Turk J Med Sci
35 (2005) 417-419

SHORT REPORT

Autoimmune Polyglandular Syndrome Type II: A Case Report

Özlem YERSAL[1], Gülbin SEYMAN[1], Dilek SOYSAL[1], Hamide AYDOĞAN[2],
Serra ŞENTEKİN[1], Yiğit SÖZEN[1]
[1]İzmir Atatürk Education and Research Hospital ,1st Clinic of Internal Medicine; İzmir - Turkey
[2]Suat Seren Chest Diseases and Thoracic Surgery Hospital, İzmir - Turkey

Received: April 05, 2005

Key Words: Polyendocrinopathies; type 1 diabetes; Addison's disease

Autoimmune polyendocrine syndrome (APS) type II (Schmidt's syndrome) is defined by the coexistence of autoimmune Addison's disease with autoimmune thyroid disease and/or type 1 diabetes mellitus (1). A fraction of the patients also present with or later develop other organ specific autoimmune disorders. These include hypergonodotropic hypogonadism, vitiligo, chronic atrophic gastritis, pernicious anaemia, autoimmune chronic hepatitis and celiac disease.

Many circulating organ-specific antibodies directed against endocrine organs are detected in patients with APS II. Major relevant autoantibodies detectable at the clinical onset of the diseases constituting type II APS are- 21 hydroxylase autoantibodies (21OHAb) against adrenal cortex, thyroperoxidase (TPOAb), thyroglobulin (TGAb) and TSH receptor autoantibodies (TRAb) against thyroid; insulin (IAA), and glutamic acid decarboxylase autoantibodies (GADAb) against the endocrine pancreas (2).

Case Report

A 21 year old woman presented with weakness, fatigue, and widespread hyperpigmentation of the skin and oral mucosa, two months following delivery of her first child. She had no symptoms of nausea, vomiting or diarrhea. She had a three-year history of type 1 diabetes mellitus and had been taking mixtard insulin twice daily. She complained of hypoglycemic attacks especially in the mornings. On admission, the patient's vital signs included a heart rate of 105 beats/min, and a blood pressure of 80/60 mmHg. Because of her severe orthostatic hypotension, she could not stand up. Physical examinaton revealed generalized hyperpigmentation and darkening with prominent gingival and buccal mucosa (Figure). The thyroid gland was not palpable. Her HbA1c was 9% and fasting C peptide <0.5 ng/ml (normal range; 0.9-4 ng/ml) . AntiGAD antibody was positive at 9 U/ml (normal range; 0-1 U/ml) . Serum electrolyte levels were found within normal ranges (Table 1). As Addison's disease was suspected, baseline plasma cortisol, plasma adrenocorticotropic hormone (ACTH), plasma aldosterone levels, and rapid ACTH stimulation test investigations were performed. The patient's baseline cortisol level was low, while the serum ACTH level was high and aldosterone level was with in normal ranges. The rapid ACTH stimulation test with 250 µg cosyntropin did not cause a rise in the plasma cortisol level ; baseline, 30-minute, and 60-minute values were 1.1, 1.1 and 1.0 µg/dL, respectively. Chest X-ray , hypophysis MR and CT scan of the surrenal glands were normal. Other laboratory investigations disclosed a low serum TSH level, with high free thyroid hormone serum values . High titers of TgAb and TPOAb antibodies were also established. TRAb and antiendomysial antibodies were undetectable. C_3 and C_4 levels were within the reference ranges (Table 2). Fine needle aspiration biopsy confirmed

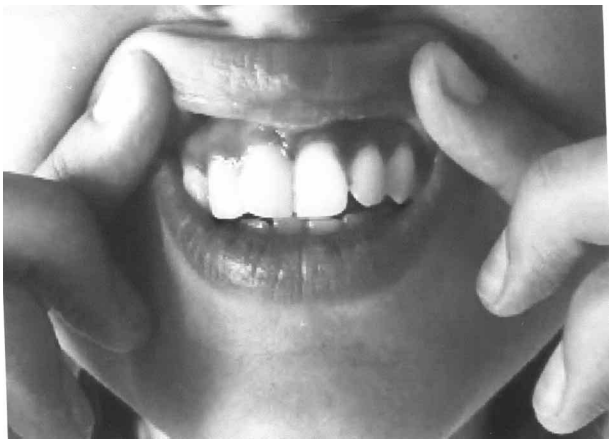

Figure. Dark pigmentalian of gum and lips.

