

Polyglandular autoimmune syndrome Type 2 – case report

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Abstract

We describe the clinical case of a 32-year-old woman with a previous diagnosis of thyroiditis, medicated with levothyroxin, and with a family history of hypothyroidism (sister).

During the first term of pregnancy, a clinical state of worsening asthenia began, with inability to gain weight (3Kg throughout the pregnancy), alopecia, and hyperpigmentation of the skin and mucosal surfaces. These symptoms persisted after delivery, and the weight loss became worse (about 20%). Hypotension was also observed by this time. Laboratory tests showed hyponatremia and hypochloremia, very high plasma ACTH levels, and very low levels of plasma cortisol and plasma aldosterone. Other hormonal plas-

ma levels were within the normal range. CT scans of the adrenal and pituitary glands were also normal. Study of autoantibodies revealed positive antithyroid antibodies. Diabetes mellitus was not present. After hydrocortisone was initiated, there was an improvement in the clinical state and laboratory results.

We discuss polyglandular autoimmune syndrome type 2 in the context of the reported clinical case, bearing in mind the rarity of appearance of symptoms during pregnancy.

Key words: Polyglandular autoimmune syndrome type 2, autoimmune thyroiditis, Addison disease.

Introduction

Autoimmune diseases of the endocrine glands are generally restricted to one gland only. However, more than one of these organs may be affected in the same patient. Three syndromes are defined, according to the pattern of the glands involved. Detection of auto-antibodies, which reflects the glands involved, is usual.

Polyglandular autoimmune syndrome type 2 is the most frequent of these syndromes, and generally manifests as diabetes mellitus type 1 or chronic thyroiditis associated with Addison disease.¹

Case Report

A 32-year-old woman with prior diagnosis of thyroiditis and under medication with levothyroxin was referred for a Medical consultation for hyperpigmentation and asthenia.

The patient had been diagnosed with hypothyroidism around 3 and half years previously, and since then, had been medicated with levothyroxin. During the first term of a first pregnancy, around 10 months before the first observation, complaints of asthenia and progressive worsening began, with difficulty gaining weight (total of 3kg throughout the pregnancy) and generalized hyperpigmentation of the skin and mucosa, without exposure to sunlight. On objective examination, there was hypotension (82/42 mmHg), asthenia (patient was only able to move using a wheelchair), accentuated cutaneous hiperpigmentação, and generalized alopecia. Laboratory results showed slight anemia (hemoglobin- 11 g/dl), normocytic, normochromic, without other alterations of the hemogram, and without alterations in renal function or transaminases, serum sodium - 130 mmol/ml, serum potassium - 5 mmol/ml, serum chloride - 96 mmol/ml, glycemia - 63 mg/dl, TSH<0.05 µU/ml, anti-microsome antibodies - 404 U/ml (reference value< 35), ACTH> 1250 pg/ml (reference value: 0-46), serum cortisol – 0.1 µg/dl (reference value: a.m.: 4.3-22,4 p.m.: 3-16.6), urinary cortisol - 3,5 µg/dl (reference value: 28-213), serum aldosterone < 1.1 ng/dl (reference value: 0-16). Remaining hormone levels, including FSH, LH, growth hormone, PTH, total, free T3 and T4 within the normal values,

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anti-thyroglobulin antibodies and TSH anti-receptor negative, anti-21-hydroxylase antibodies negative. Glycemia remained between 63-84 mg/dl and the oral glucose tolerance test was normal. Echography of the thyroid showed heterogeneity and hypoechogenicity of the glandular parenchyma, suggesting a process of the thyroiditis type. Computed tomographies (CT) scans of the sella turcica and suprarenals did not show any alterations.

Based on the clinical state and supplementary exams described, a diagnosis of polyglandular autoimmune syndrome type 2 was made, and hydrocortisone therapy was initiated. Clinically, significant progressive improvement was observed, with disappearance of the asthenia, improvement in hypotension and decrease in hyperpigmentation. Laboratory tests showed improvement in the alterations recorded in the ionogram and urinary cortisol.

