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Case Report

A case of Type 1 Diabetes Mellitus with Klinefelter's Syndrome

Klinefelter Sendromlu Tip 1 Diyabet Olgusu

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ABSTRACT

Type 1 diabetes mellitus (T1DM) is a model of chronic autoimmune disease beginning with genetic susceptibility in affected individuals and progressing to autoimmune destruction of β cells, precipitated by environmental insult. Some of the patients with T1DM have associated genetic disorders, such as Klinefelter's syndrome (KS), Down's syndrome and Turner's syndrome. This paper reports a case of T1DM accompanied by KS. The patient was a 14-year-old male who had been confirmed by absolute insulin deficiency and positive glutamic acid decarboxylase antibody (GADA). After chromosome analysis was performed because of the delay in his puberty, he was diagnosed with Klinefelter's syndrome, 47 XXY karyotype, at his follow-up.

Keywords: *1 Diabetes, Klinefelter's Syndrome*

ÖZET

Tip 1 diabetes mellitus (T1DM), etkilenen bireylerde genetik yatkınlıkla başlayan ve çevresel hasarla yıkıma uğrayan β hücrelerinin otoimmün yıkımına ilerleyen bir kronik otoimmün hastalık modelidir. T1DM'li hastalarının bazıları, Klinefelter sendromu (KS), Down sendromu ve Turner sendromu gibi genetik bozukluklara sahiptir. Bu yazıda KS'ye eşlik eden bir T1DM vakası bildirilmektedir. Hasta, mutlak insülin eksikliği ve pozitif glutamik asit dekarboksilaz antikoru (GADA) ile teyit edilen 14 yaşında bir erkekti. Ergenliğinin gecikmesi nedeniyle kromozom analizi yapıldıktan sonra takibinde Klinefelter sendromu 47 XXY karyotipi tanısı konuldu.

Keywords: *Tip 1 diyabet, Klinefelter sendromu*

INTRODUCTION

Type 1 diabetes mellitus (T1DM) is a model of chronic autoimmune disease beginning with genetic susceptibility in affected individuals and progressing to autoimmune destruction of β cells, precipitated by environmental insult (1, 2). Genetic predisposition and autoimmunity contribute to the pathogenesis of various co-morbidities (3). Some patients with T1DM have associated genetic disorders, such as Klinefelter's syndrome (KS), Down's syndrome and Turner's syndrome (4). We report a 15-year-old patient with T1DM accompanied by KS, diagnosed at his follow-up.

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CASE REPORT

A 14-year-old patient was admitted to our center with the complaint of weight loss, polyuria and polydipsia. The patient was born to a 27-year-old mother and the first child of nonconsanguineous parents. His sister was healthy, without remarkable medical history. There was no family history of diabetes and chromosomal abnormality, but his father and uncle suffered from rheumatoid arthritis. On physical examination, his height was 173 cm, weight 47,2 kg and body mass index 15,7 kg/m^2. His testicular volumes were 8 and 10 ml for the right and left one, respectively, and his penile length was 9.0 cm. Vital signs at admission were as follows: blood pressure: 100/70 mmHg; heart rate: 110 beats/minute; respiratory rate: 35 breaths/minute; and body temperature: 98.8°f (37.1°c). Physical examination revealed Kussmaul breathing (deep and rapid respiration due to ketoacidosis) with acetone odor and mild generalized abdominal tenderness without guarding and rebound tenderness. No abnormal finding was evident on the physical examination of his thorax and abdomen. Initial laboratory data were blood glucose: 301 mg/dl; venous pH: 7.24; pCO2: 25 mmHg, bicarbonate: 12 meq/l; WBC count: 18,500/ml, sodium: 143 meq/l; potassium: 3.5 meq/l; chloride: 97 meq/l; BUN: 32 mg/dl; creatinine: 1.7 mg/dl; and serum ketones were strongly positive. The results of the complete blood count and biochemical analysis are listed in Table 1.

Glutamic acid decarboxylase antibody (GAD) was positive, and islet cell autoantibodies (ICA) and insulin autoantibody (IAA) were all negative. HLA genotypes were DRB1*03, DRB3 and DQB1*02. Type 1 diabetes was diagnosed. Intensive insulin therapy for hyperglycemia was initiated. His blood glucose control was improved with 16 U insulin glargine and 3-6 U insulin aspart per meal. After the achievement of blood glucose control, the patient was discharged and examined every three months. At his follow-up, testicular volume and penile length were the same measured as before, 10 ml and 9 cm, respectively. Although he was 15 years old and in puberty, and lack of secondary sexual characteristics was mentioned. The patient's follicle-stimulating hormone level was 24.05 mIU/ml (normal range: 0.95-11.95 mIU/ml) and total testosterone was 526.94 ng/dl (normal range: 142-923 ng/dl). Having borderline intelligence level and delaying his puberty, for differential diagnosis, chromosome analysis was performed. The result was a karyotype of 47, XXY, so Klinefelter's syndrome was diagnosed. Testosterone therapy was planned to start at his follow-up. The parents' of this patient consent was obtained for this case study.

