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Multiple long-term complications as a result of poor glycaemic control in type 1 diabetes — a case report

Liczne przewlekłe powikłania jako rezultat niedostatecznej kontroli glikemii u pacjenta z cukrzycą typu 1 — opis przypadku

ABSTRACT

We present a case of a 54-year-old patient with type 1 diabetes affected by multiple microvascular and macrovascular complications. Over the course of the disease, he developed diabetic nephropathy that resulted in renal transplant, proliferative retinopathy of both eyes, and sensory polyneuropathy. He also suffered from arterial hypertension and diabetic foot syndrome, complicated by an amputation of fourth left toe.

With the implementation of intensive insulin therapy (IIT), a decrease in prevalence of diabetic complications has been observed. Tight metabolic control, especially during early years of the disease, significantly reduces the risk of their development. However, there are patients who suffer from multiple complications, despite receiving IIT. One of the most important aspects of effective diabetes management is patients' education and their active participation in the treatment. (Diabet. Klin. 2015; 4, 5: 199–203)

Key words: type 1 diabetes mellitus, diabetic complications, metabolic memory, diabetes education, patient's compliance

STRESZCZENIE

W pracy przedstawiono przypadek 54-letniego pacjenta chorującego na cukrzycę typu 1 z wieloma powikłaniami o charakterze mikroangiopatii i makroangiopatii. W przebiegu choroby u pacjenta rozwinęła się nefropatia cukrzycowa, która doprowadziła do przeszczepu nerki, retinopatia proliferacyjna obu oczu i polineuropatia czuciowa. Cierpiał też na nadciśnienie tętnicze oraz zespół stopy cukrzycowej, powikłany amputacją czwartego palca lewej stopy.

Wprowadzenie intensywnej insulinoterapii (IIT) doprowadziło do zmniejszenia częstości powikłań o charakterze mikroangiopatii i makroangiopatii u pacjentów z cukrzycą typu 1. Ścisła kontrola metaboliczna, szczególnie w pierwszych latach choroby, istotnie obniża ryzyko ich wystąpienia. Pomimo tego u części chorych poddanych IIT nadal rozwijają się liczne powikłania. Jednym z najistotniejszych aspektów opieki nad pacjentami z cukrzycą jest ich edukacja i aktywny udział w procesie leczenia. (Diabet. Klin. 2015; 4, 5: 199–203)

Słowa kluczowe: cukrzyca typu 1, powikłania cukrzycy, pamięć metaboliczna, edukacja pacjentów z cukrzycą, zdyscyplinowanie chorego

Introduction

Type 1 diabetes (T1DM) is usually diagnosed in children and adolescents, what entails the need of lifelong care. The only method of treatment is replacement of endogenous insulin with injections of the exogenous hormone.

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Over the course of the disease, most patients develop long-term diabetic complications, which is dependent on metabolic control of the disease, including not only blood glucose concentration, but also blood lipids and arterial blood pressure [1]. It is established that poor glycaemic management, indirectly assessed by the concentration of haemoglobin A_{1c} (HbA_{1c}), increases the risk of development and progression of long-term complications [2, 3].

The standard treatment for patients with T1DM includes tight glycaemic control with insulin, along with diet, physical exercise, blood glucose self-monitoring, and patient's education. The Diabetes Control and Complications Trial (DCCT) and its follow-up, the Epidemiology of Diabetes Interventions and Complications (EDIC) study, have proven the superiority of intensive insulin therapy (IIT) over conventional treatment in achieving and maintaining near-normal concentration of blood glucose and its influence on development of long-term complications. IIT is also reported to reduce early stages of diabetic retinopathy, neuropathy, diabetic kidney disease, as well as more advanced stages of microvascular complications and cardiovascular disease [3].

Many studies have reported high prevalence of long-term diabetes-associated complications [4]. However, nowadays, when intensive diabetes therapy is considered the gold standard of treatment, it is rather uncommon to observe multiple microvascular and macrovascular complications in one patient with T1DM.

Case report

A 54-year-old patient with T1DM diagnosed 33 years before, currently treated with IIT, was admitted to hospital in February 2014 due to the diabetic foot syndrome.

Two months prior to the hospitalisation, he presented at the doctor's office complaining of painless reddening of fourth left toe. There was no history of preceding trauma. It quickly progressed to ulceration and despite surgical treatment necrosis and bone lesions developed. In January 2014, the patient underwent the amputation of fourth left toe. One week later he was admitted to hospital with fever, fatigue, loss of appetite, dehydration, and fluctuations of blood glucose concentration. Infection of the amputation site with *Staphylococcus aureus* was then diagnosed. After two weeks, he was referred to the Department of Endocrinology, Diabetology, and Internal Medicine for further treatment and adjustment of diabetes control.