Table 1. Initial and subsequent complete blood count and electrolyte values

	Day 1	Three months later	After minerolocorticoid theraphy
Sodium (mmol/l)	142	127	136
Potassium (mmol/l)	4.66	7.6	5.2
Chloride (mmol/l)	102	95	97

Table 2. Results of additional investigations

	Result	Normal range
Cortisol (µg/dl)	1.1	5-25
ACTH (pg/ml)	819	10-70
Aldosteron (ng/ml)	29	29.4-161.5
Post ACTH cortisol (ug/dl)	1.1	>20
FT3 (pg/ml)	6.44	1.8-4.6
FT4 (pg/ml)	4.3	0.93-1.7
TSH (µIU/ml)	0.009	0.27-4.
TgAb (U/l)	44.83	0-28.7
TPOAb (U/ml)	>1020	0-10
TRAB (U/l)	4	0-9
C_3 (g/l)	0.93	0.9-1.8
C_4 (g/l)	0.21	0.16-0.50

lymphoid/mononuclear cell infiltration of the thyroid gland . She had a combination of type 1 diabetes mellitus , autoimmune thyroid disease and Addison's disease, which is defined as autoimmune polyglandular syndrome type II. She was given propranolol and oral methylprednisolone, 2/3 in the morning and 1/3 in the afternoon. Therapy resulted in a rapid improvement in the patient's condition. At the outpatient visit after three months her blood examination revealed hyponatremia and hyperkalemia. Treatment began with fludrocortisone (0.1 mg/day). After mineralocorticoid therapy her serum electrolyte levels reached normal ranges (Table 1).

Discussion

Autoimmune endocrine gland disorders may regularly coexist with other endocrine autoimmune diseases (3). Neufeld and Blizzard organized and classified these clinical conditions and defined them as polyglandular autoimmune diseases, also termed autoimmune polyendocrine syndromes (APS) (4).

Oegle first reported the association between Addison's disease, caused by bilateral tuberculous destruction of the adrenal glands, and diabetes mellitus in 1886 (5). Schmidt's excisional biopsy detected lymphocytic infiltration of the adrenal cortex and thyroid gland in a patient who died from adrenal insufficiency in 1926 (6). From that time, the coexistence of Addison's disease and autoimmune thyroid disease has been known as Schmidt's syndrome. In 1931, Rowntree and Snell described the first case with Addison's disease, hyperthyroidism and diabetes mellitus and revealed the relationship between these three glands (7).

APS II typically occurs in early adulthood with a peak onset during the third or fourth decades and is three times more common in females than in males. This patient with type 1 diabetes mellitus, autoimmune thyroid disease and Addison's disease, has the three major components of Schmidt's syndrome. Ten percent of Schimidt's syndrome patients have all three major components of the syndrome(8).

Patients with an autoimmune disease must be considered at risk for other autoimmune diseases. Söderbergh et al. reported 40% of 97 patients with autoimmune Addison's disease had other clinically evident organ specific autoimmune disorders (9). In the patient, we detected association of type 1 diabetes mellitus and Addison's disease and she was screened for the other autoimmune diseases. We noticed that she also had autoimmune thyroid disease.

In the patients who have type 1 diabetes and adrenal failure together, an unexpected fall in insulin requirement may be the earliest sign of adrenal failure (10). The patient developed recurrent hypoglycemia attacks without any change in the treatment or physical activity. Hypoglycaemia attacks are considered to be caused by enhanced insulin sensitivity secondary to glucocorticoid deficiency.