Table 1. Laboratory findings on the admission of the patient

Parameters		
Blood biochemical analysis	**Patient's result**	**Normal range**
Fasting plasma glucose (mg/dL)	301	70-105
Ketone (mmol/L)	1.5	0-0.6
Hemoglobin A1c (%)	13.35	4-6.0
Alanine transaminase (U/L)	12	0-26
Aspartate transaminase (U/L)	20	5-34
Albumin(g/dL)	4.1	3.4-4.8
Creatine (mg/dL)	0.62	0.3-1
Potassium (mmol/L)	3.5	3.5-5.2
Sodium (mmol/L)	143	132-145
LDL-cholestrol (mg/dL)	84	60-130
HDL-cholestrol (mg/dL)	46	37-75
Triglyceride (mg/dL)	64	30-125
Spot urinalysis		
Microalbuminuria (mg/gr creat)	10.9	0-30
Creatinine (mg/dL)	167.02	24-362

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

DISCUSSION

The patient was at a young age and had typical hyperglycemia symptoms, severe hyperglycemia with ketoacidosis, and lean body habitus with a body mass index of 15,7 kg/m^2. He had the positive autoimmune marker of type 1 diabetes, such as GAD antibodies. Atkinson et al. showed that 64 kDa autoantibodies were highly predictive of T1DM (5), and GADA is measurable in 70%-80% of patients with new-onset T1DM. The patient had HLA genotypes of DRB1*03 and DQB1*02 that comprise a high risk for type 1 diabetes mellitus. His father and uncle suffered from autoimmune disease; there was no family history of type 2 diabetes. All the above points supported the diagnosis of type 1 diabetes mellitus.

The association between KS and type 1 diabetes mellitus has been reported recently. KS is classically known to be associated with abnormalities of glucose metabolism; about 19% of the patient reported having impaired glucose tolerance, and 8% have overt type 2 DM (6). In a Danish study, out of 832 patients with KS, 15 had type 1 diabetes (7). According to a study from India, among 260 patients of T1DM, five patients (1.9%) had KS (8).

Some patients with T1DM have associated genetic disorders like Down's syndrome, Turner's syndrome and Klinefelter's syndrome. Autoimmune diseases like thyroid disorders, adrenal disorders, celiac disease, myasthenia gravis, connective tissue disorders, systemic lupus erythematosus and rheumatoid arthritis (9). Hormonal imbalance in KS may predispose hypogonadal males to develop defects in T cell activity that lead to autoimmune disorders (10).

There are many studies that denote a dramatically increased risk of type 2 diabetes in KS. There are a few reports on KS accompanying type 1 diabetes mellitus. The present patient with T1DM was diagnosed as KS at his follow- up. Although he was at puberty at the onset, on consecutive examination, the delay in puberty, such as lack of secondary sexual characteristics and delay on testicular volume, was realized. For differential diagnosis, chromosome analysis was performed. The karyotype result was 47, XXY karyotype. Hence, Klinefelter's syndrome was diagnosed.

In conclusion, KS should be considered in male patients with a delay at puberty, especially those diagnosed with T1DM, because of the coexisting that is reported in the recent reports.

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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REFERENCES

1. Redondo MJ, Eisenbarth GS. Genetic control of autoimmunity in type 1 diabetes and associated disorders. Diabetologia 2002; 45: 605–22.
2. Mayer-Davis EJ, Kahkoska AR, Jefferies C, Dabelea D, Balde N, Gong CX, et al. ISPAD Clinical Practice Consensus Guidelines 2018: Definition, epidemiology, and classification of diabetes in children and adolescents. Pediatr Diabetes. 2018; 19 Suppl 27(Suppl 27): 7-19.
3. Andreoletti L, Hober D, Hober-Vandenberghe C, Fajardy I, Belaich S, Lambert V, et al. Coxsackie B virus infection and beta cell autoantibodies in newly diagnosed IDDM adult patients. Clinical and Diagnostic Virology 1998; 9: 125–33.
4. Kordonouri O, Klinghammer A, Lang EB, Gruters-Kieslich A, Grabert M, Holl RW. Thyroid autoimmunity in children and adolescents with type 1 diabetes: a multicenter survey. Diabetes Care 2002; 25: 1346–50.
5. Atkinson MA, Maclaren NK, Holmes L, Scharp DW, Lacy PE, Riley WJ. The natural history and predictive value of Mr 64,000 autoantibodies for insulin-dependent diabetes mellitus. J Autoimmun 1990; 3: 41-5.
6. Bojesen A, Høst C, Gravholt CH. Klinefelter's syndrome, type 2 diabetes and the metabolic syndrome: the impact of body composition. Molecular Human Reproduction 2010; 16: 396–401.
7. Bojesen A, Juul S, Birkebaek NH, Gravholt CH. Morbidity in Klinefelter syndrome: a Danish register study based on hospital discharge diagnoses. Journal of Clinical Endocrinology and Metabolism 2006; 91: 1254–60.
8. Kota SK, Meher LK, Jammula S, Kota SK, Modi KD. Clinical profile of coexisting conditions in type 1 diabetes mellitus patients. Diabetes Metab Syndr 2012; 6(2): 70-6.
9. Barera G, Bonfanti R, Viscardi M, Bazzigaluppi E, Calori G, Meschi F, et al. Occurrence of celiac disease after onset of type1 diabetes: a 6-year prospective longitudinal study. Pediatrics 2002; 109: 833–8.
10. Ansar Ahmed S, Penhale WJ, Talal N. Sex hormones, immune responses, and autoimmune diseases. Mechanisms of sex hormone action. Am J Pathol 1985; 121(3): 531-51.