



## A Type 1 Diabetes Mellitus Patient Presented with Insulin Edema Only after Intensive Lifestyle Changes: A Case Report and Brief Review of the Literature

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### Abstract

Insulin edema is considered a rare type of generalized edema that occurs after initiation or intensification of insulin treatment in patients with Diabetes Mellitus (DM). In this case report, we presented clinically significant edema that resulted in the dramatic and abrupt improvement in glycemic control after intensive improvement in lifestyle in a 13-year-old girl, with DM type 1 who had positive anti-Glutamic Acid Decarboxylase (anti-GAD) antibodies. She had poor glycemic control during 2 years of insulin therapy, and lifestyle improvements with no changes to her medications types or doses, she developed generalized body edema, and face puffiness that resolved spontaneously, without any intervention, and only observation of the patient.

### Introduction

Generalized edema is a rare complication of insulin therapy, which usually occurs in newly diagnosed type 1 diabetic patients and after the initiation of insulin therapy, also it can be presented in patients with type 2 diabetes after the intensification of insulin therapy generalized edema must be differentiated from other causes of edema such as cardiac or renal disease which are the most common causes of body edema, and must initially be ruled out [1]. Here we report a 13-year-old, girl, who was diagnosed with DM type I in 2016. Her DM was uncontrolled for 2 years, and she had a history of multiple admissions to the pediatric intensive care unit, due to Diabetes Ketoacidosis (DKA). She recently presented with generalized body edema including the face, of no apparent cause, after sudden glycemic control with only lifestyle modifications, and became compliant with her medications, without any change in insulin types or doses.

### Case Presentation

A 13-year-old Saudi girl diagnosed with type 1 diabetes in 2016, had positive anti-GAD antibodies, and in the last 2 years, had uncontrolled blood glucose with a high Hemoglobin A1c (HA1c) level of more than 15%. Her lifestyle was unsatisfactory, including the consumption of many junk foods and a lack of any physical exercise. Despite her insulin dose of 1.5 units/kg/day, she still had uncontrolled blood glucose and was frequently admitted to the Pediatric Intensive Care Unit (PICU) with Diabetic Ketoacidosis (DKA) with a total of 5 admissions since her diagnosis, and HA1c level reached 16.9% on one occasion. We decided to provide her with intensive psychological support and give her frequent clinical appointments with the Pediatrics Endocrinology Clinic and a diabetic educator. She decided to change her lifestyle to prevent any diabetic complications and to improve her quality of life, therefore, she changed the types of food she consumed, eliminated most carbs, become physically active, walking around for an hour per day. In September 2020 she was admitted to the PICU due to frequent hypoglycemic attacks, with no history of fatigue or decreased energy, no symptoms of cough, shortness of breath, and chest pain, and no history of new medication use. A physical examination determined she had pitting edema on her lower limbs, lower back, and a puffy face. She had warm skin with no tingling or burning sensations at the site of edema and no pain, aching, or numbness. Another systemic exam showed she was within normal, a bodyweight of 58 kg, and had a BMI of 23 kg/m<sup>2</sup>, with no abnormalities in her chest or heart. A normal thyroid exam and showed no lipohypertrophy at the injection site. Investigations were conducted to rule out any organic cause of the edema, included renal function test, liver function test, and cardiac exams with ECG. All were normal apart from her albumin being on the lower side with a level of 35 g/L. Other labs tests showed a high HA1c level of 15.8%. ACTH and cortisol tests were performed to rule out Addison disease and the results were within normal ranges. The celiac

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profile showed negative antibodies. Thyroid function tests revealed a low FT4 level of 8.2 pmol/L and positive thyroid antibodies. Insulin doses were adjusted with the total daily dose decreasing from 1.5 to 1.3 and then 0.7 units/kg/day to control her blood glucose level, and her long-acting insulin dose was changed to another type of long-acting insulin (Tresiba) to minimize her hypoglycemic attacks. On clinical follow-up, she showed much improvement in her glycemic status, and her edema resolved without any medical interventions. Her last measured HA1c level was 7.8%, levothyroxine was initiated with a dose of 50 mic daily, and her last FT4 level was 10.3 pmol/L. Her hemoglobin A1c level decreased from 15.8% to 9.1% and then decreased again in December 2020 to 7.9%.