The patient had a history of multiple microvascular and macrovascular complications.

He suffered from diabetic kidney disease for 8 years. Between 2008 and 2009, he was subjected to peritoneal dialysis, complicated by three incidents of peritonitis. Because of that, he was switched to haemodialysis in 2009. In June 2011, he underwent simultaneous pancreatic and renal transplant, followed by pancreatic graft loss secondary to venous thrombosis one week later. However, the function of the transplanted kidney was preserved at the time of admission.

Proliferative retinopathy affecting both eyes occurred at the age of 45. It was treated twice with laser photocoagulation 9 years before. The patient also underwent surgical treatment of cataract of the right eye in 2013. He complained of severely affected vision and difficulties with reading.

Symptomatic polyneuropathy occurred at the age of 44. He reported sensory neuropathy, with almost total loss of sensation in both feet, along with "tingling" and pain in the hands.

The patient presented arterial hypertension developed 28 years earlier. Despite him receiving combination therapy, it was poorly controlled at the time of admission.

The patients had experienced three episodes of ulcerations in the course of diabetic foot syndrome. They had affected the patient's left heel and medial surfaces of both feet. In any of the cases there had been no need for amputation.

Of relevant past medical history, he had undergone type C hepatitis treated with interferon between 2009 and 2010. He was receiving complex hypotensive treatment (bisoprolol, indapamide, ramipril, amlodipine) and atorvastatin, as well as immunosuppressive medications (everolimus, prednisone, mycophenolate).

Before admission, the patient was treated with IIT (insulin lispro 3 × 14 IU, insulin isophane human 24 IU). He did not adhere to the doctor and dietician's recommendations regarding diet and blood glucose self-monitoring.

On physical examination, body mass index (BMI) 29.65 kg/m^2 and blood pressure 146/92 mm Hg were found. Left foot was swollen, with features of an ongoing inflammation at the site of amputation and ulcers of the sole. There was a significant deformation of the abdomen with a longitudinal scar in the midline (Fig. 1). The transplanted kidney could be palpated in the left iliac fossa.

The patient's blood glucose concentration was poorly controlled. Fasting blood glucose ranged from 86 to 294 mg/dL and postprandial glucose from 250 to 300 mg/dL. The results of laboratory studies are presented in Table 1.

Doppler ultrasound of the lower limbs revealed few calcified atherosclerotic plaques, but otherwise

Figure 1. Deformation of the abdomen

preserved blood flow in the arteries. Feet X-ray showed osteoporosis in the bones of the left foot.

The patient was administered intravenous antimicrobial treatment, including ciprofloxacin, clindamycin, and cotrimoxazole, after which his condition improved significantly. He also received anticoagulants, analgesics, as well as alpha-lipoic acid and alfacalcidol. Debridement of the infected wound was performed several times. Insulin therapy was modified — insulin isophane human was changed to insulin glargine, and the doses of both long-acting and rapid-acting insulin were modified to the patient's needs (insulin lispro 8 IU – 10 IU – 10 IU, insulin glargine 30 IU). After that, a satisfactory control of blood glucose concentration was achieved. Before discharge, the patient was educated about the importance of proper glycaemic control and risks of non-compliance with the recommendations.

Discussion

IIT has been the gold standard of treatment for patients with T1DM for over 20 years. It made metabolic control of diabetes easier, and, consequently, a decrease in prevalence of diabetic complications has been noted in recent years [4–6]. Therefore, multiple diabetes-related complications in one patient are not commonly observed nowadays. In the study conducted by Morgan et al. [7], all five major complications were present in only 0.1% of patients. In contrast to these findings, our patient developed a large number of complications, including nephropathy, retinopathy, and polyneuropathy, as well as diabetic foot syndrome and hypertension.

