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Case Report

A rare case report and literature overview: autoimmune polyglandular syndrome type II

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ABSTRACT

Autoimmune diseases are a heterogeneous group of diseases with chronic humoral immune response against different tissue formation. Autoimmune polyglandular syndrome (APS) is also characterized by multiple organ autoimmune dysfunction. 43-year-old male patient was admitted with complaints of anorexia, malaise, rapid darkening on skin under the sun. The patient, stating in his medical background that levothyroxine TB with the diagnosis of hypothyroidism was started three years ago, had hypotension and hyperpigmentation. Hyponatremia, hyperkalemia, autoimmune hypothyroidism, primary adrenal insufficiency and atrophic gastritis was detected in examinations, significant improvements were observed in the general condition of the patient on whom glucocorticoids, and then levothyroxine TB replacement treatments were applied, and in blood pressure and laboratory parameters. Therefore, other organ autoimmunity should be sought in patients admitted with any autoimmune disease and be considered in follow-ups. We aimed to review the literature about APS and remind APS by this case.

Keywords: Autoimmune polyglandular syndrome, Chronic autoimmune thyroiditis, Adrenal insufficiency

INTRODUCTION

Organ-specific autoimmune diseases are associated with the contribution of environmental factors in people with a genetic predisposition.[1] These individuals constitute specific cellular and humoral response against their own tissues, and one or more organs may be affected by this situation. However, there are still many questions remaining pathophysiologically unanswered about autoimmunity in APS development. Previously it was thought that organs from the same embryonic origin and sharing common specific antigens were affected. However the fact that the adrenal gland, and the thyroid and pancreatic glands, which are affected in APS-2, have respectively mesodermal and endodermal origins, does not verify this hypothesis. Furthermore, why autoimmunity focuses solely on the proteins in endocrine tissues but not on the proteins in the organs originating from the same germ layer and why multiple organs are affected at different times cannot be explained sufficiently.[2,3] Autoimmune polyglandular syndrome (APS) is also characterized by multiple organ autoimmune dysfunction. It is classified into four main types: APS type I; begins in childhood and is characterized by mucocutaneous candidiasis, hypoparathyroidism and adrenal insufficiency. APS type II or Schmidt syndrome; is more common in the adult population. It is often characterized by primary adrenal insufficiency, Graves' disease or autoimmune hypothyroidism, diabetes mellitus type I and primary hypogonadism. APS type III; is characterized by insulin dependent diabetes mellitus that develops without

Addison's disease and autoimmune thyroiditis disease, and APS type IV are the combinations which do not include the features of the previously reported groups. We aimed to present the 43-year-old male patient who was diagnosed with APS type II (primary adrenal insufficiency, autoimmune thyroiditis and atrophic gastritis) in this case.

CASE REPORT

The 43-year-old male patient was admitted to endocrinology clinic with complaints of anorexia, malaise, rapid darkening on skin under the sun. It is stated in his medical history that he was diagnosed with hypothyroidism; levothyroxine treatment was started 3 years ago. Due to the patient's continuing complaints under treatment with levothyroxine, the drug treatment was discontinued and the patient, who had not received any treatment for two years, was admitted to the clinic. In the patient's physical examination, his height was 172 cm, weight: 70 kg, body mass index (BMI): 24 kg/m², TA: 90/70 mmHg, pulse: 78 min and his thyroid gland was grade 1b palpable. Hyperpigmentation was present in the incision in the arm, the body curves and oral mucosa was normal. Other systemic examination was normal. In the tests performed; it was found that TSH was 35 µIU / ml (0.35 to 4.4µIU/ml); FT3 was 2.51 pmol/L (2.63-5.7 pmol/L), FT4 was 9.1pmol / L (9-19 pmol/L), AntiTPO (antithyroid peroxidase hormone) was 498 (0-5.6) IU / ml; AntiTg (antithyroglobuline) was 118 (0-4.11) IU / ml; serum Na(sodium) was 132 (136-145) mmol / L and potassium was 5.1-5.5 (3.5 to 5.1) mmol / L, glucose was 94 (80-100) mg / dL; serum creatinine level was 0.8 mg/dl (0.5-0.9); calcium 9 mg/dl (8.8-10.2); PTH (parathormone) was 35 pg/ml (10-72); serum cortisol was 0.8-1.0 µg/dL (3-19) and ACTH was 515 pg / ml (15-50) and serum testosterone was 7.68 ng/ml (1.66-8.77). The patients with hypocortisolemy were admitted to the endocrinology clinic. The cortisol values at 30th and 60th mins were 0.9 mcg/dl and 1 mcg/dl in short ACTH test (250 micrograms), respectively. ACTH level was found to be 515 pg/mL. No pathology was detected in the surrenal MR performed. The medical history and physical examination of the patient is incompatible with tuberculosis, his chest X-ray was normal. With the diagnosis of primary adrenal insufficiency and primary hypothyroidism, first hydrocortisone was started at stress doses, and then the dose was reduced to physiological dose (20 mcg/day). Fludrocortisone (0.05 mg / day) treatment was started on the patient with hypotension, hyponatremia and hyperpotasemia. Thyroid replacement therapy was gradually started 3 days after hydrocortisone replacement, and it was gradually increased up to 100 mcg/day. The thyroid ultrasound of the patient was consistent with chronic thyroiditis and Hashimoto's thyroiditis. In the tests of the patient screened in terms of polyglandular endocrinopathy, it was detected that serum vitamin B12 level was 399 pg/ml (normal 145-914) and anti-parietal cell antibody was 1/320 positive. Since the anti-parietal cell antibody was positive, an upper gastrointestinal endoscopy was performed on the patient, and atrophic gastritis was revealed. The clinical and laboratory findings of the patient were incompatible with diabetes mellitus vitiligo and hypogonadism. The other autoimmune disease markers; antinuclear antibodies (ANA), Estractible Nuclear Antigen (ENA) and celiac antibodies were negative. In the follow-up of the patient, Na was 138 mEq/L, K was 4.1mEq/L and TA was 120/80 mmHg. The patient, whose general condition was stable, was screened with routine endocrinology polyclinic follow-up.

