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The Diabetes Mellitus in Autoimmune Polyendocrine Syndromes

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I. Introduction

Autoimmune polyendocrine syndromes are defined by the association in the same patient of at least two endocrinopathies with other non-endocrine autoimmune disorders. There are several types, the most common is polyglandular autoimmune syndrome type II

Some diseases are not serious and require a good follow-up; Others, on the contrary, are more severe and involve the functional and sometimes vital prognosis of the affected patients(1).

The endocrine system appears particularly vulnerable mainly to the thyroid gland, the pancreas and the adrenal cortex. Although the occurrence of these autoimmune pathologies separately is frequent,their manifestation in the context of autoimmune polyendocrine syndromes remains very rare. Among them, diabetes mellitus should be sought systematically and treated efficaciously(2)(3).

The objective of this work is to study the phenotypic, evolutionary and therapeutic characteristics of diabetes mellitus during autoimmune polyendocrine syndromes

Population, methodology:

This is a retrospective study of patients with diabetes mellitus in autoimmune polyendocrine syndromes followed during the last ten years. We appreciated the following characteristics: Sex, age, the first pathology present before the onset of diabetes mellitus, the personal and family history, the type of PEA associated with diabetes mellitus, the autoimmune pathologies present in the time of diagnosis, glycemic balance, the evolution of diabetes mellitus, its complications, and the appearance of other associated autoimmune pathologies.

II. Results

We found 13 cases of type 1 diabetes (T1 D) associated with autoimmune polyendocrine syndromes in 21 cases of at a frequency of 61.90%. There is a clear female predominance with a sex ratio F / H of 3.3 (Fig1)

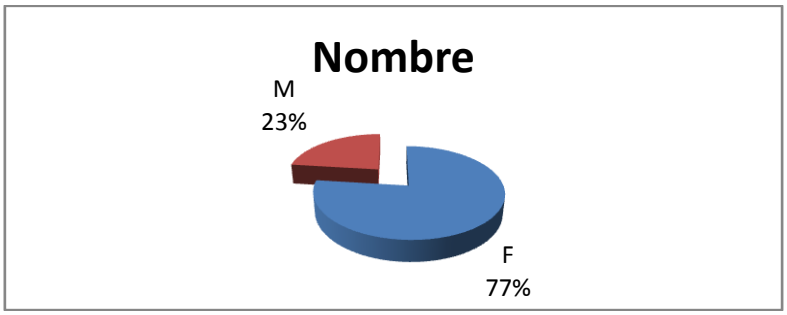

Fig 1 : Sex ratio

The average age of diabetes mellitus at diagnosis is 27.92 years (10-46). More than half of the patients (54%) have an age that varies between 20 and 39 years (Fig2).

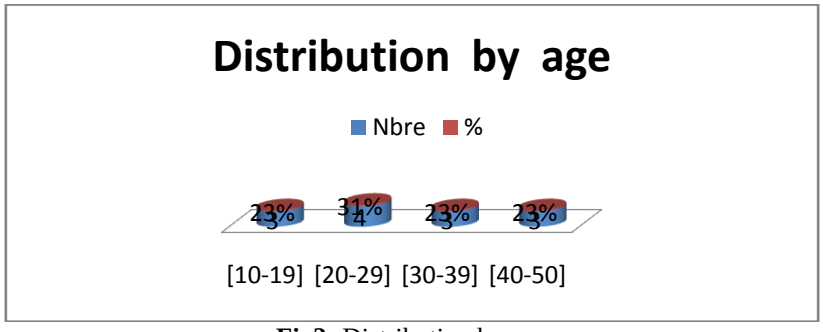

Fig2: Distribution by age

Polyglandular autoimmune syndrome type II (PGA-II) is the most frequent type (69.3%). (PGA-I) was observed in 30.7% of cases. No cases of other types of PGA (PGA III and IV) were identified. Patients with T1 D have an average age of 16.5 years. Only one patient had T1D through adulthood. The mean age of patients with PGA-II is 33 ± 0.2 years (23-46). There is a family history of autoimmunity in ¾ of cases with T1 D in 15.38% and thyroid disease in 53.84%. During (PGA I, T1D occurs before other endocrine disorders in 75% of cases. It occurs after other endocrinopathies in 25%.

