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AUTOIMMUNE POLYGLANDULAR SYNDROME TYPE I*
A Case Report

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Autoimmune polyglandular syndrome (APS) type I is a disorder that consists of three primary diseases: hypoparathyroidism (HPT), adrenocortical insufficiency (ACI) and chronic mucocutaneous candidiasis. Several other disorders may be associated. The diagnosis of APS type I was made in a 16-year-old patient with HPT, Hashimato's thyroiditis and ACI in our department. She has been observed for more than four years for other possible endocrine and non-endocrine disorders.
Key words: autoimmune, polyglandular syndrome type I, childhood.

Various autoimmune endocrinologic insufficiencies are described as autoimmune polyglandular syndrome (APS). The detection of autoantibodies against the endocrinologic gland is definitive for the diagnosis; these antibodies choose the normal gland as a target, and hypofunction develops over time[1].

APS type I consists of three primary disorders: hypoparathyroidism (HPT), adrenocortical insufficiency (ACI) and chronic mucocutaneous candidiasis; several other disorders, such as gonadal failure, alopecia, thyroiditis, malabsorption, vitiligo, chronic active hepatitis and kerotopathy may be associated[2,3]. Type II APS also consists of three primary disorders: insulin-dependent diabetes mellitus, ACI and Hashimato's thyroiditis (HT)[4].

The features of a case with type I APS are presented in this report.

Case Report

A 16-year-old girl was referred to Gazi University Hospital because of an 11-month history of fatigue, weakness and recurrent episodes of carpopedal

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spasm. She had a history of oral moniliasis at the age of five, and her menses had begun a year previously. From her family history we learned that her parents were first-degree relatives, her father had died nine years previously and her mother had had a goiter operation. On physical examination, her height and weight were both at the 50th percentile. On admission she had marked carpal spasms with a blood pressure of 90/60 mmHg. The vertical length of the right and the left thyroid lobes was 5 and 4 cm, respectively. There were brown pigmentations and deformities on her teeth (Fig. 1). Chvostek and Trousseau's signs were easily elicited. Pubertal development was graded as stage 5 according to the Tanner scale of development[5].

Laboratory investigations were in the normal range, including complete blood cell count and urinalysis. The skeletal bone age was estimated to be 16 years. Serum sodium, potassium, magnesium, blood urea nitrogen, creatinine, fasting sugar, aspartate aminotransferase, alanine aminotransferase, albumin and cortisol were in the normal ranges. Tubular phosphorus reabsorption, urine calcium excretion and urine free cortisol were also within normal limits, as were serum immunoglobulin levels, vitamin B_{12}, folic acid and antinuclear antibody. In the electrocardiogram, the corrected QT interval was measured as 0.52 seconds (normal < 0.44 second). Serum calcium (ionized) was found to be 1.6 mg/dl (normal: 4.48-4.92 mg/dl), phosphorus 7.8 mg/dl (normal: 2.7-4.5 mg/dl) and parathormone (intact) 4 pg/ml (normal: 10-65 pg/ml).

The thyroid hormones and thyroid stimulating hormone levels were found to be in the normal ranges. Thyroid antimicrosomal and antithyroglobulin antibodies

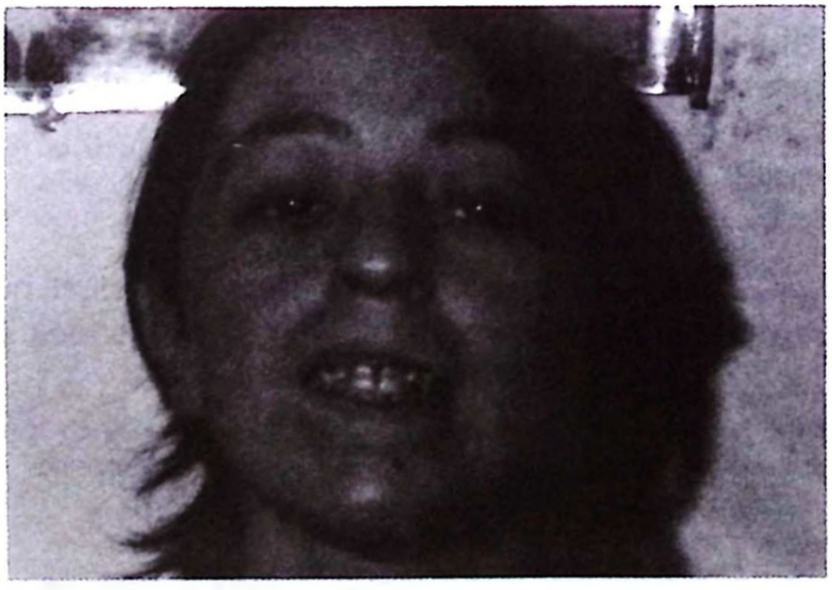

Fig. 1: The appearance of the pigmentation of the patient's teeth.

