

Coeliac Disease-Related Antibodies Appearance in a IgA Deficiency Celiac Girl after Starting the Gluten-Free Diet

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Abstract

Celiac disease (CD) is a gluten-dependent autoimmune enteropathy which occurs in genetically predisposed individuals. CD can manifest in a typical form (with gastrointestinal symptoms), with an atypical form (iron-deficiency anemia, headache, recurrent aphthous stomatitis) or be asymptomatic (silent form). Over the last decades CD prevalence increased (1.2%), mainly due to the improvement and diffusion of screening tools such as anti-gliadin, anti-endomysium and anti-tissue transglutaminase antibodies. The authors report a case of a 39 months old IgA deficiency girl with a severe abdominal distention and iron deficiency anemia, negative for CD-related antibodies, who was diagnosed celiac. Surprisingly, after six months of gluten-free diet, the patient showed the appearance of IgG class – CD specific antibodies.

Keywords: Celiac disease; igA deficiency; Abdominal distention; Iron deficiency anemia; igG-class antibodies

Introduction

Celiac disease (CD) is an autoimmune enteropathy, caused by a permanent intolerance to gluten that occurs in genetically predisposed individuals. It is a common disease as its prevalence, in Caucasian populations, is about 1.2% [1]. The demonstration of the small bowel mucosa villous atrophy, evaluated according to the Marsh classification as modified by Oberhuber et al. [2], has been the gold standard for the CD diagnosis for years. However, according to the recent ESPGHAN guidelines, in selected cases, the diagnosis could be made using anti-transglutaminase 2 antibodies (TG2), anti-endomysium (EMA) and HLA typing, without intestinal biopsy [3].

CD could be symptomatic or completely silent, the classic manifestation is characterized by gastrointestinal symptoms such as diarrhoea, abdominal pain, vomiting, abdominal distension and failure to thrive whereas the atypical forms are distinguished by extraintestinal symptoms (anemia, short stature, delayed puberty, headaches). CD may be associated with other autoimmune diseases (such as type 1 diabetes, Hashimoto thyroiditis and Addison's disease) and immunological disorders, in particular, with IgA deficiency [4].

Case Presentation

A 39 months old girl were referred to our pediatric gastroenterological unit for abdominal distention. Parents reported that their child have been suffering from two episodes of diarrhoea, with smelly and mushy stools (Type 6 Bristol stool scale), associated with growth failure and vomiting without fever throughout the previous year. Thus the girl performed blood tests during one of these episodes: complete blood count, routine radioallergosorbent test for food, and IgA TG2 antibodies resulting negative.

The girl was a full term eutocic delivered baby (birth weight: 3000 gr) firstborn of non-consanguineous parents. The pregnancy was normal and both parents were healthy. She was fed exclusively with breast milk for the first six months of her life, then weaning was started. Gluten was introduced at seven months, cow milk at ten months. Until the age of two years the girl was in apparently good health.

At our outpatient visit, the girl was overall in good conditions, showed good growth parameter (weight 13.700 kg (33° percentile), height 90.5 cm (9° percentile), BMI 16.5 Kg/m² (76° percentile), cardiac and lung examinations were normal.

	IgA AGA	IgG AGA	IgA EMA	IgG EMA	IgA TG2	IgG TG2
T0	2.59 UA/mL (nv <8)	8 UA/mL (nv <50)	Negative	ND	4.75 UA/mL (nv <50)	ND
T1	6 UA/mL (nv <15)	>100 UA/mL (nv <50)	Negative	Positive	0.01 UA/mL (nv <16)	>100 UA/mL (nv <29)
T2	<1 UA/mL (nv <10)	1 UA/mL (nv <10)	Negative	Negative	<1 UA/mL (nv <16)	10 UA/mL (nv <29)

Table 1: CD related antibodies detection. Legend: T0: at the diagnosis, on a free-diet; T1: after six months of gluten-free diet; T2: after twelve months of gluten-free diet; AGA: anti-gliadin antibodies; EMA: anti-endomysium antibodies; TG2: anti-transglutaminase 2 antibodies.

The child showed a severe abdominal distention, other physical findings were unremarkable and the blood tests revealed: a mild iron deficiency anemia (Haemoglobin: 10.5 gr/dl, iron: 26 mgr/dl (normal

value 42- 120) ferritin: 5.8 ng/dl (normal value 8- 200), an IgA deficiency (serum IgA: 3 mg/dl) and CD screening resulted negative (Table 1). In order to explain clinical and serological findings (abdominal distension and iron deficiency anemia associated with IgA deficiency) CD was suspected. Moreover allergological evaluation (based on radioallergosorbent test and skin prick test) and sweat test for cystic fibrosis were negative.

Subsequently the girl performed an upper intestinal endoscopy with multiple duodenal biopsies (three from the duodenal bulb and three from the distal duodenum). Histological evaluation of bulb and duodenum specimens showed a total villous atrophy (type 3c according to Marsh modified classification). She started the gluten free diet (GFD), experiencing a prompt clinical improvement.

After six months of GFD, blood tests were performed. As expected they showed the disappearance of iron deficiency anaemia but, surprisingly, the IgG class – CD specific antibodies appearance (Table 1).

After 12 months of GFD, the girl showed a full recovery of good health, with a marked improvement of anthropometric parameters and the disappearance of CD- related antibodies (Table 1).

Discussion

CD is a very common disease, that can manifest itself with intestinal or extraintestinal symptoms, but sometimes it could be completely silent [5].

In this case, the little girl suffered from iron deficiency anemia. The girl's growth was good, still not enough considering her parents height. In this clinical picture the most important sign was the abdominal distension, that was so suggestive for us to perform an upper endoscopy even in the absence of CD- related antibodies. Sometimes abdominal distension is reported as the only CD related clinical sign [5]. This finding can be possibly explained by both the hypotonia of the abdominal muscles and bowel distension, which could be both considered as CD-related complications.

Moreover the girl suffered from IgA deficiency as well, despite not reporting respiratory symptoms or high frequency of upper respiratory

infections. IgA deficiency is the most common primary immunodeficiency. In patients with IgA deficiency, CD is more frequent than in general population [4], so it is very important to perform IgG, besides IgA tests. Some authors have even suggested that the IgA deficiency can be deduced from very low values of IgA anti-TG2 [6].

It is well known that CD may lead to intestinal malabsorption as one possible complication. In this case is emblematic that IgG CD-specific autoantibodies, that were absent at the time of diagnosis, appeared only after three month of GFD. A possible hypothesis could be that severe malabsorption caused an important loss of protein that jeopardized the serum CD-specific autoantibodies titre.

In conclusion CD is a frequent and multiform disease that can be associated with IgA deficiency so, in order to avoid missing diagnosis, it is important to perform IgG based tests. Nevertheless, if the clinical signs and symptoms are so emblematic of CD as showed in this child, the upper endoscopy could be advisable even in the absence of CD-specific autoantibodies.

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