In 2/3 of the cases (61.53%) of PGA-II, T1D preceded the other endocrinopathies. T1D is diagnosed at the same time as other endocrinopathies in 23.05%. In 15.38% the DT1 appears metachronically. In the four patients (100%) with PGA-I , the coexistence of T1D and an autoimmune thyroid disease was observed. In two cases, in addition to T1D and autoimmune thyroid disease, there is an autoimmune hypophysitis complicated with GH deficiency and hypergonadotropic hypogonadism.

T1D is associated with autoimmune thyroidopathy in all cases of PGA-II (46% baseline disease, 54% autoimmune thyroiditis). In 44.44% of cases, there is another autoimmune disease including 33.3% non-endocrine affections (Biermer's anemia, myositis, vitiligo). All patients had unbalanced diabetes mellitus with an average glycated hemoglobin level of 7.8 ± 0.10% The balance sheet noted the presence of non-proliferative retinopathy-type microangiopathic complications in 7.7% of T1D patients after an average duration of 6.3 ± 0.4 years.The evolution was marked by the appearance of other autoimmune pathologies in 76.9%. 61.53% were endocrine autoimmune diseases (Graves' disease 20%, Hashimoto thyroiditis 38%, hyperparathyroidism 1.5% and autoimmune ovaritis 2%. 46.15% developed non-endocrine autoimmune pathologies: Biermer anemia 32%, celiac disease 10% myositis 4%, rheumatoid arthritis 8%.

III. Discussion

The endocrine glands appear to be particularly susceptible to autoimmune attack as shown by the frequency of endocrine autoimmune diseases. Immunopathological mechanisms involve both cellular and humoral immunity. They can act at different levels of hormonal metabolism. The most frequent occurrence of the hormone-producing cell is usually found in the enzymes responsible for hormone synthesis. The action of antibodies on hormone receptors results in stimulation or blockage of the hormonal secretion .More rarely autoantibodies neutralize circulating hormones. Autoimmunity can affect only one endocrine gland (4)(5), but it is not uncommon that it affects several glands in the same patient performing a polyendocrine syndrome. Each of these pathologies can be divided into a series of stages beginning with genetic susceptibility, confrontation with favorable environmental factors, active autoimmunity, which will be followed by clinical endocrine abnormalities, indicative of the presence of a disease(1)

Previously, autoimmune polyendocrinopathies were classified according to the old and complex classification of Neufeld and Blizzar (6). This reflected the clinical phenotype of patients at diagnosis. Thus, it excluded the possible evolution of the symptomatology over time, the possible existence of asymptomatic humoral reactions and the heterogeneity of family segregations.

This syndrome could be termed "iceberg" by Betterle (7) since part of the endocrine abnormalities is expressed by obvious clinical diseases and the other part by responsible humoral responses of a frustrated clinical expression or a simple evolutive risk. Thereafter, Georges Eisenbarth (8)proposed a more logical simplified classification where only the forms of autoimmune polyendocrinopathies characterized by their monogenic determinism APECED (Autoimmune Polyendocrinopathy-Candidiasis-Ectodermal Dystrophy) or APS type 1 and the IPEX syndrome (Immune dysregulation, Polyendocrinopathy, Enteropathy, X-linked syndrome) to other clinical expressions conditioned by a polygenic predisposition and grouped under the name API-2 (Autoimmune Polyglandular Syndrome, type 2) or PEA II.

T 1D is an autoimmune disease that is characterized by progressive destruction of Langerhans beta cells, pancreatic cells, which are the only ones to secrete insulin. . When the autoimmune reaction is triggered, there appears to be a gradual destruction of these langerhansian cells.When more than 80% of these cells are altered, symptoms appear .The glycaemia rises resulting in poly-polydipsic syndrome, and insulin deficiency leads to weight loss, and the appearance of ketones associated with this hyperglycemia (9).