## Discussion

Insulin edema is a known complication of the initiation or intensification of insulin therapy. It was first described in 1928 [2] and occurs in both type 1 and type 2 diabetes mellitus, especially in newly diagnosed cases of type 1 diabetes mellitus [1]. It is a benign transient condition that is usually self-limiting and resolves spontaneously with a rare or no need to use any intervention, treatment, or diuretic therapy [3]. Although the manifestations can vary widely from mild peripheral edema to cardiac failure and massive serosal effusions and may occur in local areas, such as the periorbital, pretibial, and sacral regions, or as generalized edema, there was a young patient who is diagnosed as a newly diagnosed type 1 diabetes, when generalized edema and pericardial effusion developed after initiation of insulin therapy, the treatment was only supportive and all symptoms resolved within 20 days [3,4]. As well, it can be presented at any age with the youngest age was reported was a 9 years old male who developed insulin edema few days after diagnosis of type 1 diabetes and was treated as a case of DKA [2]. There are no criteria or a risk stratification system for the diagnosis of insulin edema, and it is diagnosed by the exclusion of other common causes of body edema. However, aged being from 20 to 40 years, poor control diabetes either by having frequent hypoglycemia or following DKA treatment, newly diagnosed diabetes with higher doses of insulin therapy, poor glucose control, and low body mass index have been suggested as risk factors for insulin edema [5,6]. The true incidence of insulin edema remains unknown but some reports have estimated the incidence to be in the range of 3% to 3.5% [1]. There have been several presentations of insulin edema, William et al. reported a 15-year-old girl with a history of poorly controlled type 1 diabetes mellitus who presented with generalized anasarca which was started gradually over her limbs till extend to all of her body including her face and genitalia associated with a significant increase in her weight, her labs were within normal level apart of albumin which was in the lower normal, these symptoms were noticed after 1-week of compliance with insulin therapy [7]. Furthermore, another adult patient with latent autoimmune diabetes was reported to have insulin edema associated with neuropathy. She was a 35-year-old, diagnosed with diabetes mellitus and subsequently developed latent autoimmune diabetes, she was on an oral hypoglycemic agent and her glucose level was high with an HbA1c of 13%. She was admitted to the hospital under plastic surgery service when she presented with a painful discoloration of her right finger. During that admission developed DKA, after treatment of the DKA insulin was initiated and after 3 days she developed significant pitting edema up to her umbilicus associated with neuropathy that was diagnosed by nerve conduction studies. Other causes of edema were excluded, and because her edema was severe so, she was treated with furosemide diuretics and fluid restriction [6]. Another adult

case was reported by Wong and Balakrishnan. The patient was a 40-year-old woman, newly diagnosed with type 1 diabetes mellitus who developed generalized edema just after diagnosis and treatment initiation [1]. Sugiyama et al. [8] reported that a 50-year-old female patient, who is known to have Acute Myelogenous Leukemia (AML) post bone marrow transplantation and type 2 diabetes mellitus, was on multiple medications as prophylaxis and treatment from transplant rejection. Her blood glucose become poorly controlled so; intensive insulin therapy was given to her, after by around 4 weeks found to have insulin edema over her lower limbs. The same presentation was found in a 57-year-old male patient with a 5-year history of type 2 diabetes, he was poorly controlled and his urinalysis showed positive ketones and protein. He developed bilateral lower limb edema which was induced by the rapid improvement of glycemic control with insulin therapy [9]. Despite that, insulin edema is a rare finding and usually, it is self resolved, although it can be serious with significant complications as in this patient who was a 35-year-old woman diagnosed recently with type 1 diabetes who presented with polydipsia and polyuria for over 1 year, and at the last 2 months before presentation, she lost approximately 2 kg of weight. She presented with signs of severe DKA indicated by Kussmaul's breathing and low pH levels and was treated with insulin. On the 2<sup>nd</sup> day, her renal function started to deteriorate, she had high creatinine levels and then presented with generalized edema, serous effusions, and acute renal failure. This case was different due to the presence of more serious complications [10]. Pediatric patients also can have insulin edema; a case report of a 12-year-old boy newly diagnosed with type 1 diabetes, presented with edema of the lower extremities approximately one week after the initiation of insulin therapy. This case was considered a typical presentation of insulin edema that appeared soon after the initiation of insulin therapy in a patient newly diagnosed with DM type 1 [11]. Furthermore, Hirshberg et al. [12] reported a 49-year-old female, who was diagnosed with diabetes mellitus and developed severe generalized edema following the initiation of insulin therapy. The edema was severe enough to be treated with diuretics but unfortunately, it was impossible to continue the treatment because of the severe side effects of this medication the patient experienced. Even the patients who are on an insulin pump can develop insulin edema; Greco et al. described the case of a 39-year-old woman with poorly controlled type 1 diabetes mellitus who developed generalized edema with severe weight gain a few days after the start of an insulin pump therapy [3].

## Conclusion

Several cases have been reported about generalized edema in patients with diabetes. However, most of the cases reported on patients with either newly diagnosed type 1 or type 2 diabetes mellitus that developed edema after the initiation or intensification of insulin treatment or even after sudden compliance with insulin therapy. There were no case reports about the development of insulin edema after only improvements in the patient's lifestyle and without any change in insulin dose.

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