Because methylprednisolone has a weak minerolocorticoid effect, fludrocortisone is frequently added to the therapy regimen. The patient had normal electrolyte values at the beginning and the weak minerocorticoid effect of methylprednisolone seemed to be adequate. Three months later, blood examination revealed hyponatremia and hyperkalemia and mineralocorticoid therapy was started . Her electrolyte levels returned within normal ranges.

Autoimmune thyroid diseases (Hashimoto's thyroiditis, primary myxedema, asymptomatic autoimmune thyroiditis, Graves disease, isolated ophthalmopathy) occur in 60-70% of patients with APS II(11). This patient had high free thyroid hormone levels with low TSH levels and high titers of TgAb and TPOAb antibodies . Her thyroid biopsy was consistent with autoimmune thyroiditis. Thyroxine therapy may precipitate Addisonian crisis in patients with Schmidt's syndrome through increasing cortisol clearance and metabolic rate (12).

In APS II there is an association between organ specific autoantibodies and the presence of pre-existing disease. Autoantibodies may be detected before the symptomatic phases of the autoimmune diseases. The detection of autoantibodies and appropriate interventions prevent morbidity and mortality from other diseases such as diabetic ketoacidosis and Addisonian crisis.

In conclusion; all patients with an autoimmune disease should be considered at risk for the other autoimmune diseases. Early detection of the disease may reduce morbidity and mortality significantly in the patients with autoimmune polyglandular syndrome. Many syndrome diseases can be treated with respective substitution therapy.

Corresponding author:
Özlem YERSAL
251 sok. No:25/6
Hatay, İzmir - TURKEY
e-mail: yersal1978@yahoo.com

References

1. Desmond A. Schatz, William E.Winter. Autoimmune polyglandular syndrome II: clinical syndrome and treatment. Endocrinol Metab Clin N Am 31: 339-352, 2002
2. Falorni A , Laureti S, Santeusanio F. Autoantibodies in autoimmune polyendocrine syndrome type II. Endocrinol Metab Clin N Am 31: 369-389, 2002
3. Lam-Tse K , Batstra R , Aanstoot J et al. Pediatric Endocrinology Reviews 1: 22-37, 2003
4. Neufeld M, Maclaren NK, Blizzard RM. Two types of autoimmune Addison's disease associated with different polyglandular autoimmune(PGA) syndromes. Medicine (Baltimore) 60:1653–60,1981
5. Oegle J W. On disease of the brain as result of diabetes mellitus. StGeorge's Hosp Report 1: 157–88, 1866
6. Schmidt MB. Eine biglandulare Erkrankung (Nebennieren und Schild-drüse) bei Morbus Addisonii. Verh Dtsch Ges Pathol 21: 212–21, 1926
7. Rowntree LG, Snell AM. A Clinical Study of Addison's Disease. Mayo Clinic Monographs. Philadelphia: W.B. Saunders, 1931
8. Betterle C, Dal Pra C, Greggio N. Autoimmunity in isolated Addison's disease and in polyglandular autoimmune diseases type 1, 2, and 4. Ann Endocrinol 62: 193-201, 2001
9. Söderbergh A, Winqvist O, Norheim I et al. Adrenal autoantibodies and organ specific autoimmunity in patients with Addison's disease; Clinical Endocrinology 45: 453-460, 1996.
10. Vincent McAulay, Brian M Frier. Addison's disease in type 1 diabetes presenting with recurrent hypoglycaemia. Postgrad Med J 76: 230-232, 2000.
11. Betterle C, Lazzarotto F, Presotto F. Autoimmune polyglandular syndrome type 2. The tip of an iceberg?. Clin Exp Immunol. 137: 225–233, 2004.
12. Leland Graves III, Robert M Klein, Anne D Walling. Addisonian crisis precipitated by thyroxine therapy: A complication of type 2 autoimmune polyglandular syndrome. South Med J 96: 824-827, 2003.