T 1D can be isolated or associated with other autoimmune diseases. It then falls within the framework of the polyendocrine syndrome . The disappearance of insulin-producing cells probably involves phenomena of necrosis and apoptosis induced by immunocytes. The lysis of the β-cells of the pancreas is probably but not exclusively due to the cytotoxic action of CD8 + T lymphocytes even if cytotoxic CD4 + has been described (10).

When diabetes mellitus occurs during PG I, it usually occurs in young subjects (children, adolescents), with a peak frequency in peripubertal period .

The initial symptoms are noisy with the cardinal signs: polyuria, polydipsia, polyphagia, weight loss. In PG II, it occurs in young adults. It is not uncommon to see type 1 diabetes appear in a subject around thirty. Like juvenile T1D, it has an autoimmune component, characterized by the presence of autoantibodies in the

blood. These antibodies cause a slow and progressive destruction of the beta cells of the pancreas. It does not necessarily require insulin as soon as it is diagnosed and may therefore lead to a belief in type 2 diabetes. It may take between 6 months and 6 years for insulin to become necessary for treatment (11).

Clinical presentation is progressive (slow T 1 D). The improvement of screening conditions by carrying out systematic or targeted assessments in populations at risk, leads to the easier discovery of this type of diabetes (11).

LADA patients are exposed to the same complications as T 2 diabetics with the same degree of cardiovascular risk, although BMI is generally lower. The delay in insulin exposure exposes these subjects to the degenerative complications of diabetes. Glycemic disorders of diabetes are the main cause of microangiopathic complications. Although they do not have an exclusive role in macroangiopathic complications, they contribute significantly to the development and progression of cardiovascular complications (12) .

In addition, the associated autoimmune diseases influence the achievement of glycemic objectives. Graves' disease causes hyperglycemia by excess thyroid hormones that stimulate neoglucogenesis and glycogenolysis (13).

Hyperglycemia can be induced by the use of certain drugs, especially corticosteroids, in the management of non-endocrine autoimmune disease such as myositis. In addition to corticosteroids, other immunosuppressive drugs may also cause hyperglycaemia

The onset of celiac disease, like type 1 diabetes, influences the glycemic control and more specifically the development of hypoglycemia. Indeed, the damage to the mucous membranes and their inflammation following the autoimmune process triggered can influence the absorption of the nutrients, alter the glycemic control and thus cause hypoglycemia. The body mass index also alters the glycemic control (14).

There may also hypoglycemia in Addison's disease (especially in the morning fasting) explained by adrenocortical deficiency(15)

The development of autoimmune hepatitis exacerbates hyperglycaemia and increases the complications of diabetes mellitus, which is a source of severe morbidity in subjects with autoimmune polyendocrinopathies and makes the prognosis very pejorative (16).

The management of diabetes, alone or in the context of PEA, is similar. As it is complex, a multidisciplinary medical team with a diabetologist or endocrinologist, a diabetes educator, a nutritionist and a psychologist is essential to optimize care (17).

Therapy should be adapted to an individual level taking into account age, programs, environment and abilities.

Indeed, insulin is the inescapable treatment of type 1 diabetes. This treatment must be implemented as soon as the diabetes mellitus is discovered. The evolution of the patients can be enamelled of complications, likely to precipitate the progression of the disease or even life threatening. Follow-up of these patients is as important as treatment .Genetic counseling and care of patients' families is a necessity.

Since the onset of DT1 can be predictable with high reliability, using a combination of immunological (anti-islet AC), genetic (susceptible and protective HLA genotypes), and metabolic (oral glucose tolerance test and first phase Of insulin responses) parameters . efforts are made to prevent and / or improve it

IV. Conclusion

T1D during autoimmune polyendocrinopathies is rare. It is becoming more and more diagnosed and treated early. Although the clinicobiological tables are well defined at the present time, the fact remains that the pathophysiological aspect still retains many areas of shadow . The treatment of diabetes and other autoimmune pathologies proposes to alleviate the deleterious effects of the hypofunction of the different glandular components and to control the autoimmune phenomena without really putting an end to the initial triggering process.

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