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A Rare Case of Association between Pseudohypoparathyroidism and Type 1 Diabetes Mellitus

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ABSTRACT

Background and Objective: Type 1 diabetes mellitus (T_1DM) as an autoimmune disease is associated with hyperglycemia and pseudohypoparathyroidism with hypoglycemia. In this study, we report a rare case of association between type 1 diabetes and pseudohypoparathyroidism.

Case Report: A 12.5-year-old female patient with a one-month history of polyuria and polydipsia was admitted with severe lethargy and vomiting, and due to high blood sugar and metabolic acidosis, Diabetic Ketoacidosis (DKA) was diagnosed. She was first treated with DKA protocol and then Basal- Bolus Protocol of insulin. The patient had a history of seizures due to hypocalcemia at the ages of 8 days and 2 months. In re-examination during hospitalization due to hypocalcemia-hyperphosphatemia and high parathyroid hormone, the diagnosis of false hypoparathyroidism was proposed and treatment with oral calcium tablet and calcitriol capsule was done and she was discharged after seven days with a good general condition.

Conclusion: In patients with pseudohypoparathyroidism, in the event of a disturbance in glucose status, the pattern is usually hypoglycemia, but in our patient, this association was in the form of hyperglycemia and DKA in the context of T_1DM, which is an indication of the rare association of these two diseases. Therefore, one should think about early diagnosis and proper treatment of this rare association.

Keywords: *Pseudohypoparathyroidism, Type 1 Diabetes Mellitus, Hypocalcemia, Parathyroid Hormone.*

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Introduction

Type 1 diabetes mellitus (T_1DM) is a disorder in which the body is not able to produce enough insulin and includes 5-10% of all patients with diabetes mellitus. This type of diabetes is caused by the autoimmune destruction of beta cells in the pancreas, which mainly occurs sporadically (1, 2). T_1DM has very serious short-term and long-term complications. Disease management includes regular visits, control of blood glucose with insulin, regular blood sugar measurements, lifestyle changes, and regular screening for complications and co-morbidities (3).

Pseudohypoparathyroidism is a rare inherited disorder caused by an inadequate response to parathyroid hormone (PTH). A defect in G protein, which is the stimulus required for the activation of cyclic adenosine monophosphate (CAMP), causes this inadequate response. As its characteristics, people with pseudohypoparathyroidism may have an abnormally round face, short stature, abnormally short fingers, and mental retardation, and the combination of these symptoms is called Albright's phenotype. pseudohypoparathyroidism is generally referred to as a set of disorders that are characterized by hypocalcemia and hyperphosphatemia, but unlike primary hypoparathyroidism, PTH level is high in these patients (4).

The two main subtypes of pseudohypoparathyroidism are type Ia and type Ib. In pseudohypoparathyroidism, resistance to hormones other than PTH such as TSH, gonadotropins, glucagon, and GHRH are also commonly seen. The most common disorder in these patients is resistance to PTH in the kidney, which appears as hypocalcemia, hyperphosphatemia, and increased PTH (5).

The association of T_1DM and pseudohypoparathyroidism is a very rare comorbidity that has not been widely reported. The only reported case is a 12-year-old girl from India in 2012, who was reported by Saikia et al. with a history of recurrent seizures. She had a round chubby face, short neck, short arms and legs, which is the typical phenotype of Albright with pseudohypoparathyroidism. Chvostek and Trousseau symptoms were positive in the patient. In the X-ray of her wrist, she showed metacarpal shortening. Serum calcium was 3 mg/dL, phosphorus was 11.2 mg/dL, and PTH = 468 pg/mL. With further investigations in this child, they noticed the simultaneous presence of hypothyroidism and T_1DM (6).

Considering the timely diagnosis of these two diseases in the control of related complications such as hypocalcemia and glucose regulation despite the rarity of this association, the purpose of this study is to report a case of association between pseudohypoparathyroidism and T_1DM in a 12.5-year-old girl.

Case Report

This study was approved by the ethics committee of Babol University of Medical Sciences with code IR.MUBABOL.REC.1401.054. The patient was a 12.5-year-old girl, who was admitted to the emergency room with complaints of polyuria and polydipsia since a month ago, and fatigue, anorexia since a week ago and nausea and vomiting since the day before the visit. At the time of visit, her blood sugar was 512 mg/dl, which was accompanied by severe lethargy, rapid breathing, and increased heart rate. Abdominal examination of the patient was normal without organomegaly. The results of preliminary tests are given in

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Table 1. Due to high blood glucose and severe metabolic acidosis, she was diagnosed with severe diabetic ketoacidosis (DKA) and was treated with DKA protocol.

