

## Insulin edema in a child with diabetes mellitus type 1

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Despite the essential role of insulin in the management of patients with diabetes mellitus type 1, insulin use can cause a variety of adverse effects, such as hypoglycemia and weight gain. Herein, we describe an adolescent girl with type 1 diabetes mellitus diagnosed one year ago, who presented with edema of the lower extremities approximately two weeks after an increase in the insulin dose; other causes of edema were excluded. Spontaneous recovery was observed in the patient.

**Key words:** type 1 diabetes mellitus, insulin edema, adverse drug reaction.

Insulin is essential for the treatment of type 1 diabetes mellitus. While insulin has an essential role in the management of patients with insulin deficiency, its clinical use may lead to adverse effects. Crucial fluid retention can occur rarely with insulin therapy. It could be attributed to increased vascular permeability and shifted renal sodium handling in addition to the anabolic effect of insulin<sup>1</sup>. In the majority of these cases, the edema followed soon after the initiation of insulin therapy or a substantial increase in the insulin dose. Insulin edema is usually seen in newly diagnosed patients or poorly controlled diabetic patients after starting intensive insulin therapy<sup>2</sup>.

Extensive edema formation is an uncommon complication of insulin therapy, and only a few pediatric cases with insulin edema have been reported thus far<sup>3-6</sup>. This condition should be differentiated from other causes of edema, including cardiac or renal disease, which could be seen as a complication of the disease<sup>7</sup>. It has been reported in newly diagnosed type 1 diabetes that the edema can occur shortly after the initiation of intensive insulin therapy<sup>1</sup>. The extent of the edema varies from marked ankle edema to overt cardiac failure with ascites or pleural effusions<sup>7</sup>.

Herein, we describe insulin edema in an adolescent girl with diagnosed diabetes mellitus type 1.

### Case Report

A 14-year-old girl diagnosed with type 1 diabetes mellitus one year ago admitted with a three-week history of bilateral edema of the legs. She was treated with 1 u/kg/day insulin NPH (*neutral protamine Hagedorn*), but despite regular use, she did not have good glycemic control. The total insulin dose was increased to 1.5 u/kg/day one month before admission. Physical examination at the time of admission revealed body temperature: 37°C, pulse: 75 beats per minute, respiratory rate: 20 per minute, and blood pressure: 120/80 mmHg. Her weight was 53 kg (weight before edema: 49 kg). She had severe edema (+++) in her legs that extended to her lower abdomen (Fig. 1). Her urinalysis showed glucose +++, ketones ++, protein negative, and random blood glucose 350 mg/dl; alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), urine microscopy, and her 24-hour protein excretion (45 mg) were normal, but HbA1C of 16.5% suggested uncontrolled diabetes.

In order to rule out other possible causes of edema, further investigations were performed, which were all normal. Aldosterone and renin measurements performed via radioimmunoassay were normal: aldosterone: 150 pg/ml (normal range: 12-340 pg/ml) and renin activity: 0.6



Figure 1. Insulin edema of the legs in the patient with diabetes mellitus type 1.

ng/ml/hr (normal range: 0.5-1.9 ng/ml/hr). The electrolytes were in the lower limit of normal [sodium (Na): 134 mEq/L (normal range: 130-145 mEq/L) and potassium (K): 4.5 mEq/L (4.5-5.5 mEq/L)], whereas renal function tests were normal [blood urea nitrogen (BUN): 20 mg/dl (5-20 mg/dl) and creatinine: 0.7 mg/dl (0.6-1.0 mg/dl)]. Echocardiographic examination, chest X-ray, abdominal computed tomography (CT) scan, and Doppler sonography were all normal. No additional medication was taken, and insulin edema spontaneously recovered four weeks after glycemic control.

### Discussion

Insulin therapy is the treatment of choice in patients with type 1 diabetes mellitus; however, it can be associated with a variety of complications. Insulin edema is a rare complication, which may be neglected and underreported<sup>1</sup>. Although this complication is usually mild and self-limiting, development of pleural effusion and progression to cardiac failure have been reported<sup>2</sup>.

Peripheral edema can be associated with chronic insulin over-treatment in young diabetic

patients<sup>7</sup>. Although it seems that there is no sex predominance in insulin edema, insulin edema was found more common in females at younger ages<sup>8</sup>, similar to our patient and a recent paper from Turkey<sup>1</sup>.

Sodium retention and increased vascular permeability are two mechanisms that could be involved in insulin edema<sup>9</sup>. Fluid retention due to transient inappropriate hyperaldosteronism has also been reported in a case with insulin edema<sup>10</sup>. In our case, plasma aldosterone and renin were normal. Other mechanisms that could be responsible for insulin edema are thiamine deficiency with high output cardiac failure or an increase in glycogen-associated water stores, which were excluded in this case<sup>9</sup>.

In the patients with insulin edema, no specific medication is usually needed, and it can resolve spontaneously, as was observed in this presented patient. However, some instruction on fluid and salt restriction is necessary. Diuretic therapy may only be indicated in severe decompensated cases<sup>1</sup>.

It is recommended that pediatricians be aware of the existence of insulin edema and its occurrence as a complication of insulin therapy in type 1 diabetes mellitus, especially in newly diagnosed patients<sup>2</sup>.

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