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Late Diagnosed Type II Autoimmune Polyglandular Failure Syndrome: A Case Report

Tanısı Geciken Tip II Otoimmün Poliglandüler Yetmezlik Sendromu: Bir Olgu Sunumu

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Abstract

Autoimmune polyglandular syndrome (APS) type II is the term descibing a group of diseases with two or more concurrent endocrine disorders. It is more prevalent in female gender. The most common pathologies include primary adrenal insufficiency (Addison's disease), autoimmune thyroid diseases (Graves' disease, Hashimoto's thyroiditis), type 1 diabetes mellitus (DM) and primary hypogonadism. Replacement of deficient hormone is the basis of treatment.

The present paper discussed autoimmune polyglandular syndrome based on the symptoms in a 25-year-old female patient who was followed in the intensive care unit because of impaired consciousness considered to have resulted from potential drug/substance addiction. Antidepressant therapy was recommended for the patient and she was diagnosed with APS on further evaluation. *Turk Jem 2014; 1: 13-16*

Key words: Autoimmune polyglandular syndrome type II, adrenal insufficiency, hypothyroidism, depression

Özet

Tip II otoimmün poliglandüler sendrom (OPS), iki yada daha fazla endokrin bozukluğun birlikte görüldüğü, kadın cinsiyette daha sık görülen bir grup hastalığa verilen isimdir. Sıklıkla görülen patolojiler; primer adrenal yetmezlik (Addison), otoimmün tiroid hastalığı (graves, hashimato), tip 1 diyabetes mellitus (DM) ve primer hipogonadizmdir. Tedavi eksik olan hormonların yerine konulmasıyla sağlanır. Bu yazıda olası ilaç/madde bağımlılığına bağlanan şuur bozukluğu nedeni ile yoğun bakımda izlenen, antidepressan tedavi önerilen ve sonraki değerlendirilmesinde tip II OPS tanısı konulan 25 yaşındaki bayan hastanın bulguları ışığında OPS tartışılmıştır. *Turk Jem 2014; 1: 13-16*

Anahtar kelimeler: Tip II otoimmün poliglandüler sendrom, adrenal yetmezlik, hipotiroidizm, depresyon

Introduction

The etiology of autoimmune polyglandular syndrome (APS), which is known as autoimmune dysfunction of multiple endocrine organs, remains spare. However, underlying genetic features and autoimmunity are considered to play a role in the pathogenesis. APS is usually divided into two subgroups: type I and type II. Type I comprises chronic mucocutaneous candidiasis, type 1 includes diabetes mellitus (DM), autoimmune hypoparathyroidism, and adrenal insufficiency. Adrenal insufficiency together with autoimmune thyroid diseases (Graves' disease or autoimmune hypothyroidism) and/or presence of type 1 DM is the clinical characteristic of type II disease. Pernicious anemia, vitiligo, alopecia, celiac disease, myasthenia gravis, primary hypogonadism, autoimmune diabetes insipidus, and lymphocytic hypophysitis may accompany the clinical picture in both type I and type II APS (1).

Although it generally displays polygenic inheritance, some human leukocyte antigen (HLA) types have been reported to pose a risk for APS. Clinical presentation depends on sum of the existing diseases. Clinical progress may either be slow or the patients may present with acute and life threatening clinical pictures. Therefore, patients with one or more endocrine deficiencies should be carefully examined for APS and the patients and their relatives should be evaluated to make an early diagnosis. Replacement of the deficient hormone is the rule for treatment (2).

There are numerous case reports and observational studies showing the relationship between thyroid dysfunction and psychiatric disorders (3,4,5,6).

In the present paper, we reviewed the literature based on the case of a patient with a history of hypothyroidism and amenorrhea, who was followed for impaired consciousness, and subsequently, recommended antidepressant therapy, and was diagnosed with APS type II on further evaluation.

Case Reports

A 25-year-old female patient presented to the endocrinology department with the complaints of absence of menstrual periods for 3 years, darkened skin color, weakness, and low blood pressure. Her medical history revealed irregular levothyroxine use for hypothyroidism for 5 years, which she has not been receiving in the past one year.

