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A case of autoimmune polyglandular syndrome type II with new added type 1 diabetes mellitus

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Abstract: Type II autoimmune polyglandular syndrome (APS) is a group of disease with two or more concurrent endocrine disorders. Type 1 diabetes mellitus can occur as a component of the disease. Antibodies are often positive in patients with type 1 diabetes mellitus and other component of type II APS. If the autoantibodies of diabetes mellitus and other diseases were found negative while following the cases with type II APS, it is recommended to repeat these analyses every 2-3 years. We aimed to present a patient who has been diagnosed at our clinic with type II APS include Hashimoto thyroiditis, primary adrenal insufficiency and premature ovarian insufficiency and new added type 1 diabetes mellitus to her disease.

Keywords: Type II autoimmune polyglandular syndrome, type 1 diabetes mellitus, antibodies

INTRODUCTION

Autoimmune polyglandular syndromes (APS) are the diseases which are defined as the autoimmune dysfunction of multiple endocrine organs. Type II APS is usually seen in adults and it is a syndrome of which hereditary susceptibility interacts with the environmental factors, and it is determined by multiple gene loci [1]. The most common components of type II APS include primary adrenal insufficiency (Addison), autoimmune thyroid disease, type 1 diabetes mellitus (DM) and primary gonadal insufficiency [2,3]. Autoimmune DM (type 1) may appear as a component of all types of APS, primarily APS type II, and its treatment is the same with the treatment of other type 1 diabetic patients [4]. Herein, we planned to present a patient, who formerly has been diagnosed at our clinic with type II APS due to the presence of Hashimoto thyroiditis, primary adrenal insufficiency and premature ovarian insufficiency and in whom now the clinical picture was accompanied by type 1 DM.

CASE REPORT

Medical history of the 25-year-old female patient that admitted to the clinic for irregular menstruation revealed irregular drug use for irregular menstruation and hypothyroidism for 5 years and progressive darkening of the skin color for the last 3 years. On her physical examination, hyperpigmentation was observed on her tongue, gingiva and oral mucosa. Laboratory analyses were consistent with primary hypothyroidism and hypergonadotropic hypogonadism with elevated antimicrosomal antibody (537 Uml/L). She did not respond to ACTH stimulation test, which was performed for low serum basal cortisol and high ACTH (993 pg/ml) levels. Considering that the patient has Hashimoto thyroiditis, primary adrenal insufficiency and premature ovarian insufficiency, levothyroxine 100 mcg 1x1, prednisolone 10 mg 1x1, and fludrocortisone 0.1 mg were started. Based on high blood glucose levels during follow-up visits at the hospital, a single dose baseline insulin therapy was commenced; however, insulin therapy was discontinued as she developed hypoglycemia. She had been discharged based on the laboratory analyses which indicated negative glutamic acid decarboxylase antibody (Anti GAD) and islet cell antibody (ICA). Her blood glucose level was normal during periodic policlinic visits. Two years after the initial diagnosis, the patient presented with weight loss of 6 kg in the last 6 months, polyuria and polydipsia. Her physical examination was unremarkable except for tachycardia, acidotic breathing and cutaneous and gingival

pigmentation. Laboratory findings were as following: glucose: 497 mg/dl, sodium: 131 mmol/L, potassium: 4.7 mmol/L, acetone: positive, HbA1C: 12.3%, C-peptide: 0.76 ng/ml, and insulin: 0.49 µU/mL. Arterial blood gas analysis revealed a pH of 7.23 and HCO_3 of 13 mmol/L, which suggested diabetic ketoacidosis leading to hospitalization of the patient. Ketoacidosis picture improved with insulin therapy and IV hydration. Intensive insulin therapy was started. Glucocorticoid and levothyroxine doses were modified. Anti-GAD antibody was negative but ICA was positive. Bringing the patient's blood glucose under control, she was discharged recommending coming for control visits at the policlinic.

DISCUSSION

The prevalence of type II APS is 1:20.000. Although it appears at any age, it is more common between the ages 30 and 40 and in females [2, 3]. The disease is associated with HLADR3 and/or DR4 haplotype and shows autosomal dominant inheritance [1,5]. The second component is seen years after the initial component determined in the patients [6]. We know that, hypothyroidism and irregular menstrual cycles have begun years before our patient's hospital presentation and adrenal insufficiency accompanied these components while she was staying at our clinic [7]. Type 1 DM was determined in our patient approximately 2 years after diagnosing her with type II APS.

Adrenal insufficiency is expected in all patients with type II APS, whereas autoimmune thyroid disease is expected in 69-82% and type 1 DM in 30-52% [4]. Togetherness of Addison, autoimmune thyroid disease and/or type 1 DM is the classical characteristic of the disease [1]. The most common combinations are type 1 DM / autoimmune thyroid disease by 41%, autoimmune thyroid disease /Addison disease by 14.6%, type 1 DM/vitiligo by 9.9% and Type 1 DM/Addison disease 3.3%. Concurrent type I DM and autoimmune thyroid disease usually manifests with hypoglycemia due to decreased insulin need and increased insulin sensitivity [8]. In the patients with type 1 DM, ICA and Anti-GAD antibody are usually positive. ICA positivity is more specific for type 1 DM because Anti-GAD positivity can be seen also in Addison disease by 5-7% [9]. It has been demonstrated that approximately 27% of the patients with type 1 DM is associated with polyglandular involvement [10]. Type 1 DM could be now forecasted due to advance immunogenetic and antibody screening methods [11]. Despite the assumption that genetic researches are more beneficial for type I APS versus type II APS, screening for HLADR3/DR4 is important in determining susceptibility to type 1 DM regardless of the type of APS [12]. If the autoantibodies of other diseases were found negative while following the cases with type II APS, it is recommended to repeat these analyses every 2-3 years [13]. In fact, ICA was found positive when our patient presented with ketoacidosis although Anti GAD and ICA were negative two years ago when the patient was considered to have type 1 DM.

In conclusion, questioning all APS patients that have type 1 DM or other components, as well as their families, for the presence of other autoimmune diseases and performing necessary genetic or autoantibody screening tests are important for early diagnosis and treatment of the disease.

Author Contributions

All authors contributed to the diagnosing, threating of the patient and writing of this paper.

Conflict of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of the research reported.

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