The patient was diagnosed with T1DM in 1981, when IIT was not the standard method of treatment. Therefore, satisfactory metabolic control during first years of the disease was very difficult to achieve. This might have had a significant influence on the subsequent development of complications. An observational

Table 1. Results of the laboratory tests

Parameter	Result	Standard value	PDA recommendations
HbA_{1c} (%)	9.8	≤ 7	≤ 8
Total cholesterol [mg/dL]	209	130–200	< 175
LDL cholesterol [mg/dL]	105	100–159	< 100
HDL cholesterol [mg/dL]	67	35–55	> 40
Triglycerides [mg/dL]	169	40–200	< 150
WBC [$10^3/\mu L$]	7.39	4–10	
RBC [$10^6/\mu L$]	4.39	4.5–6.0	
Haemoglobin [g/dL]	10.8	14–18	
Haematocrit (%)	33.8	40–54	
PLT [$10^3/\mu L$]	203	130–350	
CRP [mg/L]	61.7	0–10	
Fibrinogen [mg/dL]	842	200–400	
Urea [mg/dL]	60	10–50	
Creatinine [mg/dL]	1.6	0.7–1.1	
GFR [ml/min]	48	80–200	

CRP — C-reactive protein; GFR — glomerular filtration rate; HbA_{1c} — haemoglobin A_{1c}; HDL — high density lipoprotein; LDL — low density lipoprotein; PDA — Polish Diabetology Association; PLT — platelets; RBC — red blood cells; WBC — white blood cells

follow-up of DCCT, EDIC study, has revealed the existence of a phenomenon called "metabolic memory" [3]. Patients initially treated with IIT continued to show significantly lower rate of long-term complications, comparing with those previously assigned to conventional treatment, even though their metabolic control deteriorated [8–11]. That disparity was explained mainly by differences in HbA1c between the two groups during DCCT. In the presented case, the patient had already been receiving IIT for several years. Despite that, he developed multiple complications, which is most probably associated with inadequate glycaemic control in the early years of the disease.

Another factor contributing to sufficient metabolic control is patient's comprehensive education and their conscious participation in the treatment process. Intensive diabetes therapy combines IIT with dietary interventions, physical activity, and frequent self-monitoring. Its success is dependent not only on the physician's experience, but also — or maybe predominantly — on the patient's attitude to disease and treatment. The association between patient's diabetic knowledge and risk of developing long-term complications has been described by Araszkiewicz et al. [12]. The patients underwent a teaching programme followed by a test, and during a mean follow-up of 7 years, development of microvascular complications was assessed. Those who developed retinopathy and albuminuria were found to present significantly lower diabetic knowledge, comparing with patients who remained free from microangiopathy.

It is worth accentuating that despite undergoing the same training programme, not all patients benefitted from it. This may implicate the need to revise existing education schemes and implement interventions tailored to the patient's individual needs and concerns. A study by Hermanns et al. [13] suggests that programmes focused not only on glycaemic control, but also on emotional aspects of diabetes, are more effective in translating knowledge into everyday self-management, resulting in greater reduction of disease-related distress and an increase in diabetes empowerment.

It should be highlighted that although the presented patient received IIT, the treatment was based on fixed doses of insulin, regardless of actual concentrations of blood glucose. This regimen is easy to follow, but does not provide ideal glycaemic control. Flexible intensive insulin therapy (FIT), in contrast, is more complex, but more effective in maintaining proper metabolic control [14]. FIT obliges patients to adjust insulin doses to the predicted carbohydrate intake, planned exercise, and current blood glucose, requiring comprehensive knowledge and conscious cooperation with the doctor. The efforts result in more dietary freedom and better self-care, as well as lower risk of long-term complications [14].

Due to the patient's non-compliance, the implementation of FIT in the reported case was impossible, therefore limiting the possibility of achieving tight glycaemic control.

Although tight metabolic control does not entirely prevent the development of chronic complications, a great number of patients have been reported to survive decades of diabetes without developing complications at all. The Golden Years Study [15] described a group of patients suffering from T1DM for over 50 years. Apart from diabetic retinopathy, which was present in 43% of patients, and cardiovascular disease, present in approximately 1/3 of them, the patients were free from long-term complications. The group was characterised by normal body weight, low insulin dose, and high HDL cholesterol. In the 50-year Medalist Study [16], nearly one half of the patients did not report microvascular complications. In accordance with the aforementioned study, this group had significantly higher HDL cholesterol level and lower insulin dose, as well as lower triglycerides, comparing with those who developed complications. Physical activity was also associated with reduced risk of complications. Of note, there was no significant difference between the two groups regarding concentration of HbA_{1c}, BMI, total cholesterol, or LDL cholesterol level. This lack of association between the development of complications and most metabolic parameters may suggest the role of other determinants, such as genetic factors, protecting certain patients from complications.

Conclusions

Tight metabolic control of diabetes, especially during early years of the disease, reduces the risk of long-term complications. However, despite better methods of treatment, there still are patients who develop multiple complications. In most cases, the key factor influencing the outcome of the disease is patient's awareness and their cooperation. Proper education, covering not only basic skills and knowledge, but also psychosocial aspects, as well as encouraging patient to actively participate in the treatment, are crucial in effective management of diabetes.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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