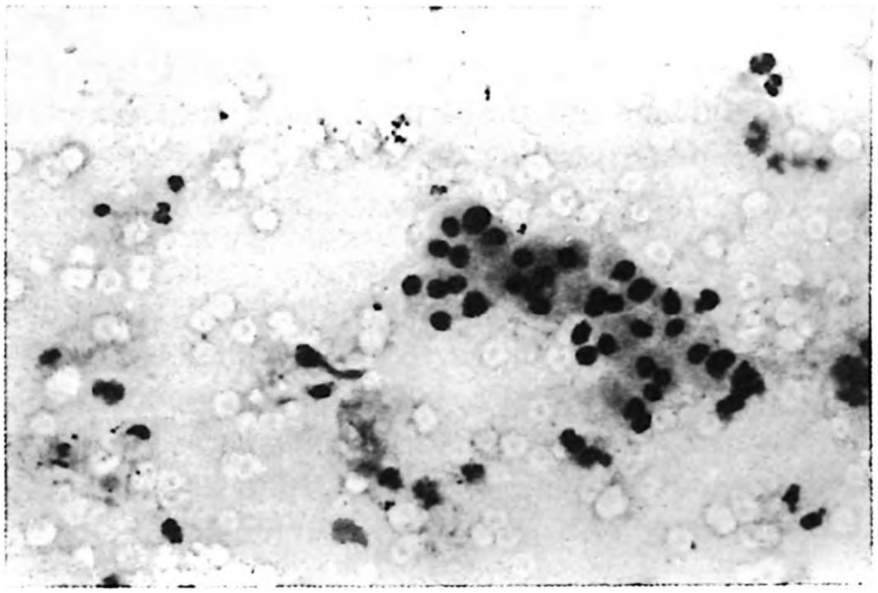

Fig. 2: A cluster of Hurtle cells with abundant granular eosinophilic cytoplasm and uneven nuclei. The background of the smear shows erythrocytes and polymorphonuclear leukocytes of blood origin.
(Aspiration biopsy material taken from thyroid tissue) (x 400, Hemotoxylen and Eosin).

were 287 mg/dl (normal < 50 mg/dl) and 44 mg/dl (normal < 50 mg/dl), respectively. Thyroid ultrasonography showed the right lobe as 17 x 59 x 11 mm, and the left lobe as 17 x 48 x 9 mm without a solid or cystic nodule. Fine needle thyroid aspiration biopsy was consistent with HT (Fig. 2).

The patient's basal adrenocorticotropic hormone (ACTH) value was elevated (84 pg/ml; normal 10-60 pg/ml). Before and after the ACTH stimulation test, cortisol levels measured as 17.79 ng/dl and 18.54 ng/dl, respectively, and these values were much lower than expected. Follicle stimulating hormone, luteinizing hormone, total estriol and dehydroepiandrosterone sulfate were within normal limits. Chest x-ray, brain tomography, adrenal tomography and parathyroid scintigraphy were all reported to be normal.

Intravenous calcium gluconate and oral 1.25-dihydroxy-vitamin D_3 were administered to treat the hypocalcemia and tetany. On the third day of admission, serum calcium and phosphorus levels returned to normal. Our patient was treated daily with hydrocortisone per oral 20 mg/m²/day. L-thyroxine was given at a dose of 100 µg/day to treat the goiter. Five months later, the patient suffered from orthostatic hypotention with a plasma sodium level of 124 mEq/L (normal: 136-146 mEq/L), potassium 5.8 mEq/L (normal: 3.5-5.1 mEq/L) blood renin activity 50 ng/ml (normal < 4.3 ng/ml/hr), and her basal ACTH level was higher than normal. These findings led us to the diagnosis of mineralocorticoid insufficiency, and flurocortisone therapy at adose of 0.1 mg/day was initiated.

Discussion

A rare disorder, type I APS is diagnosed when two or three of HPT, ACI and mucocutaneous candidiasis are present. A number of endocrine and non-endocrine autoimmune disorders such as gonadal failure, alopecia, autoimmune thyroid disorder, vitiligo, chronic active hepatitis and keratopathy are associated with this syndrome[1,3,6].

The initial diagnosis of our case was HPT and goiter. HT was then diagnosed by thyroid fine-needle aspiration biopsy and the patient's high level of thyroid antimicrosomal antibody. In type I APS, HPT is the primary finding in 90 percent of patients, and HT can be seen in 10 percent patients[4,6]. Because of suspected complaints we further investigated probable ACI. In one month glucocorticoid deficiency and in six months mineralocorticoid insufficiency were found. ACI can be seen in two-thirds of cases[4]. Glucocorticoid and mineralocorticoid deficiences can be seen either at the same time as or five years after presentation with the disease[4,7].

Gonadal failure is another finding that can be seen in type I APS, and women are affected more commonly at older ages[8]. The gonadal functions of our patient were considered to be normal.

The most common nonendocrine disturbances seen with this syndrome are deformation of the teeth and nails and mucocutaneous candidiasis[9]. From the patient's history we learned that she had once had white plaque in her mouth, which could have been oral candidiasis, and her teeth were pigmented.

Cellular and humoral immune system disturbances have also been reported in type I APS. High levels of immunoglobulin G and immunoglobulin E and lower levels of immunoglobulin A may be seen[1,10,11]. The increased activity of suppressor T-cells may be responsible for these immunoglobulin disturbances[9,11]. However immunoglobulin levels and T lymphocyte subgroups were normal in our patient, and she had anergy for candida antigen.

It is possible that some autoimmune disorders other than HPT, HT, ACI and endocrine or non-endocrine disorders could be seen at a later age with type I APS. This fact should always be kept in mind during the clinical follow-up of patients with APS.

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