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Celiac Disease: A Food Allergy? Contra!

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Celiac disease (CD) is primarily a malabsorption disorder manifested as diarrhea, steatorrhea, malnutrition, muscle wasting, abdominal distension, poor growth, irritability, hypoproteinemia, and anemia [1-3]. The jejunal mucosa typically shows flat mosaic appearance, subtotal villous atrophy, and increased intraepithelial lymphocytes. CD is caused by ingestion of gluten, the major protein in wheat, rye, barley, and oats. Wheat flour contains 6-8% protein, 90% of which is gluten which comprises gliadin (the offending fraction in CD) and glutenin in equal parts [4].

The onset of symptoms is usually during early childhood after a few to several months of ingesting gluten-containing food [5], but it may be delayed to adulthood [6]. The offending quantity of gluten and the severity of manifestations vary widely from one patient to another, but in general the disease is usually severer in young children.

Possible Causes of CD

It is not clear why certain subjects develop such type of gluten intolerance. Several theories have been postulated [3, 7] but none of them gained sufficient support. They include proteolytic enzyme deficiency causing accumulation of cytotoxic degradation products of gluten, abnormal glucosylation of gluten leading to lectin-like toxicity of enterocytes, and abnormal immune response that may be linked to genetic predisposition plus environmental factors (e.g., infection with adenovirus type 12).

Immunologic Abnormalities in CD

CD is associated with a variety of abnormal humoral and cellular immunologic findings [7] that are mostly inconsistent and seem to be secondary rather than the primary underlying mechanism of the disease. During active disease, the mucosa contains increased numbers of various immunoglobulin-bearing plasma cells and the serum contains high titers of antiglutens antibodies that decrease following institution of a gluten-free diet [8–11]. Increased levels of serum IgA antibodies to gliadin, endomysium, and reticulin are the most specific findings (noted in more than 95% of CD patients) and correlate well with the disease activity [12–14].

Is CD a Food Allergy?

In clinical practice, 'allergy' generally denotes atopy or IgE-mediated hypersensitivity. In that context, the link between CD and allergy is weak. An increase in the incidence of atopic disorders in adults with CD has been reported [15], which can be partly secondary to an increased intestinal mucosal permeability that is frequently noted in CD patients [16, 17]. As with many other diseases (e.g., autoimmune, renal, and dermatologic disorders), the presence of characteristic immunologic findings does not qualify CD to be considered an 'allergy'. As an adverse reaction or intolerance to dietary gluten, CD is often referred to as 'gluten-sensitive enteropathy', which may imply hypersensitivity or allergy. However, 'gluten-induced enteropathy' would be a more appropriate term.

CD patients do not usually react clinically to oral gluten challenge as rapidly or as acutely as patients with wheat allergy; the latter in fact can be life-threatening. Also, whereas wheat allergy is usually temporary, CD is invariably permanent. CD patients seldom show immediate wheal-and-flare response to intradermal injection of gluten [18] though they may show a late (Arthus-type) response [9, 20].

Serum total IgE level is also usually normal in CD patients [15, 21, 22]. We [22] studied food-specific antibodies in the sera of 17 CD patients in whom the diagnosis was confirmed by jejunal mucosal biopsy. Comparison was made with sera from 12 clinically-diagnosed CD patients, two pools of normal sera, and serum from a child with severe systemic hypersensitivity from ingesting wheat. Levels of specific IgE antibodies to crude wheat and to α -gliadin in CD patients (whether biopsy-proven or not) were very similar to normal controls and were markedly lower than in the wheat-allergic subject (fig. 1). We noticed, however, that most CD patients had elevated levels of specific IgD antibodies to crude wheat, but not to α -gliadin or to a few other foods tested. The significance of this

