weight 61 kg, height 162 cm, BMI 23 kg/m², BP 120/70 mmHg, HR 90/min). Blood glucose profile showed fluctuation of glycaemia throughout the day (from 43 to 342 mg/dl). Interestingly, there were significant discrepancies between the results noted by the patient and those obtained from the glucose meter's memory (tab. 1). Due to lack of correlation between low HbA1c (suggesting a tendency to hypoglycaemia) and several episodes of hyperglycaemia the insulin dose was not modified. Taking into account unreliable measurements of blood glucose level made by patient, she underwent psychological evaluation and was recommended to attend psychotherapy.

Tab. 1. Blood glucose profile

Hour	Patient's notes	Results from glucose meter's memory
0-1	283	83
2-3	257	108
4-5	294	HI
7-8	293	no result
11-12	57	97
16-17	248	565

Laboratory findings on admission (tab. 2) revealed low HbA1c 4.9%, normal fructosamine level, anaemia, vitamin D deficiency and presence of *E. coli* (ESBL +) in the urine sample. Ultrasound examination detected small stones in the right kidney and post-void residual urine. Urinary tract infection was diagnosed and, as the patient refused to be treated orally, intravenous antibiotics and spasmolytics were started, which relieved dysuria.

Taking into account all the above mentioned facts, in spite of present indications for a pancreas transplanta-

Tab. 2. Laboratory results

Parameter	Value	Normal value
HbA1c (%)	4.9	7
Fructosamine ($\mu\text{mol/l}$)	234	205-285
C-peptide (ng/ml)	0.69	1.1-4.4
Haemoglobin (g/dl)	10.3-11.3	12-16
Creatinine (mg/dl)	0.5	0.5-0.9
eGFR (ml/min)	153	> 60
25(OH)D (ng/ml)	6.8	30-100
PTH (pg/ml)	31.8	14.9-56.9
Ca (mmol/l)	2.15	2.09-2.54
P (mg/dl)	4.03	2.7-4.5
AST (IU/l)	20	5-31
ALT (IU/l)	15	5-31
CRP (mg/l)	0.6-3.8	< 5
WBC ($\text{K}/\mu\text{l}$)	4.52-7.28	4.5-10
Procalcitonin (ng/ml)	0.02-0.03	< 0.5

tion, the patient was disqualified from the procedure because of recurrent urinary tract infections connected probably with the neurogenic bladder and psychological issues. She was discharged with the recommendation of further urological and psychological treatment.

DISCUSSION

The world's first pancreas transplantation was described in 1966 at the University of Minnesota (5). Initially, graft and patient survival was dismal mainly due to immunological complications. Over the decades, it has significantly improved and now 3-year patient survival rate exceeds 90% (6). The frequency of pancreas transplantation increased as a result of significant improvement in surgical techniques, graft preservation techniques, immunosuppression and management of posttransplant complications. Since 1966 there were 23000 pancreas transplantations performed worldwide (7). Candidates for pancreas transplantation are divided into 3 categories according to their renal function and hence the need for kidney transplantation. In the first group (75% of cases) pancreas and kidney transplantations are performed simultaneously (SPK), in the second one kidney is transplanted previously to pancreas (PAK – 18%). Pan-

creas transplantation alone (PTA) is performed unfrequently (7%) (6), however more and more often, sometimes even in patients with type 2 diabetes.

In the qualification process not only indications, but also specific (in contrary to general surgical) contraindications such as severe cardiovascular disease, recurring infections, cancer, mental disorders or high insulin resistance should be taken into account. The above mentioned contraindications are mostly connected with the complications of immunosuppressive regimens that are used lifelong and entails appropriate compliance. This raises the issue of benefits and potential risk associated with this therapeutic method.

In the presented case pancreas transplantation alone would be considered. There was a consistent failure of blood glucose control leading to marked hyperglycaemia and episodes of severe hypoglycaemia with loss of consciousness. Yet, there were also recurrent urinary tract infections due to neurogenic bladder caused by probably uneradicable bacteria, what must be considered as a contraindication not specific for a PTA, but in general for an immunosuppressive treatment. It cannot be excluded, however, that after urologic treatment (probably cystostomia), eradication of bacteria and long-lasting period free of infection this contraindication may not longer persist.

What is more, utmost importance, as non-compliance is connected with more frequent rejection and graft loss (8). Therefore, identification of behavioural patterns and emotional states is essential. In the presented patient, discrepancies between the notes and real glucose results reveal emotional imbalance. This can be a risk factor for non-compliance in terms of immunosuppressive treatment. Our patient was recommended to attend psychotherapy which hopefully would change her attitude and help to deal with the disease.

CONCLUSIONS

The presented case illustrates that multidisciplinary approach which is crucial in the qualification process. The indications and possible benefits of the transplantation should be balanced against the contraindications and potential complications.

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