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Review

Debut of Polyglandular Autoimmune Syndrome Type 2 (Schmidt Syndrome) in a Patient with Chronic Kidney Disease of Unknown Etiology in Peritoneal Dialysis

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Abstract

Schmidt Syndrome refers to the combination of autoimmune adrenal insufficiency (Addison's disease) with autoinmune thyroiditis, and is part of a larger syndrome known as autoinmune polyendocrine syndrome type II or polyglandular autoinmune syndrome type II (PAS II). Schmidt Syndrome as a 1:20,000 prevalence in general population with 3:1 ratio of females to males affected. It is autosomal dominant inheritance with variable penetrance. Associated with certain HLA antigens HLA-DR3, HLA-DR4, non HLA gene M-ICA and CTLA-4. The diagnosis of the Schmidt Syndrome is the same as that of the individual disorders. The treatment includes of primary hypothyroidism and the Addison disease. We present the evolution, the clinic and the treatment of a patient diagnosed with Schmidt Syndrome.

Keywords: Addison disease; Hashimoto's thyroiditis; Peritoneal dialysis; Polyglandular autoimmune syndrome; Schmidt Syndrome

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Introduction

Autoimmune polyglandular syndrome is a rare disease, that is defined by the presence of two or more glandular insufficiencies caused by autoimmune mechanisms and that may be associated with other pathologies and immunological phenomena. It is characterized by the presence of circulating organospecific antibodies and lymphocytic infiltration of the affected gland. It is classified into 4 types. Polyglandular syndrome type 2 (Schmidt Syndrome) includes adrenal insufficiency associated with autoimmune thyroid disease or type 1 diabetes mellitus [1-3].

A 36-year-old woman with end-stage renal disease of unknown etiology in long-standing peritoneal dialysis who went to the emergency room for marked arterial hypotension and was subsequently diagnosed with autoimmune polyglandular syndrome. We present the evolution, the clinic and the treatment of the syndrome.

Case Report

A 36-year-old patient with the following background: end-stage renal failure in the peritoneal dialysis program since March 2010, diagnosed in 2009 with autoimmune thyroid disease with fine needle aspiration suggestive of Hashimoto's thyroiditis and presence of anti-TPO antibodies in blood. In September 2014, a total parathyroidectomy and bilateral total thyroidectomy was done. After the biopsy was made, she was diagnosed with classic multifocal papillary carcinoma and confirming lymphocytic thyroiditis. The patient was treated by the endocrinology service with iodine 131 without incidents. In February 2016 she went to the emergency department for presenting vomiting and dizziness, upon arrival the physical examination was: blood pressure 60/40 mmHg, skin pallor, analytically: leukocytes 5400 (4000-10000), eosinophils 8%(0.5-6), hemoglobin 12.7 g / dl (12-16), hematocrit 37.6% (37-49), platelets 224,000(138000-381000), albumin 3 mg / dl (4-5.2), glucose 95 mg / dl (74-105), urea 52 mg/dl (13-50), uric acid 3.6 mg / dl (2.4-6.4) potassium 3.6 mEq / L(3.6-4.9), lactic dehydrogenase 249 IU / ml (200-418), Sodium 127 mEq / L(137-148) thyrotropin stimulating hormone 13.68 mUI / L(0.35-5.5), T4 1.45 ng / dl(0.89-1.76), parathyroid 32 pg / ml (10-55), cortisol 2.3 µg / dl (5.27-22.45), protein C reagent 0.4 mg/dl, negative tumor markers, autoimmunity was negative.

The patient received the following peritoneal dialysis pattern: 3 exchanges of 2000 cc with physioneal 35 to 1.36%, and negative balances of -700-800 ml / day. An echocardiogram was performed with the following findings: undilated cardiac chambers. Hyperdynamic left ventricular function. Chest radiology: rule out acute pathology. Abdominal ultrasound: kidneys of small size 6 cm, difficult to delimit, intra-abdominal fluid in relation to peritoneal dialysis.

Under suspicion of an undiagnosed adrenal insufficiency syndrome, ACTH, cortisol, aldosterone and anti-alpha 21 hydroxylase levels were requested, these being negative important elevation of ACTH (1812 pg/ml) and a low cortisol (2.3 µg/dl). A Synacthen test was done and it was positive, with a clear absence of elevation pf plasma cortisol. Water replacement is performed, treatment is initiated Fludrocortisone 0.1/day and Hydrocortisone 50 mg /8 hour, gradually improving the patient, and being discharged home at home with maintenance treatment 7 days later after stabilization. Subsequently, the immunological study reflects the presence of positive anti-adrenal antibodies being diagnosed the patient of autoimmune adrenal insufficiency, diabetes mellitus was ruled out, Anti GAD/64k, Anti-IA, and Anti insulin antibodies were negative. Two sisters of the patient, aged 32 and 40, were studied and were positive with anti-TPO antibodies, one of them asymptomatic and the other with clinical hypothyroidism.

