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Case Report

The rare complication of type 1 DM, which is insulin-dependent edema: Four patient case reports presenting with the same clinical manifestation

Tip 1 DM'nin nadir görülen komplikasyonu insüline bağımlı ödem: Aynı klinik tablo ile başvuran dört hasta olgu sunumu

Seyran Bulut[1], Zeki Beyzade[2], Mutluhan Yiğitaslan[2], Rabia Meral[1], Eren Er[1], Bumin Dündar[3]

[1]*Tepecik Training And Research Hospital, Pediatric Endocrinology, İzmir, Turkiye*
[2]*Tepecik Traininng And Research Hospital, Pediatric Clinic, İzmir, Turkiye*
[3]*Katip Celebi University , Pediatric Endocrinology, İzmir, Turkiye*

ABSTRACT

Insulin is the essential hormone in managing Type 1 Diabetes Mellitus (DM). Severe complications can be seen during treatment. Insulin-dependent edema is a rare complication that can be seen regularly in patients with new diagnoses or poorly controlled diabetes shortly after the start of intensive insulin therapy. It can present itself in various clinical forms, from minimal peripheral edema to heavy pericardial, pleural edema and even heart failure. Although insulin-dependent edema has been known for a long period, the number of cases reported in the literature is very few. We are reporting four cases with poorly controlled type 1 diabetes that developed insulin edema.

Keywords: *İnsulin, edema, type 1 DM*

ÖZET

İnsülin, tip 1 DM'in yönetiminde esansiyal hormondur. Tedavi sırasında ciddi komplikasyonlara neden olabilir. İnsüline bağlı ödem de sıklıkla yeni tanı veya kötü kontrollü diyabetlilerde yoğun insülin tedavisi başlandıktan kısa bir süre sonra ortaya çıkan nadir bir komplikasyondur. Hafif periferal ödem olabileceği gibi ağır perikardiyal, plevral ödem ve kalp yetmezliğine kadar değişen spekturumlarda karşımıza çıkabilir. İnsüline bağlı ödem; uzun bir süredir bilinmesine rağmen literatürde bildirilen vakalar sınırlıdır. Bu nedenle insidansı bilinmemektedir. Biz de bu bildiride, kötü kontrollü eski tanı tip 1 diyabetli dört vakamızda gelişen insülin ödemini sunduk.

Keywords: *İnsülin, ödem, tip 1 DM*

INTRODUCTION

Insulin is crucial in the management and treatment of Type 1 Diabetes Mellitus (DM), characterized by insulin deficiency. The most common side effects include hypoglycemia and weight gain (1). Insulin-dependent edema is a rare complication and is observed peripherally or generalized (pericardial, pleural, acid) after excluding heart failure, renal and liver diseases. It is seen as a result of intensive insulin therapy in newly di–

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Correspondence / Yazışma: Seyran Bulut · SBÜ Tepecik Eğitim ve Araştırma Hastanesi, Pediatrik Endokrinoloji Kliniği, İzmir, Türkiye · seyranbulut@hotmail.com

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agnosed or poorly controlled patients with DM (2,3). In adults, the first case was reported in 1928, whereas in children, the first case was reported in 1979 (4,5). There are very few case reports about insulin-dependent edema in childhood. Thus, the incidence is unknown. The uncertainty regarding its pathophysiology still remains. It regularly recovers by itself. In this case study, we present four poorly controlled type 1 DM patients with edema as a rare complication of insulin.

CASE REPORT

Case 1

A 16-year-old female patient who had been followed up by our clinic due to Type 1 DM presented with swelling in her legs. Physical examination revealed a weight of 55,3 kg (25-50 p), height of 162 cm (25-50 p), blood pressure of 110/70 mmHg, and pulse rate of 80/bpm. At the systemic examination, lung sounds were usual, there was no hepatosplenomegaly and had a +2 pitting edema on the anterior side of the tibia. Patient history was as follows: diagnosed with type 1 DM 11 years ago, used a single dose long-lasting insulin glargine and three doses of fast-acting insulin lispro after carbohydrate counting to determine dose. Angiotensin-converting enzyme (ACE) inhibitor therapy was previously started by pediatric nephrology due to high blood pressure levels. The patient was evaluated as a result of peripheral edema. Blood test showed no hypoalbuminemia. 3-month average blood glucose was 10%. Proteinuria was not present in the 24-hour urine. A chest x-ray did not reveal pleural effusion. Heart functions were normal. Echocardiogram did not exhibit pericardial effusion. The patient did not appear to have her DM controls regularly, she had not been feeding with the appropriate diet and a high carbohydrate intake led to an increased amount of insulin dosage. The patient's diet was re-arranged. Diuretic treatment was started. After one week of follow-up, the edema was seen to have regressed.

Case 2

A 17-year-old female patient who was being followed-up with type 1 DM for three years also presented to our clinic with edema on her legs. Patient history revealed that a lack of appearance to her endocrinology controls and, within the last one year had four spells of diabetic ketoacidosis resulting in admission to the hospital ward and revision of the patient's insulin therapy. Before this presentation, the patient had been admitted to the hospital with heavy diabetic ketoacidosis one week earlier and insulin therapy was reorganized. Physical examination of the patient showed a weight of 60 kg (25-50 p), the height of 156 cm (3-10p), blood pressure of 112/79 mmHg, and pulse rate of 92/bpm. Both of the anterior tibias had +2 pitting edema. Lung auscultation revealed a decrease in lung sounds at the base of the right lung. Peripheral edema etiology was explored. Blood tests did not indicate hypoalbuminemia; proteinuria was not present in the 24-hour urine. Chest X-ray revealed pleural effusion at the base of the right lung. A thorax ultrasound calculated the pleural effusion at the right lung as 16 mm. The patient did not exhibit any signs of respiratory distress. Heart functions were evaluated, there was no pericardial effusion. Blood sugar was observed to be regulated with 1.9u/kg/day insulin treatment. Three-month average blood glucose was 16.3%. After one week of observation, the edema spontaneously regressed.

