VIA MEDICA
ORIGINAL ARTICLE
ISSN 2450–7458
e-ISSN 2450–8187

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Type 1 diabetes and autoimmune-related conditions: a Portuguese research in pediatric age

ABSTRACT

Background. Type 1 diabetes (T1D) is the most common chronic metabolic disease among children and the autoimmune process can induce the development of additional autoimmune diseases. We performed a retrospective study of the clinical records and analytical determinations of pediatric patients with T1D during a five-year-period.

Methods. We identify 102 patients, similar gender distribution. In 98% was performed, at least, one tracking of other autoimmune disease. We found positive autoantibodies in 31%: thyroid antibodies (n = 16), antibodies for celiac disease (n = 10), and antinuclear antibodies (n = 5). Antibodies positivity occurred in mean 3.6 years after T1D diagnosis. Other conditions associated were pulmonary hemosiderosis, vitiligo, IgA deficit, uveitis, and positive *Anti-Saccharomyces* cerevisiae antibodies.

Conclusions. Despite the antibodies' positivity we highlight the possibility of other less common autoimmune-related conditions. The screening of comorbidities is fundamental to perform an earlier diagnosis and prevent complications. (Clin Diabetol 2021; 10; 5: 386–388)

Key words: type 1 diabetes, autoimmune conditions, tracking comorbidities, antibodies determination

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Clinical Diabetology 2021, 10; 5: 386–388
DOI: 10.5603/DK.a2021.0031
Received: 14.11.2020 Accepted: 03.02.2021

Introduction

Type 1 diabetes (T1D) is the most common chronic metabolic disease among children and the autoimmune process can also affect other organs, resulting in the development of additional autoimmune diseases [1]. Comorbidities of T1D include autoimmune thyroid diseases, pernicious anemia, celiac disease, and vitiligo [2, 3].

Adrenal insufficiency (AD) may be associated with T1D as part of the autoimmune polyglandular syndromes, divided into type 1 and 2. Autoimmune polyendocrinopathy syndrome type 1 (APS1) is characterized by several endocrine deficiencies including hypoparathyroidism, AD, gonadal failure as well as diabetes; diabetes is generally a later manifestation. APS2, also known as Schmidt syndrome, is characterized by T1D, AD, and hypothyroidism and is more common in females [4].

These diseases are associated with the presence of specific auto antibodies in blood serum, which can be detected before the development of clinically overt disease [2]. In pediatric age, some auto antibodies may be detected at diagnosis of the disease: anti-glutamic acid decarboxylase (anti-GAD), anti-islet cell (ICA), anti-insulin (IAA) [3]. Bodie et al emphasize the key role of these antibodies in the qualification of the disease, assessment of its activity, and the risk of progression and prediction of the symptomatic phase of the disease [1].

Clinicians must be aware of the symptoms and risk factors associated with common comorbid autoimmune diseases so that screening can be performed if there is clinical suspicion of the disease outside of the recommended screening intervals [4].

We aim to characterize the presence of autoimmune-related conditions in a Portuguese population of T1D patients of pediatric age.

Material and methods

A retrospective descriptive study was performed in the Unit of Endocrinology of Centro Hospitalar de Trás-os-Montes e Alto Douro, Vila Real, Portugal. Medical records and analytical determinations of the patients were retrospectively assessed for five years. All children until 18 years with diagnosis and/or follow up during the period of the study were included. Information about gender, age, age at diagnosis, presence of autoantibodies, and timings of determination were collected. Information about other pathologies associated with T1D in these patients, namely autoimmune diseases were also collected. The statistical analysis was performed with Microsoft Excel 2011.

Results

We identified 102 T1D patients of pediatric age with similar gender distribution: 54 girls and 48 boys (53% *vs* 47%). Age ranged between 1 and 18 years, mean age of 8 years. One hundred patients had at least one autoantibody determination (98%). The autoantibodies' positivity occurred in a mean of 3.6 years after the diagnosis. However, during the first year of the disease, 26% (n = 27) had already positive determinations of at least one antibody.

In our center ICA, IAA and/or GAD was performed at least once in 54 patients (52.9%). From these, 90.7% had one or more positive results (n = 49).

