Frequency and correlation of autoimmune endocrine diseases in adolescent patients

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Abstract

Autoimmune endocrine diseases represent widespread problem nowadays. Autoimmune endocrinopathies often occur together in the same person and are clusters, as autoimmune polyglandular diseases. Mostly one autoimmune endocrine disorder develops clinically earlier than other.

According to the articles, published in the Pubmed and Google Scholar database, between several autoimmune endocrine diseases, autoimmune diabetes and autoimmune thyroid diseases coincidence often together, most likely due to shared genetic predisposition. Indeed, several loci and genes have been shown to contribute to the joint susceptibility to autoimmune diabetes and autoimmune thyroid diseases. Early identification and treatment of another autoimmune endocrine disease is very important and sometimes even life-saving. Early identification autoimmune thyroid disease when autoimmune diabetes is already diagnosed is recommended according new guidelines. (TCM-GMJ September 2017; 2(2):P28-P30)

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Introduction

Epidemiologic analysis indicates that nowadays a lot of people are affected by autoimmune diseases, in which autoimmune endocrine disorders take an important place.

Burnet and Medawar were awarded the 1960 Nobel Prize in Physiology or Medicine for discovering immunological tolerance. In their Nobel Lecture, Medawar and Burnet define immune tolerance as “a state of indifference or non-reactivity towards a substance that would normally be expected to excite an immunological response”. But, in some cases, the body mistakenly creates antibodies and T lymphocytes against its own cells and tissues. This misguided destruction leads to autoimmune diseases; for instance, T lymphocytes cells that destroy insulin-producing cells in the pancreas cause Type 1 diabetes. The term used to describe this autoimmunity had been used by Paul Ehrlich, German physician and scientist over a century ago. Although he had given it a much more terrifying name: horror autoxicosis (literally, ’the horror of self-toxicity’).

Baruj Benacerraf discovered that the major histocompatibility complex (MHC) plays an important role. A lot of human patients with autoimmune diseases carry particular genetic variants of the histocompatibility antigens. The autoimmune endocrinopathies are organ specific autoimmunity diseases in which the target organs are endocrine glands such as the thyroid, pancreas (β cells), adrenal, ovaries, pituitary gland and etc. Organ-specific autoimmune endocrine disorders may present as single diseases or may cluster in various syndromes. Associations of multiple autoimmune disorders have been classified in different syndromes. Historically, Schmidt (1962) first described the association of Addison’s disease and thyroiditis. Carpenter and coworkers in 1964 included diabetes type 1 in the syndrome. Other non-endocrine autoimmune associations, not always described in syndromes, are also well recognized. Vitiligo, for example, seems to accompany multiple autoimmune endocrinopathies.

Indeed, autoimmune endocrine disorders frequently occur together in the same patient and this association is classified as an autoimmune polyglandular syndrome (APS).

Autoimmune Polyglandular Syndromes

There are several types of APS: APS type I and type II can be clearly separated clinically, but some authors prefer to subdivide APS II and III on the basis of the association of some autoimmune disorders but not others. APS Type I- Chronic candidiasis, chronic hypoparathyroidism, Addison’s disease, (At least two present); APS Type II- Addison’s disease, (always present) and thyroid autoimmune disease and/or type I diabetes mellitus. APS Type III- Thyroid autoimmune disease associated with other autoimmune diseases (excluding Addison’s disease and/or hypoparathyroidism). APS Type IV- Combination of organ-specific autoimmune diseases not included of in the previous groups.
Some authors divide APS III into three subcategories:

A – Autoimmune thyroiditis with immune-mediated diabetes (T1DM) mellitus (also known as polyglandular autoimmune syndrome type 3 variant).

B – Autoimmune thyroiditis with pernicious anemia.

C – Autoimmune thyroiditis with vitiligo and/or alopecia and/or other organ-specific autoimmune disease.

The autoimmune polyglandular syndrome is associated with organ-specific autoimmune diseases (celiac disease, hypogonadism, and myasthenia gravis), organ-nonspecific or systemic autoimmune diseases (sarcoïdosis, Sjogren syndrome, rheumatoid arthritis).

Type I APS- is a monogenic autoimmune syndrome, caused by defects in a gene identified as the autoimmune regulator (AIRE) and is inherited autosomal recessive disease; Its gene is located on chromosome 21. APS type I usually occurs in children at the age of 10-12.

The prevalence of APS II increases gradually in the first decade of life and reaches the highest values between 25-40 years of age; Women are three times more likely to develop it than men;

Type III APS- It mainly affects women in their 30s;

In patients with autoimmune polyendocrine syndromes who have a single disorder such as Addison’s disease or type 1A diabetes, the prevalence of additional autoimmune disorders is 30 to 50 times that in the general population.

It is thought, that coincidence of more than one autoimmune endocrinopathy may result from shared genetic susceptibility leading to loss of tolerance to multiple tissues;

For example, the risk of the development of both Addison's disease and type 1A diabetes is associated with a heterozygous HLA-DR4-DQ8/HLA-DR3-DQ2 genotype.

Certainly, the major histocompatibility complex (MHC), also known as human leukocyte antigen (HLA) in human, is associated with different autoimmune disorders. Especially, MHC class II genes show the strongest association with type 1 diabetes (T1D), in which DRB1*03-DQB1*0201 and DRB1*04-DQB1*0302 haplotypes in Caucasian and DRB1*0405-DQB1*0401, DRB1*0802-DQB1*0302 and DRB1*0901-DQB1*0303 haplotypes in Japanese indicate susceptibility to the disease, while DRB1*15-DQB1*0602 haplotype in Caucasian and DRB1*1501-DQB1*0602 and DRB1*1502-DQB1*0601 haplotypes in Japanese are protection factors against the disease.