Case 3

A 16-year-old female patient presented to our outpatient clinic with swelling on her feet for three days. Patient history highlighted a diagnosis of type 1 DM 5 years ago, did not have regular follow-ups and admission to the hospital with diabetic ketoacidosis one week ago. Physical examination revealed a weight of 60 kg (25-50 p), height of 159 cm (25-50p), blood pressure of 122/84 mmHg, and pulse rate of 88/bpm. Lung, heart and abdominal examinations did not show any pathological findings. Bilateral +1 pitting edema on the anterior tibia. When researching edema etiology, blood tests did not show hypoalbuminemia and proteinuria was not present in the 24-hour urine. Heart functions were normal and there was no pericardial effusion. The insulin dose was arranged at 1.8u/kg/day to regulate blood sugar levels after ketoacidosis treatment a week earlier. Three month average blood glucose was 15.2%. Blood glucose was observed to be regulated with the current insulin therapy.

Case 4

A 12-year-old female patient was being followed up with type 1 DM by our clinic. The patient, who had not come to her control for six months, presented to the emergency services with weakness, fatigue and weight loss. Finger-stick blood glucose revealed a blood glucose of 380 mg/dl and a blood gas with a ph of 7.21 and hc03 of11.7. The patient was evaluated as having mild ketoacidosis. Six hours later, insulin therapy from 1u/kg/day was started after the patient requested oral intake. HbA1C was 15.6%. During the patient's follow-up, the insulin dose was increased to 2u/kg/day according to blood glucose levels. After high insulin treat–

ment, bilateral 2+ edema was observed on the back of the feet. There was no respiratory distress. The patient was evaluated regarding edema etiology. Proteinuria was not present. There were no signs of pericardial, pleural effusion or acid. During follow-up, edema declined without additional treatment after one week. The consent of the participants' parents was obtained to conduct this case study. The clinics of the patients are shown in Table 1.

Table 1. Comparision of patients' findings and laboratory values

	PATIENT 1	PATIENT 2	PATIENT 3	PATIENT 4
Physical examination	+2 tibial edema	+2 tibial edema	+1 tibial edema	+2 tibial edema
Proteinuria	None	None	None	None
Pleural effusion	None	16 mm on the right lung	None	None
Pericardial effusion	None	None	None	None
Acid	None	None	None	None
HbA1c (%)	10	16,3	15,2	15,6
Treatment	Furosemide	No	No	No

DISCUSSION

Edema is a rare complication in newly diagnosed type 1 DM or in poorly controlled DM patients that require intense treatment. The severity of peripheral edema is various; they are light in the majority of cases. Edema is an infrequent complication that is widely accepted to be a consequence of starting insulin treatment or increasing dosage. A vast majority of cases in the literature have reported edema in patients with a fresh diagnosis of type 1 DM after the start of insulin treatment, whereas our cases were previously diagnosed with type 1 DM and had poor control.

The incidence of edema due to insulin usage in children with type 1 DM is currently unknown. The foremost reason for this is that these cases are not being reported. Between the years 1979-2001, only 10 cases were reported. The patients ranged from 10 to 16 years old. Six (60%) of individuals had poorly controlled DM (6). Our patients were similar to these cases as they also had previous DM diagnoses, skipped insulin doses, and later edema was followed when intense treatment began.

The pathophysiology behind insulin-dependent edema is not clear. In 1928, Leifer et al. (5) stated that insulin-dependent edema can be caused by glycogen build-up in tissues leading to secondary liquid retention. Subsequent years revealed that insulin has an antinatriuretic effect on distal nephrons. In addition, insulin, with its antidiuretic effect can increase renal sodium absorption by stimulating Na-K ATPase. Thus, insulin usage can increase vascular permeability (1,7). The loss of albumin in circulation by rising capillary leakage can contribute to edema formation. Furthermore, it is another hypothesis for insulin-dependent edema in hyperaldosteronism (8). However, there are also reports in the literature of cases with normal aldosterone levels. Our patients did not have hypokalemia; therefore, aldosterone levels were not examined. Literature review revealed patients with insulin-dependent edema have low body weight. This can mainly be attributed to weight loss seen in newly diagnosed type 1 DM patients. However, in comparison to the literature due to our patients having old diagnoses and a poorly controlled DM, their body weight SDS is between 0 and 1.

Genetic predisposition has been put forward as a possible etiology for insulin-dependent edema. In a study by Suzuki et al. (10), four patients with insulin-dependent edema were compared with 197 patients without edema. All patients with edema were recorded to have a 3243 tRNA mutation. The limitation of salt and water consumption is the main approach for insulin-dependent edema (2,3). Literature review has shown that edema generally regresses in approximately seven to 20 days. This finding was in line with our findings obtained in this study, as our patient's edema also regressed in seven days. We applied diuretics to only one of our patients. Edema regressed in our other three patients without the need for diuretic treatment. We continued with insulin treatment as planned.

In conclusion, insulin is vital in the treatment of type 1 DM. Insulin is known to regularly cause hypoglycaemia and weight gain as a complication, along with rarer incidences of peripheral and generalized edema. After excluding heart, liver and renal diseases, insulin can be attributed as an etiology of edema after insulin treatment. This entity is generally self-limiting; therefore, a careful physical examination must be performed.

Patient Consent Form / Hasta Onam Formu

The parents' of this patient consent was obtained for this study.

Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

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