Contents lists available at ScienceDirect

Diabetes Research and Clinical Practice

journal homepage: www.elsevier.com/locate/diabres

Potential celiac disease in type 1 diabetes: A multicenter study

Adriana Franzese [a,*], *Dario Iafusco* [b], *Raffaella Spadaro* [a], *Olmina Cavaliere* [a], *Francesco Prisco* [b], *Renata Auricchio* [a], *Riccardo Troncone* [a], *Giuliana Valerio* [c]

The Study-Group on Diabetes of Italian Society of Pediatric Endocrinology and Diabetology (ISPED) [1]

[a] *Department of Pediatrics, Federico II University, Via S. Pansini 5, 80131 Naples, Italy*
[b] *Department of Pediatrics, Second University, Naples, Italy*
[c] *School of Movement Sciences (DiSIST), Parthenope University, Naples, Italy*

ARTICLE INFO

Article history:
Received 6 September 2010
Received in revised form
8 December 2010
Accepted 21 December 2010
Published on line 15 January 2011

Keywords:
Autoimmune disorders
Celiac disease
Potential celiac disease
Type 1 diabetes

ABSTRACT

Aims: To describe the prevalence of potential celiac disease (pot-CD) in young patients with type 1 diabetes mellitus (T1DM) and characterize their clinical features.
Methods: This cross-sectional multicenter study involved 8717 T1DM patients from 31 Italian centers. Information was collected on the total number of T1DM patients, CD patients and pot-CD patients. The following data were collected on pot-CD patients: gender, age at T1DM diagnosis, age at the first CD serological positivity, presence of CD-related symptoms, presence of other autoimmune disorders and treatment with gluten free diet (GFD). One thousand-three-hundred-sixty-one patients who were positive for CD serology were the control group.
Results: CD serological positivity was found in 7.2% T1DM patients. Prevalence of pot-CD was 12.2% ($n = 77$) among CD positive patients: symptoms were present in 12/77; a third autoimmune disorder was found in 15 patients. Prevalence of pot-CD in the control population was 8.4% ($n = 114$; $p = 0.005$). No difference was found with regard to clinical features. Only few symptomatic patients were on GFD both in T1DM and control patients.
Conclusions: A higher prevalence of pot-CD was found in T1DM patients, that may be ascribed to the routine screening, although the influence of genetic factors cannot be excluded.

1. Introduction

An association between celiac disease (CD) and type 1 diabetes mellitus (T1DM) has been recognized in the last decades [1], with a mean prevalence of CD in T1DM of 4.5%. The high prevalence of CD among T1DM patients, particularly children, suggests that more of a simple association may exist [2]. In fact, if the association is due to the sharing of common genetic factors [3] or if gluten itself is one of the causal factors of T1DM is still matter of debate. Screening tests based on the measurement of serum endomysial (EmA) and tissue transglutaminase antibodies (anti-TGase) are widely performed in T1DM patients in the first months from diagnosis of diabetes [4]; biopsy is then needed to confirm CD diagnosis. Following this screening policy, T1DM subjects with positive celiac-related antibodies but without diagnostic small-bowel

* *Corresponding author*. Tel.: +39 081 7464234; fax: +39 081 7464234.
E-mail address: franzese@unina.it (A. Franzese).
[1] Members of the Study-Group on Diabetes of Italian Society of Pediatric Endocrinology and Diabetology are listed in Appendix A.
0168-8227/$ – see front matter
doi:10.1016/j.diabres.2010.12.028

mucosal villous atrophy are emerging, as it is occurring in the non T1DM population. This picture is defined as potential celiac disease (pot-CD) [5–7]. However, many questions are still unanswered on its natural history, whether the same complications of CD are present in pot-CD and which is the best treatment choice. In addition, it is still discussed whether the low-grade enteropathy found in these cases [5] is the result of genetic differences or can be ascribed to a different degree of immune-regulation. T1DM population represents an ideal model for analyzing both clinical and pathogenetic aspects of pot-CD.

The aim of this cross-sectional multicenter survey was to describe the prevalence of pot-CD among patients with T1DM recruited from the majority of childhood diabetes care centers in Italy and to characterize their clinical features.