Autoimmune aspects of diabetes and thyroid disease

Between all autoimmune endocrine disorders the most common is diabetes type 1 (T1D) and autoimmune thyroid disease (AITD). Both of them are characterized by T cell infiltration and production of autoantibodies against the target organs, which result their dysfunction and/or destruction.

Most type 1 diabetes results from autoimmune destruction of pancreas β cells, which fail to produce insulin, that results hyperglycemia. These patients with T1D at diagnosis have elevated level of antibodies against β cell proteins: antibodies to glutamic acid decarboxylase 65 (GAD 65), islet cell antibodies (ICA), insulin autoantibodies (IAA), tyrosine phosphatase IA2 (ICA512) and zinc transporter 8 (ZnT8);

Although T1D mainly occurs in children and adolescent, it may also present in adult patients as Latent autoimmune diabetes of adulthood (LADA); LADA is slowly progressive forms of type 1 diabetes, with similar baseline C-peptide levels in patients with LADA and typical type 1 diabetes but a more rapid decline with type 1 diabetes. Ab-GAD 65 may be the more important predictor of insulins therapy over the short term (3 years) and antibodies will indicate the need to check for thyroid autoimmunity and consider other associated autoimmune disorders.

Autoimmune thyroid disease can present with Hashimoto thyroiditis (which may lead hypothyroidism) or Graves disease (thyroid hyperfunction). There are three major thyroidal autoantigens: thyroglobulin, TPO and TSH receptor. Circulating autoantibodies to these antigens are useful markers for thyroid autoimmunity.

There are now solid epidemiological data showing that T1D and AITD frequently occur within the same families and in the same individual (APS3v). The association between T1D and AITD is most likely due to shared genetic predisposition. Indeed several loci and genes have been shown to contribute to the joint susceptibility to T1D and AITD.

The DR3 haplotype in Caucasian and DRB1*0405-DQB1*0401, DRB1*0802-DQB1*0302 and DRB1*0901-DQB1*0303 haplotypes in Japanese confer susceptibility to T1D with AITD; Indeed The most prevalent immunological diseases in patients with DM 1 is autoimmune thyroid diseases(AITD); The prevalence of positive peroxidase antibodies(anti-TPO) is estimated to be between 2% and 10% in the general population, whereas in the population of T1D patients it is much higher.

Approximately one third of patients with type 1A diabetes have thyroid autoantibodies; Therefore, there are a lot of evidences for an increased incidence of autoimmune thyroiditis in patient s with type 1A diabetes. AITD incidence increases with longer DM 1 duration and higher anti-TPO prevalence.

Thyroid autoimmunity is highly prevalent in T1D patients of non-Hispanic white, Asian, or Hispanic origin. The strongest disease risk is conferred by female sex and older age. This risk is modulated by HLA-DRB1 and HLA-DPB1 loci.

Latent autoimmune diabetes in adults (LADA) also presented with higher rates for autoimmune thyroid disease markers, especially anti-TPO.

The presence of anti-TPO (28.6 vs.10%) and anti-TG (28.6 vs.14%) was higher in patients with LADA in comparison to healthy controls and anti-TPO in comparison to...
patients with type 2 diabetes (38.6 vs. 17.4 %). In patients with LADA the presence of autoimmune thyroid autoantibodies was associated with newly diagnosed subclinical hypothyroidism. 

The role of early identification of autoimmune endocrine diseases

Autoimmune endocrine diseases usually initiate with a single disease (i.e. Type 1 diabetes mellitus, Hashimoto’s thyroiditis, Graves’ disease, or Addison’s disease), and after a variable period of latency may develop the other components of the syndrome. Organ-specific autoantibody screening in patients with monoglandular autoimmune endocrinopathies undoubtedly makes it possible to identify patients under the risk of developing a future APS. Early identification and treatment of another autoimmune endocrine disease is very important and sometimes even life-saving. Hormonal replacement therapy remains the only form of treatment of APS. However, specific combinations of endocrine organ dysfunction require specific management. For example, thyroxine replacement can precipitate life-threatened adrenal insufficiency. Furthermore, hypoglycemia or decreasing insulin requirements in patients with type 1 diabetes may be the earliest of adrenal failure.

On the other hand, treatment of one autoimmune endocrine disorders clearly helps to correction and treatment of other coincidence autoimmune diseases. For instance, American diabetes association for children and adolescents recommends testing individuals with type 1 diabetes for antithyroid peroxidase and antithyroglobulin antibodies soon after the diagnosis and thyroid-stimulating hormone concentrations soon after the diagnosis of type 1 diabetes and after glucose control has been established, whereas subclinical hypothyroidism may be associated with increased risk of symptomatic hypoglycemia and reduced linear growth rate and hyperthyroidism alters glucose metabolism and usually causes deterioration of glycemic control. For adults’ American diabetes association recommends screening patients with type 1 diabetes for autoimmune thyroid disease soon after diagnosis and thyroid-stimulating hormone test is advised in patients with type 1 diabetes if not performed/available within the past year.

Conclusion

Autoimmune endocrine diseases represent widespread problem; They often occur together in the same individual and are called as autoimmune polyglandular diseases. Mostly one autoimmune endocrine disease develops clinically earlier than other. Between several APS, autoimmune diabetes and autoimmune thyroid disorders more often coincidence together. So, early test for autoimmune thyroid disorders, when autoimmune diabetes is already diagnosed, is recommended according new guidelines of American diabetes association dc.

There are very little information about correlation between autoimmune diabetes and autoimmune thyroid disease in adult patients in Georgia. Therefore, it is interesting to ascertain the correlation, which is subject of future research.

References