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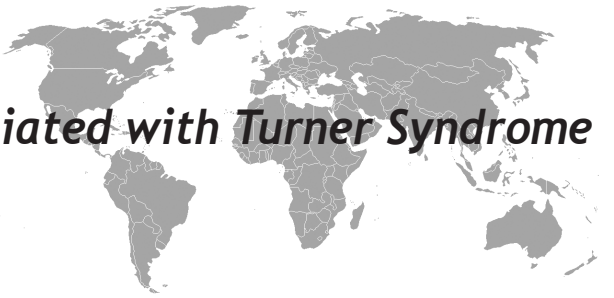
Case Report

Type 1 Diabetes Mellitus Associated with Turner Syndrome



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ABSTRACT

Turner's syndrome is a chromosomal disease frequently associated with autoimmune conditions including thyroid disease, inflammatory bowel disease, and diabetes. Recent reports have described an association with TS and type 1 diabetes mellitus. Here we report the case of a 11 -year-old girl with TS associated with T1DM. Our case is presented because of the rarity.

Key words: *Type 1 diabetes mellitus, turner sydrome, autoimmunity*

Tip 1 Diabetes Mellitus Turner Sendrom Birlikteliği

ÖZET

Turner Sendromu otoimmun troid, inflamatuar barsak hastalığı, diyabet ile ilişkili olan kromozomal bir hastalıktır. Yakın dönemde yapılan çalışmalarda TS ve tip 1 diyabet birlikteliği tanımlanmıştır. Bu yazıda 11 yaşında bir vakada TS ve T1DM birlikteliği nadir olması nedeniye sunulmuştur.

Anahtar kelimeler: *Tip 1 diabetes mellitus, turner sendromu, otoimmunite*

INTRODUCTION

Turner's syndrome (TS) is a chromosomal disease frequently associated with autoimmune conditions, including thyroid disease, inflammatory bowel disease and diabetes (1). Many of the patients with type 1 diabetes mellitus (T1DM) have associated genetic disorders (2, 3). Our case may suggest a genetic relationship between the two disorders.

CASE

A 11-year-old girl was admitted to the hospital with complaints of polyuria, polydipsia, decreased appetite, weight loss of 8 kg for a few weeks. She was born at term by normal vaginal delivery (birth weight 3400 g) from a healthy mother as first children of the family. There was no consanguinity between the parents. No family history of diabetes was reported. Physical examination at the time of admission revealed a temperature of 36.2°C, a pulse of 99 beats per minute, a respiratory rate of 22 per minute, and a blood pressure of 90/60 mm/Hg. The patient's height was 119 cm (-3.23 SDS) and her weight was 22.5 kg (-2.93 SDS).Calculated body mass index was 15.8 kg/m^2 (-0,62 SDS). She had second degree of dehydration. Respiratory, cardiovascular and neurological systems, thyroid examination was normal. She was prepubertal at Tanner stage 1. She had skeletal abnormalities included a webbedneck, shield chest, and

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cubitus valgus. Laboratory evaluation revealed normal-complete blood count, renal, hepatic test results. Blood glucose was 593 mg/dL (normal range: 60-110 mg/ dL). Blood gas analysis showed a pH of 6.7 and HCO^3 2.8 mmol/L. Blood ketone was 2 positive. The diagnosis of diabetic ketoacidosis was made, and after appropriate fluid-electrolyte and insulin therapy, multiple dose (4 times daily) insulin injection treatment (1 U/kg/day) was started. Glycosylated haemoglobin A1c was %12,3 (normal range:4-6%) C-peptide level was <0.02 ng/ ml(normal range) .Pancreatic autoantibodies (Islet cell autoantibodies, glutamic acid decarboxylase antibodies and anti-insulin autoantibodies) were pozitive. High resolution chromosome analysis revealed a karyotype 45XO. Echocardiogram was normal. Therefore, the patient was diagnosed as T1DM associated with Turner's syndrome. FSH was 6.99 mIU/mL(normal range:2.5-7.04), LH 2.91 mIU/mL(normal range:0.1-12), and E2 <20 pg/ mL. Gluten sensitive enteropathy and Hashimoto thyroiditis were not determined.

DISCUSSION

Type 1 diabetes mellitus is a model of chronic autoimmune disease beginning with genetic susceptibility in affected individuals and progressing to autoimmune destruction of B cells, precipitated by environmental insult (4). Genetic predisposition, autoimmunity and viral infections are the main etiopathological factors implicated in the pathogenesis of T1DM (5,6). These factors are also known to contribute to pathogenesis of the various co morbidities. Many of the patients with T1DM have associated genetic disorders like Turner' s syndrome.In T1DM ;autoimmune diseases (AID) like thyroid disorders, adrenal disorders, celiac disease, myasthenia gravis and connective tissue disorders are also found to be coexistent as well as autoimmune impairment of non-endocrine tissue.Using these specific antibodies, organ specific autoimmunity may be detected before the development of clinical disease. Early detection has potential bearing on prevention of unrecognized disease and the significant morbidities thereof (2-4).

Turner Syndrome is a rare genetic disorder, affecting approximately 1 in 2.500 female live births due to total or partial absence of the X chromosome in germinal and somatic line (7). Cardinal stigmata are reduced final height with webbing neck, cubitus valgus and ankle swelling associated with some classical clinical features :premature ovarian failure and less constantly phenotypic particularities such as congenital malformations, acquired cardiovascular, otological (hearing impairment), autoimmune and metabolic diseases (8,9)

We present a case detailing the association between TS and T1DM. Gonc et al.(10) described a 3.5-year-old girl with TS and T1DM who presented with diabetic ketoacidosis. As our case her Anti-islet cell and anti-insulin antibodies were positive and C-peptide level was low. Children with TS are at increased risk of developing a wide range of AID (11,12). The commonest diseases among these subjects are ulcerative colitis, Hashimoto thyroiditis and T1DM, coeliac disease, juvenile rheumatoid arthritis , addison's disease , psoriasis, vitiligo and alopecia areata have also been reported(13-19).

T1DM used to appear the most common AID associated with TS, as showed in a Danish study based on administrative data (17). There is no clear evidence for an increased prevalence of T1DM in these patients. The reason for the increased incidence of diabetes in TS women is probably due to deranged insulin secretion by mechanisms that are not entirely clear, and is not related to autoimmunity against pancreatic b-cells(20). It has been suggested that the abnormalities of the X chromosome may influence immune tolerance, leaving TS patients more susceptible to autoimmune disease (21). Although there is no clear association between major histocompatibility complex (MHC) polymorphisms and TS a number of polymorphisms in MHC may render these individuals susceptible to autoimmunity, which has no effect in normal individuals.

Increased stress interferes with the hypothalamic pituitary axis and induces catecholamine production resulting in neuroendocrine disequilibrium, subsequently affecting the immune system. It can be argued that stress levels are increased in individuals with TS due to psychological factors and this may cause immune dysfunction, leading in the process to predisposition to autoimmunity. However, no studies have been conducted in this area and therefore the role of stress in predisposition to autoimmunity in these individuals is unknown. Turner's syndrome subjects seem to have an increased susceptibility to infections, which may be due to defective immunoregulation, predisposing in the process to autoimmunity. However, this remains a hypothesis which could be tested by a longitudinal study investigating the prevalence of autoimmunity TS sub-

jects with repeated infections (20). In conclusion ıt is therefore proposed that all patients with TS and should be investigated for diabetes. Further investigations will be required to determine whether there is a significant association between TS and T1DM.

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