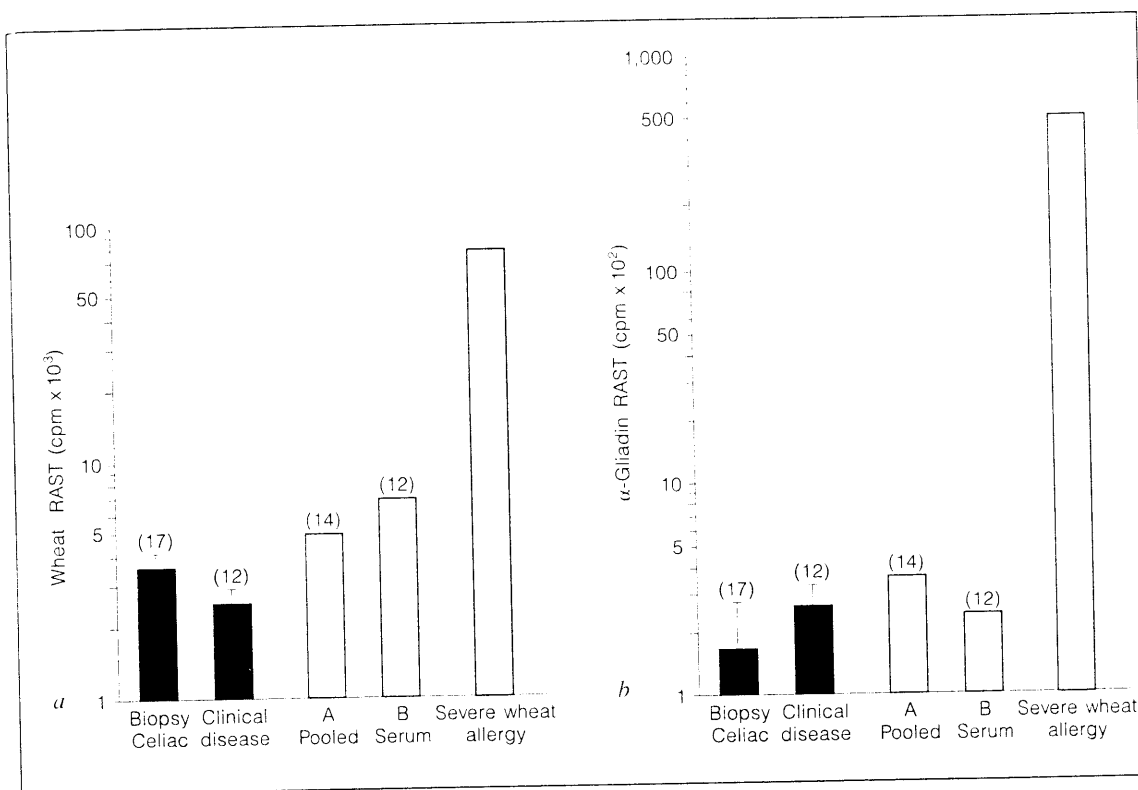


Fig. 1. Serum IgE antibodies to crude wheat (a) and to α -gliadin (b) in 17 biopsy-proven celiac patients compared with 12 clinically-diagnosed celiac patients, two pools of normal controls, and a wheat-allergic child.

Table 1. CD is not an allergic disorder

Clinical reaction to oral gluten challenge usually is not as rapid or as acute as in case with wheat allergy
 CD is invariably permanent, whereas wheat allergy is usually temporary
 Serum total IgE level is usually not elevated
 Intradermal testing with gluten or wheat may cause late, Arthus-type, response but seldom an immediate wheal-and-flare response
 Levels of specific IgE antibodies to wheat proteins are not elevated

finding is not clear, particularly since the role of IgD in general is unknown. Neither specific IgD nor IgE antibody level showed a relationship to the presence or absence of precipitating antibodies to wheat.

Conclusion

In the clinical context of considering 'allergy' synonymous with atopy, i.e., IgE-mediated hypersensitivity, CD should not be classified as an allergic disorder for the reasons listed in table 1. The mechanism of CD is yet to be determined. To avoid potential misunderstanding, the term 'gluten-sensitive enteropathy' should be substituted with 'gluten-induced enteropathy'.

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