DISCUSSION

The organ-specific autoimmune diseases characterized by lymphocytic infiltration and specific autoantibodies result in endocrine hyperfunction or hypofunction. Clinical signs of the disease are usually limited to a gland. In addition; not infrequently, individual or familial infiltration of multiple endocrine glands can also be seen. APS is divided into four groups by Betterle et al. Type 3 is sub-divided into four groups including; 3A, 3B, 3C, 3D (Table 1).[4]

Looking at the history of the disease, the relationship between thyroiditis and Addison's disease was first revealed by Schmidt in 1926. In 1964, Carpenter et al. added type 1 diabetes to the syndrome.

APS type 2 is associated with genes which are generally transmitted with familial inheritance and that regulate the antigen presentation to T cells. APS type 2 is usually hereditary in families associated with characteristic HL.[3] However, it is also known that environmental factors play an important role in the emergence of the disease.[5] There are studies suggesting that abnormal expression of the gene encoding Cytotoxic T-lenfositantij-4 (CTLA-4) predisposes to autoimmune polyglandular syndrome type 2.

Autoimmune polyglandular syndrome type 2, is more common than Type 1, and typically more common in adults. Insulin-dependent diabetes mellitus and thyroid dysfunction (autoimmune hypothyroidism or Graves' disease) are the most common clinical presentations. Addison's disease is the third major component of these disorders.[6] Disorders of other endocrine glands may clinically develop in the majority of the patients with Addison's disease. In our case also; Addison's disease was accompanied by autoimmune hypothyroidism and atrophic gastritis.[7] Among the components of polyglandular syndrome type 2 that are less frequent, are primary hypogonadism and hypophysitis[8]. Additionally, pernicious anemia, vitiligo and celiac disease are the other rare diseases that may be associated with this syndrome.[9]

Table 1: Classification of autoimmune polyglandular syndrome.

APS 1	APS 2	APS 3				APS 4
Chronic candidiasis	Addison's disease should certainly be present	Autoimmune thyroid disease should certainly be present (Hashimoto's thyroiditis, primary myxoedema, asymptomatic autoimmune thyroiditis, Graves' disease, pretibial micom, endocrine ophthalmopathy)				APS involvement not meeting the definitions of APS type 1,2,3
	APS 3A	APS 3B	APS 3C	APS 3D	APS 3A	
And/or chronic hypoparathyroidism	Autoimmune thyroid diseases	Endocrine diseases	Gastrointestinal or hepatic autoimmune diseases	Skin, neural or neuromuscular autoimmune diseases	Collagen vascular or autoimmune haematological disorders	
And/or Addison's disease	And/or type 1 diabetes mellitus	Type 1 DM Adenosine and neurohypophysis diseases Premature ovarian failure Hirata syndrome	Atrophic gastritis Pernicious anaemia Celiac disease Chronic inflammatory bowel disease Autoimmune hepatitis Primary biliary cirrhosis Sclerosing cholangitis	Vitiligo Alopecia Autoimmune thrombocytopenia Autoimmune Hemolytic anaemia Anti-phospholipid syndrome Myasthenia Gravis Stiff-Man Syndrome Multiple Sclerosis	Systemic lupus erythematosus Discoid lupus erythematosus Rheumatoid arthritis Seronegative arthritis Systemic sclerosis Sjogren's syndrome Werlhof syndrome Antiphospholipid syndrome Vasculitis	
Two or more of the diseases above should be present		Addison's diseases houl				

OPS Type 2 treatment is done separately for each of the diseases in this group. In the follow-up of patients, other components that can be seen in this syndrome should be kept in mind and attention should paid in this regard. Thyroid hormone replacement therapy alone in hypothyroidism accompanied by adrenal insufficiency may reveal symptoms of adrenal insufficiency. In our case, the patients with no clinical improvement after levothyroxine therapy had ended his treatment. When the patient was re-evaluated in our clinic, first we started hydrocortisone therapy, and then levothyroxine therapy.

CONCLUSIONS

APS is characterized by endocrine and non-endocrine organs' disorders with autoimmune-origin, and has a wide clinical spectrum. Due to its inclusion of a large group of diseases, it is important to evaluate the clinical and laboratory parameters of patients at admission carefully. Since autoimmune disorders can further increase over time, long term follow up of patients is crucial10. APS should especially be taken into consideration in the presence of multiple autoimmune diseases, and patients should be screened in a detailed manner in this respect also.

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