

Case Report

Autoimmune Polyglandular Syndrome (Type - III) : Case Report

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ABSTRACT

Autoimmune polyglandular syndromes are constellations of multiple glandular insufficiencies. There are four types - I, II, III and IV. Type II is the commonest. The

case reported here has features of type III, which is a rare occurrence.

KEY WORDS: autoimmune polyglandular syndrome type-III, insulin resistance

INTRODUCTION

Autoimmune polyglandular syndromes (APS) are constellations of symptoms and signs of multiple glandular insufficiencies. Four types of APS exist. Type I, III, and IV are relatively rare while type II is more common^[1]. Type III does not involve the adrenal cortex but two of the followings: autoimmune thyroid disease, type 1 diabetes mellitus (DM), rheumatoid arthritis, autoimmune liver disease, pernicious anemia, vitiligo and alopecia^[2]. This case belongs to type III because of the presence of type 1 diabetes, hypothyroidism, rheumatoid arthritis and vitiligo along with a probable association of autoimmune hepatic involvement and is reported because of its rarity.

CASE REPORT

A 14-year-old Saudi girl was admitted to the Department of Medicine, King Khaled General Hospital, Hafr Al Batin, with the complaints of upper abdominal pain, vomiting and increase in respiratory rate of one day duration. She was a known case of type 1 DM with insulin resistance, deforming rheumatoid arthritis and hypothyroidism under therapy with raised hepatic transaminases-possibly due to autoimmune liver disease. She had not attained menarche but had all other signs of puberty. She was previously admitted one month ago for diabetic ketoacidosis (DKA) when her liver function tests were deranged in the form of raised transaminases with normal bilirubin level. Her viral markers were non-contributory. At discharge, she was put on 150 units of insulin per day. She had missed her morning dose of insulin on the day of present admission.

On clinical examination, her weight was a 58.5 kg. She was conscious, oriented, afebrile, severely dehydrated, having Kussmaul's breathing with absence of pallor, cyanosis, icterus, thyromegaly, acanthosis nigricans and edema. She had vitiligo on extensor surface of both elbows and around the neck. Per abdomen examination showed epigastric and right hypochondrial tenderness. Respiratory, cardiovascular and central nervous system revealed no significant findings.

Investigations showed neutrophilic leucocytosis which reverted back to normal the next day. She had normal liver, renal and other biochemical parameters. Her blood gas analysis revealed severe high anion gap metabolic acidosis. Urine for acetone was positive. Her thyroid microsomal antibodies were positive. Sonography of abdomen failed to reveal any pathology. Her serum calcium, magnesium, phosphate, parathormone, cortisol, luteinizing and follicular stimulating hormone were all within normal range.

She was treated with standard protocol for DKA and broad spectrum antibiotics. She required 10 units of iv insulin per hour and subsequently more than 200 units of insulin per day when shifted to subcutaneous therapy. Insulin resistance was considered because of the high dose required. She was given a trial with metformin (500 mg) BID which lowered her insulin requirement significantly, but unfortunately, her hepatic transaminases went up and hence this oral anti-hyperglycemic agent was discontinued. Though used for a short period metformin helped in achieving a better glycemic control.

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DISCUSSION

Autoimmune polyglandular syndromes (APS) comprise a group of autoimmune disorders of the endocrine glands that result in failure of the glands to produce their hormones^[1]. In 1980, Neufeld and Blizzard organized and classified these syndromes into four main types defined as polyglandular autoimmune disease, also termed autoimmune polyglandular syndromes-APS^[3]. The polyglandular diseases are a series of organ-specific autoimmune illnesses characterized by the presence of circulating organ-specific antibodies, even in the absence of overt clinical disease^[4,5]. Genetic factors are also involved in the pathogenesis of APS^[1,4,6]. APS II and III are associated with HLA class II genes, with apparently distinctive HLA alleles for each. These APS are often observed in individuals in the same family, suggesting its inheritance could be due to an autosomal dominant trait with incomplete penetrance. HLA alleles are not seen in APS I and the mode of inheritance is autosomal recessive^[1].

APS I is characterized by the classic triad of mucocutaneous candidiasis (90 to 100%), hypoparathyroidism (80 to 85%) and Addison's disease (70 to 75%) appearing in a chronological order^[2]. For diagnosis at least two of the three major components need to be present^[3,7]. It is a rare condition. Prevalence is one in 25,000 population^[8]. Female to male ratio ranges from 0.8 - 1.5:1. It usually occurs in children.

APS II is characterized by the presence of autoimmune Addison's disease (100%) in association with either autoimmune thyroid diseases (originally described by Schmidt) and/or type 1 DM^[2,3,5,9]. It is the most common type encountered clinically. Approximately 14 to 20 people per million population are affected. The female to male ratio is 4:1. It occurs primarily in adulthood^[10].

APS III - in which a direct association of autoimmune thyroid disease (Hashimoto's thyroiditis, Grave's disease) and type 1 diabetes is found in absence of Addison's disease^[1,2]. It is a very rare condition. The exact worldwide prevalence of APS III is unknown. There is no racial or ethnic difference, in frequency of percentage, reported. It is typically observed in middle-aged women but can occur in persons of any age. The hallmark of APS III is the absence of Addison's disease^[1].

APS IV is a rare syndrome characterized by the association of autoimmune combinations not falling in the above categories^[11]. For example, Addison's disease with one or more minor components (rheumatoid arthritis, autoimmune liver disease, primary gonadal failure, pernicious anemia, celiac disease, vitiligo, etc.) excluding other major components of APS I, II and III. In all the

above types minor components are present in variable degrees.

The reported case is an adolescent girl with type 1 DM since the age of 11 years, who developed hypothyroidism at the age of 12 years and rheumatoid arthritis at the age of 10 years. She has vitiligo and probably autoimmune liver disease. The absence of goiter and the presence of microsomal antibodies in this patient probably denotes autoimmune atrophic thyroiditis. Insulin resistance in this patient could be due to anti-insulin antibodies which should be suspected in such patients with marked insulin resistance. Anti-insulin receptor antibody syndrome also known as type B insulin resistance (approximately 25 patients reported)^[11] is characterized by marked insulin resistance, hyperglycemia and acanthosis nigricans. Approximately, one third of patients also have other autoimmune diseases. The course of the DM is variable with occasional spontaneous remissions^[11]. Although acanthosis nigricans was not present in this case, possible association of this syndrome could not be ruled out as only specialized laboratory facilities can quantify the anti-insulin receptor antibodies to facilitate this diagnosis. The combination of type 1 DM, hypothyroidism, rheumatoid arthritis, vitiligo and autoimmune liver disease suggest APS III in this patient. It is mandatory to consider other glandular hypofunction while evaluating patients with any type of endocrine hypofunction, because multiple glandular involvement is quite frequent. Screening (organ-specific autoantibodies or HLA typing) of their family members is equally important.

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