Discussion

Polyglandular autoimmune syndrome type 2 (PAS type 2) is hereditary in around half of cases, and various forms of genetic transmission are described (recessive autosomic, dominant autosomic and polygenic).^{2,3}

This syndrome is also known as Schmidt syndrome (hypothyroidism and Addison disease) and occurs with a prevalence of 1.4-2 per 100000 inhabitants.⁴

In the majority of patients (around 50%), diabetes mellitus type 1 (DM1) is the first manifestation of polyendocrinopathy,⁵ appearing after autoimmune thyroiditis, sometimes simultaneously with Addison disease.⁶

Associated with the “major” components of this syndrome, other autoimmune diseases may also emerge, though less frequently. These include hypogonadism, vitiligo, alopecia, chronic hepatitis and chronic atrophic gastritis.⁷

The patient presented in this case report does not, so far, show any evidence of DM1, however, she has autoimmune thyroiditis and Addison disease which feature the Schmidt syndrome.

It is now known that the presence of auto-antibodies precedes the appearance of symptoms of Addison disease by several years,⁸ and various states of alteration of the immunological system are established, until the appearance of symptoms (1 genetic susceptibility, 2 asymptomatic – absence of laboratory alterations, 3 symptoms and laboratory alterations

under stress, 4 permanent symptoms and laboratory alterations).^{7,8} This disease is therefore recognized as an instructive model for the alterations observed in PAS.^{7,8}

Adrenal anticortex antibodies were discovered in 1957.⁹ Subsequently various criteria suggestive of autoimmune disease were indicated, including typical histopathological alterations and the presence of another autoimmune endocrinopathy. The presence of these antibodies in the initial clinical phase is described in around 80% of patients with PAS.⁷

The standard test for detecting adrenal cortex antibodies has a sensitivity of around 70% and very high specificity.¹⁰

In the patient presented here, no anti-suprarenal antibodies were detected. The recommendations are repetition of the dose of these antibodies, although the time interval between doses has not been defined.⁸ It is also recognized that after several years of evolution of the disease, no auto-antibodies may be detected in some cases.⁷

Typically, the imaging exams of the suprarenal show an absence of lesions, as in the case presented here, or atrophy over the course of the disease, excluding other causes of suprarenal insufficiency, namely tuberculosis and neoplasms.⁷

The most specific signal of primary suprarenal insufficiency is hyperpigmentation of the skin and mucosa. The majority of the symptoms of cortisol deficiency, i.e. fatigue, anorexia, weight loss and weakness, occur in insidious and non-specific form.¹⁰ In some patients, initial symptoms may also include abdominal pain, nausea, vomiting and diarrhea.⁷ In the laboratory tests, hyponatremia, hyperkalemia, hypoglycaemia, normocytic anemia, mildly normochromic, low aldosterone values and increased plasma rennin are common. As a screening test, serum cortisol levels can be taken in the morning, the ACTH serum value being used to distinguish between primary and secondary renal insufficiency. In patients in whom suspicion of suprarenal insufficiency is maintained, and assuming the previous levels are within the normal values, the ACTH test should be carried out.^{7,10}

Addison disease generally causes infertility due to chronic anovulation, although some patients can remain fertile with appropriate therapy. Reported cases of obstetric success are rare.¹¹

In an even rarer form, the PAS can complicate

pregnancy and may be confused with *hyperemesis gravidarum* by causing hypoglycemia and alterations of the ionogram during the first term of pregnancy.¹² In the case described here, the clinical state of suprarenal insufficiency developed during pregnancy, without evidence of any complication or clinical manifestation in the newborn infant, as has been described.¹³

The treatment for this syndrome is hormone replacement therapy, depending on the affected glands.

It is currently accepted that patients with isolated Addison disease should be monitored for the co-existence of other autoimmune endocrinopathies, and should be kept under observation if the results of the initial approach are negative^{7,8}. Direct family members of patients with PAS known to have any of the endocrinopathies described should also be screened.^{1,7,8}

The case described here is illustrative of Polyglandular autoimmune syndrome type 2 and demonstrates the need to pay close attention to the appearance of other autoimmune endocrinopathies, when one of these has already been diagnosed. Suprarenal insufficiency was manifested during the pregnancy, what seldom occurs. Some cases of Polyglandular autoimmune syndrome type 1¹⁴ and type 2¹⁵ have already been published in Portugal, but no similar cases have been found with diagnosis during pregnancy. ■

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