Autoimmunity Reviews 18 (2019) 645–646

Contents lists available at ScienceDirect

Autoimmunity Reviews

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

Diagnosis of gluten-related disorders: A new and challenging public health problem

ARTICLE INFO

Keywords:
Gluten-related disorders
Celiac disease
Wheat allergy

Dear Editor,

With great interest we read the article "Celiac disease and endocrine autoimmunity – the genetic link" by Kahaly et al. [1]. One of the main conclusions is that patients with the above autoimmune endocrine disorders should be also screened for celiac disease.

Cereal consumption have had an important role in the history of mankind. Gluten-containing cereals (wheat, rye, barley) consumption has lead to the development of some important clinical manifestations [2]. Gluten-related disorders have gradually emerged as an epidemiologically pheomenon with a global prevalence that exceeds 5% [3]. In this context, recent studies confirm that increasing numbers of consumers worldwide have started to avoid gluten-containing food in order to protect themselves from developing these gluten-related disorders and their clinical manifestations [4].

Different mechanisms are involved in the pathogenesis of the gluten-related disorders [5]. Gluten is considered to be the main structural protein of wheat and it is composed of two man fractions depending on their solubility in aqueous alcohols: the gliadins (classified into alpha/beta, gamma and omega types) and the glutenins, which are poorly soluble (divided into high-molecular-weight HMW and low-molecular-weight LMW subunits) [6].

In celiac disease a T-cell mediated autoimmune reaction is considered to be triggered by gluten-derived peptides. This autoimmune process is localized in the small bowel and it leads to the classical enteropathy and malabsorption syndrome [1]. Celiac disease is the most known gluten-related disorder. It has genetic predisposition and it is associated with other autoimmune disorders [7].

Wheat allergy (WA) represents another type of adverse immunologic reaction to proteins contained in wheat. In this process, Immunoglobulin E (Ig E) antibodies mediate the inflammatory response to several allergenic proteins such as: gliadins, HMW glutenins, non-specific lipid transfer protein [8].

Non-celiac Gluten Sensitivity (NGCS) is another type of symptomatic response to gluten ingestion. The current opinion is that there is a non-autoimmune non-allergic process. Patients affected by NGCS report both intestinal and extra-intestinal symptoms arising shortly after the ingestion of gluten-containing food in the absence of CD or WA [9–12].

Our recommendation for diagnostic tests for gluten related disorders:

1. Celiac disease

- Serology: Anti transglutaminase IgA plus IgA dosage are used as screening test; Anti endomysium as confirmatory test;
- Genetic: HLA typing is useful to exclude celiac disease (around 95% celiac patients carry the HLA-DQ2 heterodimer and the remaining 5% are HLA DQ8 carriers);
- Histology: Presence of duodenal atrophy is considered the gold standard in adult patients;
- Skin tests: not used;
- Recommendations: Gluten challenge is used in case of genetically predisposed patients following a gluten free diet.

2. Wheat allergy

- Serology: The research of Ig E against the suspected allergens is sensitive;
- Genetic: not used;
- Histology: not indicated;
- Skin tests: Skin reactions against allergens have a low sensitivity;
- Recommendations: Challenges with the suspected allergens are considered the gold standard; potentially dangerous for the patient.

3. Non-celiac gluten sensitivity

- Serology: Anti gliadin IgG positive in 50% of cases;
- Genetic: not used;
- Histology: Not strictly indicated; a mild duodenal intraepithelial lymphocytosis is possible in up to 50% of suspected cases;
- Skin tests: not used;
- Recommendations: Double blind challenge with gluten could be considered the gold standard for diagnosis.

Finally, the main take home messages are: (1).Gluten-related disorders share similar clinical manifestations making their differential diagnosis challenging. (2).For an accurate diagnosis we need to correlate the following: patient's clinical history, symptoms, histological and serological tests.

https://doi.org/10.1016/j.autrev.2019.02.008
Received 1 February 2019; Accepted 6 February 2019
Available online 05 April 2019

Conflict of interest

The authors have declared that no conflict of interest exists.
The article production was not sponsored by any grant or company.

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