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It was learned that she had been intubated and hospitalized 4 months ago in the intensive care unit of a state hospital due to loss of consciousness, breathing difficulty, and urinary and fecal incontinence. It was also learned that sodium and potassium concentrations were within the normal ranges and cranial computed tomography (CT) showed normal findings. Serum TSH level was 100 mIU/mL; the patient had received steroids for the relief of edema; been extubated 3 days later; and transferred to the neurology clinic. Electroencephalography (EEG), which was performed in the neurology clinic, demonstrated generalized basal rhythm irregularity composed of high-voltage slow activity, whereas cranial magnetic resonance imaging (MRI) demonstrated signs consistent with metabolic syndrome. No substance was detected in blood and urine samples, which were sent to forensic medicine laboratory to eliminate probable drug/substance intoxication depending on her personal history revealing that her

Figure 1. Hyperpigmentation in the skin and oral mucosa of the patient at the time she was diagnosed with adrenal insufficiency

Figure 2. Hyperpigmentation in the skin and oral mucosa 4 weeks after hospital discharge

Table 1. Laboratory parameters of the patients during hospital admission and policlinic control

Normal	Admission	Policlinic control
Hb (13.6-17.2 g/dL)	12.4	13.7
MCV (80-99 fL)	76.1	76
Ferritin (15-200 ng/mL)	10.9	51
Glucose (70-105 mg/dL)	86	84
Na (135-145 mmol/L)	134	134
K (3.5-5.1 mmol/L)	4.5	4.6
Creatinine (0.6-1 mg/dL)	0.52	0.7
Erythrocyte sedimentation rate (0-25 mm/h)	7	
Cortisol (6.7-22.6 µg/dL)	0.14	<0.4
DHEASO4 (18-391 µg/dL)	2.5	
25(OH)VITD3 (20-120 ng/mL)	5	36
ACTH (10-50 pg/mL)	993	54
fT3 (2.3-4.2 pg/mL)	2.14	
fT4 (0.61-1.12 ng/dL)	0.13	0.82
TSH (0.34-5.6 mIU/L)	102.91	7.2
HbA1C (4.8-69%)	6.14	
FSH (16.74-113.6 mIUmL*)	35.65	
LH (10.87-58.64 mIUmL*)	35.76	
Estradiol (5-37 ng/mL*)	13.78	
Progesterone (<0.08-0.78 ng/mL*)	0.09	
Prolactin (3.34-26.72 ng/mL)	52.64	

*Reference ranges are the normal ranges of postmenopausal period

Table 2. Cortisol levels before and after ACTH (Tetracosactrin acetate) test

Time (minute)	Cortisol (Normal, 6.7-22.6 µg/dL)
Basal	<0.4
30th	<0.4
60th	<0.06
90th	<0.4

ex-husband was a substance abuser and that she intermittently used antidepressant drugs. Treatment for hypothyroidism was planned and the patient was discharged with recommendation to be followed up in psychiatry and endocrinology outpatient clinics.
On the laboratory analyses performed at the endocrinology outpatient clinic, cortisol level was 0.145µg/dL and ACTH level was 993pg/mL; the patient was admitted to the endocrinology inpatient clinic being prediagnosed with adrenal insufficiency.
System questioning revealed nausea, dizziness, polydipsia, nocturia, amenorrhea, and loss of axillary and pubic hair. On her physical examination, axillary temperature was 36°C, pulse rate was 68/min and rhythmic-rhythmic; respiratory rate was 18/min, and blood pressure (BP) was 90/60 mmHg. Her general status was good, she was conscious and cooperated. Hyperpigmentation was observed on the skin, oral mucosa and gingiva. Examination of other systems was unremarkable (Figure 1).
Laboratory parameters at the time of hospitalization are shown in Table 1. Rapid ACTH test (250µg Tetracosactrin acetate) was performed to diagnose adrenal insufficiency (Table 2) and Prednisolone 1x10mg and Fludrocortisone 0.1mg were commenced considering that she had Addison's disease. It was learned that thyroid ultrasonography and scintigraphy performed at external center have been reported as autoimmune thyroid disease. Anti-microsomal antibody was 537 (0-9U/mL) and anti-thyroglobulin antibody was <20 (0-40U/mL). Considering that she had Hashimoto's thyroiditis, levothyroxine sodium 0.1mg was commenced.
The patient, who complained about amenorrhea, had high follicle stimulating hormone (FSH) and luteinizing hormone (LH) but low estrogen and progesterone levels. Premature ovarian insufficiency (early menopause) was thought and gynecology consultation was requested for the treatment. She began to receive hormone replacement therapy. Her pelvic ultrasonography revealed no pathology in the uterus and in bilateral ovarian loci. Upper abdominal and pelvic CT showed no pathological finding except for hepatosteatosis.
The patient was considered to have APS type II because of presence of Hashimoto's thyroiditis, Addison's disease and premature ovarian insufficiency (hypogonadism). The patient, whose therapy protocol was created and who was clinically stable, was discharged with recommendations for outpatient follow-up.
On her follow-up visit after 4 weeks, BP was 120/80 mmHg and pulse rate was 80/min. Her general status was good, she was conscious and cooperated. It was observed that skin and mucosa pigmentation has regressed (Figure 2). She told that she felt well psychologically.