2. Materials and methods

A cross-sectional multicenter study was performed from January to December 2008. Forty-two childhood diabetes care centers affiliated to the Diabetes Study Group of the Italian Society of Pediatric Endocrinology and Diabetology (ISPED) were invited to participate. These centers almost completely (more than 95%) ensure the care of childhood diabetes in the country. Thirty-one centers participated (15 in the north, 6 in the center and 10 in the south). Since 1995, ISPED has recommended yearly screening for CD in T1DM children and adolescents starting from the time of diabetes diagnosis, using anti-tissue transglutaminase antibodies (anti-TGase) and anti-endomysium (EmA) antibodies, tested by enzyme linked immunosorbent assay and indirect immunofluorescence method, respectively [8]. In IgA deficient patients IgG anti-TGase antibodies are instead evaluated. Patients were diagnosed as having CD when small bowel biopsy performed on at least four duodenal specimens showed mucosal villous atrophy and crypt hyperplasia, according to the criteria of the North American Society for Pediatric Gastroenterology and Nutrition [9]. Pot-CD was diagnosed in subjects with anti-TGase antibodies positivity, confirmed by EmA and normal villous architecture (Marsh 0 or Marsh 1) [10]. Each center was asked to provide information on the total number of T1DM patients, CD patients and pot-CD patients who were in follow-up during the study period. The following data regarding pot-CD patients were collected: gender, age at T1DM diagnosis, age at the first CD serological positivity, presence of CD-related symptoms, presence of other autoimmune disorders and treatment with GFD. A total of 8717 (4533 males, 52%) T1DM patients aged 13.2 ± 4.1 years (range 1–26 years) were in follow-up. The control group was recruited in the regional Celiac Disease center, located in Naples (Campania, South Italy), and was represented by 1361 EmA/anti-TGase positive patients (615 males, 45.1%) aged 13.8 ± 4.9 years (range 0.5–32 years), who underwent intestinal biopsy.

2.1. Statistical analyses

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS-15.0, SPSS Inc., Chicago, IL). The results were reported as mean ± standard deviation. The Independent-Samples' *t*-test was used to compare variables normally distributed, the chi squared test was used to compare categorical variables. A p value of less than 0.05 was considered significant.

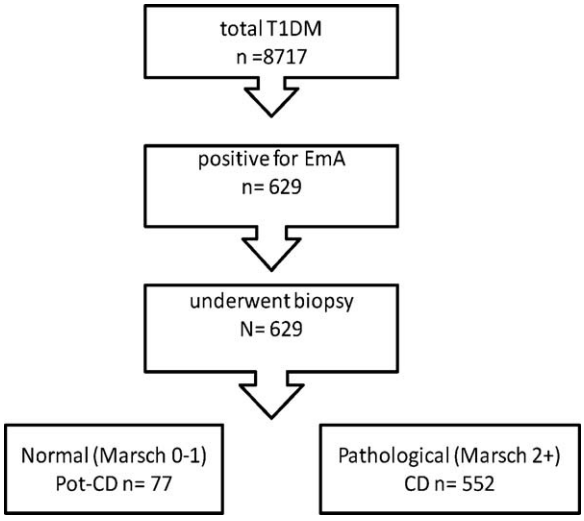

Fig. 1 – Flow chart of the study.

3. Results

Prevalence of EmA/anti-TGase positivity in the whole sample of T1DM patients was 629/8717 (7.2%). Five-hundred-fifty-two (6.3%) showed villous atrophy and were classified as CD, while 77 (0.88%, 30 males) had normal villous architecture and were classified as pot-CD (Fig. 1). Prevalence of pot-CD in the population of T1DM patients who were EmA/anti-TGase positive was 12.2%, with a higher prevalence of females (61.1%).

In the 77 pot-CD patients age at T1DM diagnosis was 5.9 ± 3.6 years (range 1–15.5 years), while age at pot-CD diagnosis was 8.3 ± 4.6 years (range 1–18 years). The first serological positivity occurred within the first 4 years since T1DM diagnosis in 58 patients (75.3%) and between 4 and 14 years in the remaining patients.

In pot-CD patients' symptoms were present in 12 subjects (15.8%): abdominal pain in 7, failure to thrive in 3 and diarrhoea in 2. Only 10 symptomatic patients were on GFD. A third autoimmune disorder was found in 15 patients (19.5%): 13 had autoimmune thyroid disease (16.9%), one multiple sclerosis and one thrombocytopenia.

The prevalence of pot-CD in the CD control population was 8.4% (114/1361), with higher prevalence of females (66.7%). Age at pot-CD diagnosis was 7.4 ± 4.1 years, range 1.5–16 years. Symptoms were present in 21 patients (18.4%): abdominal pain in 13, failure to thrive in 6 and diarrhoea in 2; only 12 symptomatic patients were on GFD. An additional autoimmune disorder, represented by autoimmune thyroid disease, was found in 6 out 114 patients (5.3%). Data are presented in Table 1.

4. Discussion

This is, to the best of our knowledge, the first report on the prevalence of pot-CD in a very large sample of young T1DM