Discussion

Autoimmune polyglandular syndrome is a rare disorder of autoimmune etiology that affects two or more glands and that may be associated with more disorders of autoimmune origin. It is characterized by immunological phenomena that cause the loss of self-tolerance to the target organ, thus inducing the formation of circulating organospecific antibodies that subsequently and in the presence of glandular lymphocytic infiltrate causes destruction of the glandular parenchyma causing failure of the affected organ. The polyglandular syndrome (autoimmune polyendocrinopathy) has been classified into 4 types (Table 1):

Type 1: Also known as APECED (Autoimmune Polyendocrinopathy, Candidiasis and Ectodermal dystrophy) a very rare entity, as a very low incidence 1/80000, and a very variable prevalence, is more frequent in populations with a high degree of consanguinity [3]. It has an autosomal recessive pattern of inheritance and is associated with the mutation of the AIRE autoimmune regulatory gene [4], located on chromosome 21q22.3. Its main components are mucocutaneous candidiasis, adrenal insufficiency and hypoparathyroidism, for its diagnosis the syndrome must have at least two of its main components, it can also be associated with other autoimmune disorders such as gonadal insufficiency, vitiligo, and celiac disease alopecia among others. Its main components usually appear at 3-5 years and before 20 years.

Type 2: It is the most frequent of the polyglandular syndromes, affects more women 3:1, and as a prevalence of 2-4.5: 100000 inhabitants. Appears in adulthood from 3-4 decade of life, is of autosomal dominant inheritance with incomplete penetrance, it is believed that there is a polygenic predisposition of chromosome 6. In some studies has been a relationship between the appearance of the disease and the presence of alleles B8 and DR3 of HLA and in adrenal insufficiency with DR3 and DR4. This makes it necessary to rule out involvement in first-degree relatives [5]. Its main components are, involvement of the adrenal gland and thyroid gland (Schmidt Syndrome) or the adrenal gland and pancreas (carpenter syndrome) may be associated with other effects of other organs such as gonadal failure, myasthenia, celiac disease [6,7].

Type 3: It is the association of thyroid disease with other autoimmune diseases that affect other organs where the adrenal is not found, depending on the affected organs it is classified in / 3A (thyroid + DM1) 3B (thyroid + gastrointestinal diseases), 3B (Thyroid + skin diseases) and 3D (thyroid + collagen diseases) all of autoimmune etiopathogenesis, as a poorly defined inheritance pattern, but seems to be dominant. It appears in adults and is very rare presentation [8].

Polyglandular Autoimmune Syndrome I	• Addison's disease • Hypoparathyroidism • Mucocutaneous candidosis	• Hypogonadism • Alopecia • Keratitis • Autoimmune hepatitis • Vitiligo • Alopecia • DM1 • Chronic thyroiditis • Malabsorption • Pernicious anemia	Occurs in childhood
Polyglandular Autoimmune Syndrome 2	• Addison disease • Thyroid disease • Autoimmune • Mellitus diabetes	Vitiligo Atrophic Gastritis Autoimmune Hepatitis Pernicious Anemia Hypogonadism Alopecia Myasthenia gravis	Adolescence and adults
Polyglandular Autoimmune Syndrome 3	3A (thyroid + DM1) 3B (thyroid + gastrointestinal diseases), 3B (Thyroid + skin diseases) and 3D (thyroid + collagen diseases)	Other endocrine affection	Adults
Polyglandular Autoimmune Syndrome 4	(adrenal involvement + hypogonadism)	• Hypogonadism • Vitiligo • Alopecia • Gastritis • Atrophic • Anemia • Pernicious • Hepatitis • Chronicle • Hypophysitis • DM1 • Disease • Celiac	Adults

Table 1: Differences between polyglandular syndromes.

Type 4: Encompasses endocrine diseases that do not appear in previous classifications such as (adrenal involvement + hypogonadism), is rare and appears in adults, and remains poorly defined genetic patron [9].

Recall that adrenal glands are divided both anatomically and functionally into two parts: cortex and medulla. In turn, the cortex is subdivided into three zones: glomeruli, produced mainly by aldosterone, the main mineral-corticoid, which contributes to the electrolyte balance through the homeostasis of sodium and potassium. The fasciculate zone is responsible for the synthesis of glucocorticoids, such as cortisol, which affects glucose metabolism and normal cellular function [10].

With the destruction of the gland, on the one hand, low levels of cortisone stimulate ACTH-CRH, increasing levels of ACTH causing hyper pigmentation. On the other hand, the deficit of cortisol decreases gluconeogenesis, producing hypoglycemia, asthenia and muscular fatigability. As the glomerular zone is destroyed, plasma renin levels and angiotensin II, increase to maintain a normal aldosterone secretion, until finally there is a deficit in mineralocorticoid secretion [11]. The treatment is hormone replacement, and sympthoms treatment [12].

Conclusion

Autoimmune polyglandular syndrome is a rare disorder of autoimmune etiology that affects two or more glands and that may be associated with more disorders of autoimmune origin. Appears in adulthood from 3-4 decade of life with involvement of the thyroid gland. Its long latent period, is mainly due to the maintenance of the function of the adrenal glands, however, once marked destruction of these occurs, symptoms such as nausea, dizziness, often symptoms that are confused with a perennial picture treated many sometimes with volume repletion. However, sustained hypoglycemia, arterial hypotension and coloration of skin should raise suspicion of a pathology that has not yet been diagnosed. Early detection is considered essential to avoid major complications. The level of ACTH, aldosterone and imaging tests provide valuable data about the disease.

Disclosure of Potential Conflicts of Interest

The authors declare that there is no conflict of interests.

Research Involving Human Participants and/or Animals

The authors declare that there was no research involving human and/or animal participants.

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