In 24 patients (23.5%) it was found only one antibody: GAD was the most prevalent (n = 35; 34.3%); ICA and IAA were positives in 26.5% (n =13) e 18.4% (n = 9), respectively (Table 1). Two or more positive autoantibodies were found in 25 patients. Positive GAD was found in 35 patients (71.4%). Besides pancreatic autoantibodies, 31.6% (n = 32) had determinations of other autoantibodies. Of these patients, 51.6% (n = 16) had positive thyroid antibodies. Anti-nuclear antibodies (ANA) were positive in 16.2% (n = 15) and one patient had positive Anti-Saccharomyces cerevisiae (ASCA). About 31% (n = 5) of patients with positive thyroid antibodies had clinical disease: hypothyroidism (n = 4) and hyperthyroidism (n = 1). Ten patients had celiac positive antibodies (32.3%) and among these four had celiac disease (confirmed with endoscopy and therapeutic proof). These are the two most prevalent autoimmune associated diseases — thyroid disease occurred in approximately 4% and celiac disease was a 5% prevalence of all sample.

Other autoimmune associated conditions were vitiligo (n = 1), pulmonary hemosiderosis (n = 1), IgA deficit (n = 1), uveitis (n = 1). GAD was positive in 85.3% (n = 87) of these patients, in association or not with other antibodies (Table 2).

Of all patients, 62 maintain follow-up until now.

Table 1. Number and percentage of positive determinations of isolated and combined autoantibodies found in T1D patients

Positive autoantibodies	n [%]
ICA	9 (18.4)
GAD	13 (26.5)
IAA	2 (4.1)
ICA + GAD	12 (24.5)
ICA + IAA	3 (6.1)
GAD + IAA	7 (14.3)
ICA + GAD + IAA	3 (6.1)
Total	49 (100)

ICA — islet cell cytoplasmic autoantibodies; IAA — insulin autoantibodies; GAD — glutamic acid decarboxylase autoantibodies

Table 2. Number and percentage of positive autoantibodies in all patients with T1D diagnosis of autoimmune related conditions

Positive autoantibodies in T1D with AI related conditions	n [%]
ICA	1 (7.1)
GAD	5 (35.7)
IAA	1 (7.1)
ICA + GAD	4 (28.6)
ICA + IAA	0 (0)
GAD + IAA	(21.4)
ICA + GAD + IAA	(0)
Total	n = 14 (100)

AI — autoimmune islet; ICA — cell cytoplasmic autoantibodies; IAA — insulin autoantibodies; GAD — glutamic acid decarboxylase autoantibodies

Discussion

According to the literature, almost a third of T1D patients develop another autoimmune condition. A high proportion of children and adolescents with type 1 diabetes have detectable organ-specific autoantibodies (eg, thyroid, adrenal) in addition to islet autoantibodies, and approximately 25% of patients with type 1 diabetes are diagnosed with another autoimmune disease which overlaps with our results [1, 4].

Autoimmune thyroid disease is the most common comorbid autoimmune condition seen in patients with type 1 diabetes, followed by celiac disease as in our sample [4].

In our sample, we routinely performed determinations of autoimmunity markers in the (98%). Despite the occurrence of positives antibodies associated with T1D in the mean 3.6 years after diagnosis, more than 26% (n = 26) are positive in the first year of the diagnosis. This fact claims the attention of tracking autoimmune-related conditions at diagnosis. Moreover, it is important to be aware of the possibility of other less common autoimmune-related conditions associated [3]. Although there is a lack of evidence on the timing of antibodies' positivity, the majority of studies explain that antibodies' positivity occurs mainly in the first years of the disease and even before the clinical presentation of T1D, which supports the evidence of the regular determination of antibodies to track these concomitant conditions [1, 4].

We found an important prevalence of positive autoantibodies, with a higher prevalence of GAD, thyroid antibodies, and celiac antibodies [1–3].

As far as we know, only another study of prevalence among T1D children has been published in Portugal. Our results following this study, showing a higher prevalence of autoimmune conditions, mainly in first years after the diabetes diagnosis, with 44% prevalence of autoimmune conditions, which is higher compared with our results [5].

Around the Europe a few studies were published. An Italian study showed that the screening programming for detecting other autoimmune diseases is very critical in the first ten years after the onset of autoimmune diabetes, with 30% prevalence which overlaps with our results [6].

Another European study (Poland) presented also a comparable percentage of autoimmune conditions in T1D children (20.8%) [7].

According to published data the prevalence of thyroiditis is approximately 3–8% and celiac disease ranges from 1 to 10% which is in line with our prevalence study (4% and 5% respectively) [5–7].

Our findings show an important prevalence of autoimmune comorbidities in T1D, with clinical spectrum since positive antibodies without clinical disease until clinical concomitant disease as described in the literature [5–7].

Conclusion

T1D patients had an important prevalence of autoimmune conditions. The tracking of these conditions should be periodically performed by antibody determination. Clinical suspicion, correct management, and screening for comorbidity are essential for earlier diagnosis and prevention of complications.

Conflict of interest

The authors have no conflicts of interest to declare.

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