Table 1. Laboratory results of the patient at the age of 2 months (hospitalization due to seizures)

Type of test	Results
Calcium	6.5 mg/dl
Calcium Corrected	6.9 mg/dl
Phosphorus	7.8 mg/dl
Alkaline phosphatase	480 IU/L
Serum Albumin	3.1 mg/dl
Blood urea nitrogen	6 mg/dl
creatinine	0.4 mg/dl

The patient was the first child of the family, born via normal delivery, with a weight of 3500 grams. There was no problem on the first day of birth, but at 8 days old, she was admitted to the neonatal ward of children hospital due to seizure. In the laboratory examination, due to low calcium (Ca= 6.5 mg/dl), she was treated with intravenous calcium and after normalization of blood calcium; she was discharged with prescription of oral calcium. She was hospitalized again at the age of 2 months due to repeated seizures. In the laboratory results, she had low calcium and high phosphorus, which was treated with intravenous calcium, and after correcting the blood calcium, the treatment continued with oral calcium.

After the age of 2 months, the patient's seizures did not recur and she had no history of re-hospitalization. At the age of 12.5 years, the patient was hospitalized with severe DKA and was treated with DKA protocol, and after that, she was treated with Basal-Bolus Protocol of insulin. During a recent hospitalization at the age of 12.5 years, the patient was again examined in terms of calcium and phosphorus status, and according to low calcium and high phosphorus and PTH and normal kidney examination, the diagnosis of false hypoparathyroidism was put forward (Table 2) and the corresponding drugs were prescribed. The patient was examined in terms of Albright's phenotype, her intelligence and appearance were normal, the patient's height was 148 cm between the 10th-25th percentile, and the patient's weight was 34 kg, on the 10th percentile, and the patient's body mass index (BMI) was 15.5 kg/m^2 on normal percentile. No signs of short metacarpal bones were seen in the wrist x-ray. So, this patient was a case of pseudohypoparathyroidism without Albright phenotype in rare association with T_1DM.

Currently, the patient is 16 years old and is being treated with drugs related to diabetes and pseudohypoparathyroidism. The level of glucose and calcium is acceptable. In terms of the status of other hormones, it was also shown that the thyroid test is normal and the patient's puberty is complete and she has regular periods.

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Table 2. Laboratory results of the patient at the age of 12.5 years old (hospitalized due to DKA)

Test	Result	Test	Result
WBC	7300 mc/lit	HB	12.4 g/dl
PLT	283000 / µL	VIT D	ng/ml 36
BS	mg/dl 512	Na	130.6 meq/L
BUN	mg/dl 11	K	meq/L 3.35
Cr	mg/dl 0.6	PTH	pg/ml 407
Mg	mg/dl 2.98	Ca	mg/dl 6.6
SGOT	IU/L 20	P	mg/dl 6.9
SGPT	IU/L 21	T4	µg/dl 9.2
ALP	IU/L 558	TSH	MIU/L 1.7
ABG pH PCO_2 HCO_3	 7 20 5	-	-

Discussion

This patient is worthy of consideration in several ways. First, this case is the rare association between pseudohypoparathyroidism and T_1DM. Another important aspect is the young age of onset of the patient's clinical symptoms. On the other hand, in pseudohypoparathyroidism due to mutations in receptors, resistance to glucagon hormone is common. As a result, it is expected that in pseudohypoparathyroidism, if there is a disturbance in blood glucose, it will be in the form of hypoglycemia, but in our patient, high blood glucose and DKA manifestations appeared for the first time, which is contrary to the usual manifestations of pseudohypoparathyroidism.

In 2012, Saikia et al. reported a 12-year-old girl with a history of recurrent seizures. She had the facial and physical characteristics of pseudohypoparathyroidism, such as round chubby face, short neck, short arms and legs, and Chvostek and Trousseau symptoms were positive in the patient, and shortness of the metacarpals was seen in the wrist x-ray, which resulted in Albright phenotype for the patient. However, our patient did not have the Albright phenotype. She also had hypothyroidism, but 2 months after the initial presentation of pseudohypoparathyroidism, the patient was diagnosed with T_1DM and treated with insulin. After 2 years of follow-up, there was no recurrence of seizures (6). Unlike this patient, there was no association between pseudohypoparathyroidism and hypothyroidism in our patient. On the other hand, there is also the association of autoimmune diseases of the endocrine glands called Autoimmune Polyglandular Syndrome, and hypoparathyroidism is one of its main criteria and is also associated with cases such as T_1DM, but our patient had co-occurrence with pseudohypoparathyroidism, which is an interesting and rare co-morbidity (7).

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In this report, a rare association between pseudohypoparathyroidism and T_1DM was introduced, which is an unusual association of these two diseases. That's because in patients with pseudohypoparathyroidism, if there is a disturbance in the glucose status, it is in the form of hypoglycemia (due to a disturbance in the glucagon receptor), but in our patient, this association was in the form of hyperglycemia and DKA. So, early diagnosis and timely treatment of this association can help with the prevention of complications and better control of diabetes.

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