Insulin Edema in Type 2 Diabetes Mellitus: A Case Report Study

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Abstract

Edema is a rare complication induced by insulin therapy, which is mostly developed after initiation or intensification of insulin treatment in diabetic patients. Edema can either be localized or generalized. Our patient was a 34-year-old woman with type 2 diabetes. She was under treatment with oral agents medication, but recently insulin therapy was initiated for her due to inability to control her hyperglycemia and development of diabetic ketoacidosis. The patient referred while suffering from bilateral lower extremity edema. During follow-up, her edema resolved spontaneously without any specific treatments. In this patient, the diagnosis of edema was based on ruling out other causes, along with more accurate blood glucose control during diabetic ketoacidosis process and spontaneous recovery. Based on our finding, it can be concluded that insulin-induced edema is not a worrisome problem and in most cases, its symptoms resolve without treatment and through restricting the consumption of water and salt.

Keywords: Insulin, Insulin regular, Human, Edema

Introduction

In the treatment of diabetic patients, the role of insulin is well known, although this treatment can be associated with some adverse effects, including hypoglycemia, weight gain and, in rare cases, edema or fluid retention. The insulin-induced edema often occurs after initiation or intensive insulin therapy (1,2), which can either be localized in pretibial, sacral, or periorbital regions or generalized (2).

Various mechanisms have been proposed for this insulin-induced adverse effect such as the direct effect of insulin on the kidney, resulting in increase of sodium reabsorption in renal tubules and consequently the RAS (renin-angiotensin- aldosteron system) was inhibited by the plasma volume expansion. Increase of microvascular permeability, induction of endothelial growth factor release, and having genetic predisposition with the 3243 mitochondrial tRNA mutation, are other

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suggested mechanisms for this complication (3). In many cases, edema is managed by reducing insulin dose or restricting dietary salt. Diuretic therapy has different effects on insulin edema (4).

We reported a 34-year-old woman with type 2 diabetes. She was under treatment with oral agent drugs, but recently insulin therapy was initiated for her. She referred due to bilateral lower extremity edema.

Case Report

Our patient was a 34-year-old woman with type 2 diabetes with a six-year period of disease, and under treatment with oral medications. She was a candidate for insulin therapy because of inappropriate diabetic control, but she did not accept this treatment. Despite the use of oral medications, the patient referred to the emergency department while suffering from nausea, vomiting, and abdominal pain. On physical examination, mild dehydration and Kusmal breathing noticed. Her BMI was 19 kg/m2, heart rate was 115/min, blood pressure 100/70 mmHg and body temperature 38.8 °C. Laboratory investigations showed blood glucose 610 mg/dl, ketonuria 3+ and acidosis (bicarbonate 6 mmol/l, PH=1), confirming diabetic ketoacidosis. Because diabetic ketoacidosis (DKA) is not common in diabetes type 2, except in sepsis, this patient has been evaluated for different infections. So she received isotonic saline and intravenous infusion of insulin. After controlling diabetic ketoacidosis, insulin glargine and aspart with a total daily insulin dose (TDD) of 28 units on day, were prescribed for her. On day 3, the patient was discharged with insulin glargine (final dose 12 units) and insulin aspart (6 units before each meal) regimens. There was no edema at the time of discharge.

Two days after discharge, the patient referred with bilateral lower extremity edema initially affected ankles and quickly involved the entire lower limbs. On examination, non-tender, pitting edema was found without skin discoloration. Other examinations were normal and patient had no other complains. To understand the cause of his edema, the patient was hospitalized. Following results were obtained. (Table 1)

Within 4 days of hospitalization, the edema was controlled without any specific treatment.

Ethical considerations

This study was approved by the ethics committee of Shahid Sadoughi university of medical science, Yazd, Iran (code: IR.SSU. REC.1399.216).

Discussion

In our patient, the diagnosis of insulin-induced edema was based on the ruling out other causes, along with more accurate blood glucose control during recovery from DKA and spontaneous recovery. On her clinical examination, we found no symptoms of heart failure, such as pulmonary rales, or third heart sound (S3) and jugular venous pressure was not raised. There was no evidence of cardiomegaly and pulmonary edema in her chest X-ray, and her echocardiography was completely normal. Normal thyroid function tests and lack of proteinuria also supported our diagnosis.

Tufton suggested that age range of 20-40 years, poor glycemic control (including both

Table 1. Laboratory data of the patient at first day of admission

Value	
BUN= 17 mg/dl	ESR= 27 mm/hr
Cr= 0.8 mg/dl	INR= 1
Bil T= 0.3 mmol/li	UA= normal, no proteinuria
Bil D= 0.1 mmol/li	TSH= 1.2 miu/li
AST= 21 u/dli	CBC= normal
ALT= 36 u/dli	Alb serum= 3.1 gr/dl
FBS= 114	BS (10 AM)= 143
BS (5 PM)= 138	BS (10 PM)= 127

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hypoglycemia episodes and following treatment of DKA), low body weight, poor nutritional status, new onset diabetes and higher doses of insulin therapy are the risk factors of insulin edema (3). Some of these observations in our patient were in tandem with previous reports. Similar to our case, the patient presented in a study by Onyiriuka et al., recovered spontaneously and without any specific treatments (5). In the previous studies, the duration of insulin therapy varied from 1 to 14 days before the onset of edema, and the edema lasted for 4 to10 days. The process of edema development in our patient was similar to that of previous studies (6-10).

Edema is a rare complication following insulin therapy, and various mechanisms have been proposed for its occurrence. In an individual with insulin- deficient catabolic state, intensive serum therapy, may lead to extravasation of fluid into the subcutaneous tissue and development of peripheral edema. It is also hypothesized that vasomotor changes induced by fast blood glucose control can be involved in the onset of edema. In addition, it has been argued that a rapid improvement in blood glucose control may result in hepatic re-oxygenation, leading to production of reactive oxygen species in the liver that contribute to cell damage and increased vascular permeability. Furthermore, insulin therapy can increase sodium tubular reabsorption in the kidney through stimulation of Na/ K/ ATPase and expression of Na/ H exchanger3 in the proximal tubule, and can cause transient inappropriate hyperaldosteronism, consequently leading to fluid retention and edema (8,9,11).

Conclusions

Edema is a rare complication induced by insulin, especially in those with poorly controlled diabetes and their blood sugar level has been controlled immediately after initiation of insulin. Based on the findings of this study, we can conclude that insulin edema is not a serious problem and occurs in diabetic patients following a better control of blood glucose, especially in low-weight ones. In addition, in most cases, it can be resolved without any specific treatment, through restricting the consumption of water and salt and accurate follow-up of the patients.

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