Discussion

APS was first defined and classified by Neufeld and Blizzard (7). First, a case of tuberculosis-related adrenal injury and type 1 DM; many years later, a case of adrenal insufficiency coexisting with thyroid disease; and years later, a patient with the involvement of three endocrine organs have been reported. Thereby, the coexistence of autoimmune thyroid disease, autoimmune adrenal insufficiency and/or type 1 diabetes has been defined as APS Type II (8,9,10). The prevalence of APS Type II has been estimated at 1.4-2 /100.000. APS Type II may appear in any age, however, occurs most frequently in the third to fourth decades of life and is 3 times more common in females (11,12). Autoimmunity has been demonstrated in more than 50 percent of patients and most autoimmune disorders were associated with HLA (1,13). These patients are at risk also for other autoimmune diseases. Some studies have reported that 40% of patients with Addison's disease develop other organ-specific autoimmune diseases (14). Ovarian failure can be seen in 10% of women with APS type II and should be considered in the differential diagnosis in case of amenorrhea in women under 40 years of age. Patients may present with dermatological signs, such as alopecia and vitiligo. Autoimmune thyroid disease has been detected in more than 15% of patients with alopecia in particular (12).
Hyponatremia, hyperkalemia, dehydration, hypotension, acidosis and hyperpigmentation are the common symptoms of primary adrenal insufficiency. Fifty percent of cases may present with adrenal crisis. Nevertheless, the patients may also present with weakness, weight loss, intermittent vomiting, abdominal pain, muscular cramps, and postural hypotension, which are the symptoms of chronic adrenal insufficiency. Clinical signs depend on time of onset of disease and severity of adrenal insufficiency (11,15). History of the present case, in fact, defines signs of chronic adrenal insufficiency, however, on previous evaluations, primarily hypothyroidism and psychiatric disorders were thought and the diagnosis of adrenal insufficiency seems to have been overlooked. There are numerous studies in the literature indicating that psychiatric problems can accompany thyroid dysfunctions. Symptom spectrum may range from tremor, panic attack and anxiety disorder to acute psychosis, and even to depression, particularly in patients with hypothyroidism (3,5,6,16). Moreover, there are many studies showing that thyroid dysfunction itself causes depression and that thyroid hormone replacement therapy decreases depression severity scores in such patients (17). A study demonstrated that untreated hypothyroidism slowed down the response to therapy in bipolar disorder (18). Again, postpartum depression was found more prevalent in women with autoimmune thyroid disease and with positive antibody (19).
Personal medical history of the present patient case revealed depression attacks, due probably to poor-treated autoimmune hypothyroidism, and intermittent antidepressant drug use. In addition, she has been evaluated in the psychiatry department when she was hospitalized 4 months ago, depression was considered, and antidepressant drug was recommended based on suspected drug or substance use.
Considering that the patient had elevated serum TSH, CK, LDH and myoglobin levels together with psychiatric disease at that time, it seems reasonable to explain current clinical condition with hypothyroidism-associated myxedema picture. Steroid use for edema and stable clinical status at that time might have caused adrenal insufficiency to be overlooked.
Of the adrenal insufficiency cases, 90% have hyponatremia and 65% have hyperkalemia. Adrenal insufficiency should be considered in the event of a morning serum cortisol concentration

<5 µg/dL in addition to the clinical symptoms. However, in practice, ACTH stimulation test should be performed in each suspected patient without waiting for the result of basal cortisol level (11). Significantly high serum ACTH concentration in addition to clinical symptoms and hypocortisolemia made us consider adrenal insufficiency in the present patient case. Cortisol response to additional ACTH stimulation could not be obtained, thus, the diagnosis of adrenal insufficiency has been confirmed.

Hormone replacement should be performed individually for each condition in APS type II. However, if these conditions co-occur, treatment of adrenal insufficiency has the priority over thyroid hormone replacement (2,20).

In conclusion, APS type II is a rarely encountered syndrome but can lead to serious life-threatening problems unless treated early. APS type II should be considered in the presence of hypothyroidism, secondary amenorrhea and hypotension. Family members should be questioned and necessary screening should be performed owing to genetic transition characteristic of the disease.

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