Case Report

Peripheral edema in a child with a new diagnosis of insulin-dependent diabetes mellitus

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ABSTRACT

Peripheral or generalized edema is an uncommon complication of insulin therapy in diabetes mellitus. The exact cause is yet not known. It is transient and self-limiting in nature. However, diuretics and aldosterone antagonists have been used in some cases. We report the case of a 14-year-old boy with newly diagnosed Type 1 diabetes who developed edema after the commencement of insulin therapy. Other causes of edema were excluded from the study. The child was managed conservatively and edema seemed to start decreasing after 72 h and completely disappear in 2 weeks.

Key words: Insulin, Edema, Type 1 diabetes

Edema is an uncommon and underreported complication, on the initiation or intensification of insulin therapy in diabetes, especially in pediatric cases. A small number of pediatric cases have been reported since 1979 [1] and in the absence of heart, liver, or renal dysfunction, edema is mostly transient and self-limiting in nature. The exact pathophysiology and the incidence of insulin-induced edema in children are not known. A review of the literature revealed only nine children and adolescents, aged 10–16 years described in six case reports from 1979 to 2001 [2]. In six out of the nine children, edema resolved spontaneously while one showed improvement after the discontinuation of insulin. The rest of the children received drugs such as furosemide and ephedrine.

Due to its benign nature, an increased awareness of this condition is required to avoid unnecessary investigations and treatment. Hence, we are reporting a case of the development of edema after the commencement of insulin therapy in a newly diagnosed Type 1 diabetic adolescent. The child was managed conservatively and no drug therapy was introduced in our case.

CASE REPORT

A 14-year-old boy, with a history of polyuria, polydipsia, excessive fatigue, and weight loss over the previous 6 months, presented to the hospital with diabetic ketoacidosis (DKA).

On admission, he weighed 38.8 kg (25th centile) with a height of 163.0 cm (50th centile) and a body mass index (BMI) of 14.60 (0.4th centile). On examination, he was dehydrated and appeared cachectic. His heart rate was 92 bpm, respiratory rate was 24 cpm, and blood pressure was 110/70 mm of Hg.

He was managed according to the local DKA guidelines, including one fluid bolus of normal saline on admission. His initial blood ketones were 5.4 mmol/l and pH was 6.9. His ketoacidosis resolved after 48 h and he was switched to subcutaneous insulin, constituting a basal-bolus of insulin glargine and quick-acting insulin novo rapid. He had a prolonged hospital stay of 14 days due to diagnosis-related anxiety and difficulty delivering diabetes education to the young person and his family.

On day 5 of his admission, he developed a non-tender and bilateral pitting edema to the lower legs (Fig. 1). There were no other features of renal, cardiac, or hepatic causes of his edema. He did not have periorbital edema. His urine was negative for proteinuria. Further investigations showed normal renal function, liver function including albumin level, and inflammatory markers. His initial screening blood tests were positive for anti-glutamic acid decarboxylase and anti-islet cell antibodies. His thyroid function tests were normal and thyroid peroxidase antibodies were negative.

He did not require any active management, such as fluid restriction, or diuretics, and edema gradually improved with an elevation of the legs. Edema started improving after 72 h. On discharge from the hospital after 9 days, there was only minimal residual edema. His weight on discharge was 44.5 kg and BMI was 16.74. After 4 weeks in the clinic, he had gained 7.45 kg and his BMI had increased to 17.41, with no evidence of edema.

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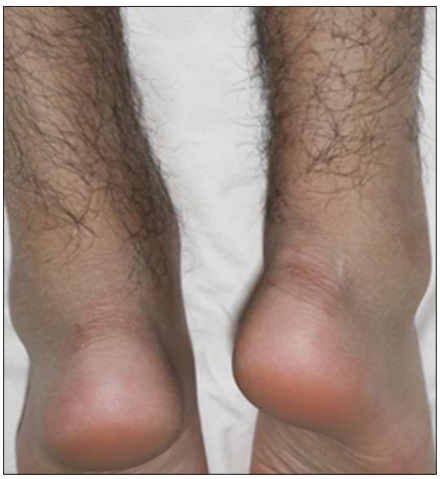

Figure 1: Bilateral pedal edema

DISCUSSION

The case of insulin edema was reported in 1928 [3], although the exact cause of insulin edema is unknown. The complication has been reported in newly diagnosed Type 1 diabetics and in poorly controlled Type 2 diabetics during the initiation or intensification of insulin therapy. However, there are very few reports with regard to the pediatric population.

This is predominantly seen in people who are underweight and newly diagnosed with Type 1 diabetes. There also appears to be a female bias in incidence. A wide variance of complications exists, ranging from mostly mild peripheral edema to rarely effusions, ascites, and cardiac failure [4], although more severe complications have been mainly confined to adult cases. Severity in pediatrics ranges from mild to generalized edema, with one reported case of pericardial effusion in an adolescent [5].

Although no precise pathophysiology of insulin edema has been identified, there are a few proposed mechanisms as mentioned below: Leifer suggested in his report that glycogen deposition in cells leads to increased fluid retention leading to edema [3]. Another postulated mechanism is insulin's effect on enhanced sodium reabsorption [6]. Kalambokis has reported in his paper that hyperaldosteronism may occur in patients with insulin edema, even in the absence of volume depletion, contributing to the development of increased sodium reabsorption and laboratory disorders including such as improving sodium and hypokalemia, hypouricemia, proteinuria, hypoalbuminemia, and anemia [7]. Fluid retention has also been suggested to be permitted by increased vascular permeability in hyperglycaemic states [8]. Insulin therapy resumes the production of gonadotropin-releasing hormone and estrogen leading to nitric oxide production in endothelial cells which causes vasodilation of capillary beds [9]. Mitochondrial mutation of the 3243 tRNA has been implicated in peripheral edema after insulin therapy; however, this is not proven in pediatric cases reported so far [10]. Refeeding edema seen in patients with anorexia nervosa shares a similar pathophysiology and can be ruled out on the basis of clinical and biochemical characteristics.

There are currently no treatment guidelines for insulin edema in pediatrics. The majority of cases within the literature were managed conservatively, with spontaneous resolution observed in most [11]. Supportive management such as in our case, with the elevation of the limbs, should be used to maintain comfort and can be combined with fluid and salt restriction if there is no improvement. In more severe and decompensated cases, adjunctive therapy with loop diuretics and aldosterone agonists should be utilized. A single case report describes the use of ephedrine where edema was refractory to diuretic therapy [12]. Other causes of edema should also be excluded from the study. In our young person, edema lasted for approximately 2 weeks, which is similar to the other cases reported in the literature. These children should be regularly monitored to ensure continued resolution and adequate glucose control.

CONCLUSION

Insulin edema should be recognized as a potential complication in the initiation or intensification of insulin therapy in children, especially in those with a history of prolonged symptoms before diagnosis and those with significant weight loss and very low BMI. We think that this is an under-reported complication. Increased awareness will prevent unnecessary investigations, help to reassure clinicians, patients, and their families, as well as, guide appropriate treatment.

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