

CHAPTER 1

IgE-mediated (and food-induced) intestinal disease

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Introduction

Despite recent advances in rapid measurement techniques of food-specific IgE antibodies in atopic individuals [1], the correlation of these findings with the diagnosis of intestinal anaphylaxis (or intestinal IgE-mediated disease) is not entirely straightforward under clinical conditions.

Positive skin tests indicate the presence of specific IgE antibodies on mast cells in the skin (antibodies attached to the Fcε-receptor on the mast cell) but only some of the individuals with such evidence of sensitization complain of allergic symptoms in general or of specific gastrointestinal symptoms after contact (e.g. ingestion) with the antigen in question. There is also no definite demarcation, as measured by skin sensitivity, between clinically sensitive and non-sensitive individuals with possible latent atopic disease [2,3]. This has to be born in mind when reviewing published reports which comment on food-induced gastro-intestinal symptoms in patients with a positive skin (IgE) test.

Despite this caveat, there seems to be no doubt — from clinical experience in humans and from evidence obtained in experimental models — that immediate and delayed IgE-mediated reactions are causing or contributing to (or both) intestinal pathology [4–8].

Experimental and clinical evidence

Increased permeability [8–11] anaphylactic mucus release from intestinal goblet cells [12] systemic shock and (local) antigen-specific mucosal mast cell degranulation [5,13–15] altered gastrointestinal motility [10,16], altered electrolyte transport and other parameters of gastrointestinal physiology [15,17,18] have been documented during chronic [19] and intermittent [5] antigen exposure in previously sensitized laboratory animals, mainly rats. Reports of IgE-mediated damage on mucosal structure have been variable. Intestinal symptoms in IgE-mediated diseases are not directly correlated with abnormal mucosal morphology (in non-parasitic models) and the lack of such changes does not exclude

the above mentioned aetiology. Release of the rat mast cell protease II (RMCP II) and other mediators of inflammation [14,15,20] are often associated with functional abnormalities without light microscopic changes. The release of IgE into gastrointestinal secretions (stool) is different in food-allergic patients compared with control subjects and can be measured directly [21,22] or after whole gut lavage with polyethyleneglycol [23], its usefulness in the diagnosis of food allergy in the individual is currently unknown.

Clinical symptoms

Based on the current definition of IgE-mediated reactions (immediate onset) the following clinical symptoms affecting the intestinal tract have been reported and the list is based on analysis of cow's milk allergy in childhood. Virtually all foods can lead to sensitization (IgE) although morphological intestinal mucosal damage similar to cow's milk intolerance have been reported only anecdotally for soy, fish, chicken, rice, wheat [24–26]. Clinical symptoms related to the intestinal tract are:

- oral allergy (burning sensation, itching, hoarseness, within several minutes of oral food contact [27];
- anaphylaxis [28,29];
- intestinal colic [30];
- gastro-oesophageal reflux, oesophagitis [26,29,31];
- vomiting [29,32,33];
- diarrhoea [29,32,34]; and
- colitis (allergic colitis, enterocolitis) [32,35–37].

Immediate clinical symptoms when caused by IgE-mediated mechanisms are rapidly elicited with small (less than 10 mL) amounts whereas delayed onset symptoms often require larger volumes over a longer period (days) [38].

Diagnostic procedures

The diagnostic procedures follow the general principles laid out in the papers on 'The diagnosis of food intolerance' and 'Food allergic disease'.

Skin testing (skin-prick test) in children above 3 years can be helpful in diagnosing IgE-mediated food-allergic symptoms, especially in cases where clinical reactions at

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onset have been severe and would not allow a repeated challenge for confirmation of diagnosis. The diagnostic accuracy of skin-prick tests in suspected food-allergic symptoms is only around 60–70%. This positive predictive accuracy is insufficient in the individual patient and additionally decreases with age. The current lack of well standardized test solutions and protocols makes it almost impossible to directly compare published studies on positive and negative predictive accuracies [2].

Intestinal biopsy for diagnosis of immediate allergic symptoms

An intestinal biopsy is only rarely indicated for the diagnosis of acute IgE-mediated symptoms but it has a role in those children with intestinal symptoms and failure to thrive, or where history and initial investigations do not provide sufficient diagnostic clues.

A picture of degranulated IgE positive mast cells on conventional histology [39,40] may be helpful in making the diagnosis. However, IgE positive mucosal mast cells are also seen in patients with a normal skin test and this feature is only of limited usefulness in the individual case [40].

The pathogenetic role of intestinal eosinophils in acute or chronic intestinal reactions is not clear and the relationship of food allergy to the hypereosinophilic syndrome needs clarification [4,41]. A sub-group of infants (under 1 year) with eosinophilic gastroenteritis and diarrhoea with atopy and evidence of IgE-mediated hypersensitivity may respond to dietary elimination therapy [41].

Evidence of rectal/colonic involvement in IgE-mediated disease

In a group of adult patients with ulcerative proctitis, IgE-specific immunoperoxidase staining techniques of rectal biopsies revealed a markedly increased number of IgE-containing cells [36]. Despite a limited therapeutic success with cromoglycate in eight out of 12 treated patients, the pathogenetic role of IgE-mediated responses in these patients remains unconvincing. The demonstration of IgE containing mucosal cells is not necessarily diagnostic for an IgE-mediated food allergic process but can also be shown in inflammatory bowel diseases and normals [42,43].

Therapy

The clinical management of patients with suspected (IgE-mediated) food-allergic disease is grounded on the

identification and elimination of the antigen in question combined with adequate nutritional replacement. Some authors (anecdotally) report positive effects of cromoglycate and other anti-allergic compounds on clinical symptoms and on intestinal permeability [11,44–47]. Prospective studies examining this form of management are lacking and this therapeutic approach is only occasionally effective in a minority of patients and has recently been reported as being absent [48].

Natural history and prognosis

The duration of clinical symptoms, for example in cow's milk allergy is variable in infancy and childhood [49–52]. Infants, who develop allergic symptoms under the age of 3 months have a better prognosis for future clinical tolerance compared with those with a later onset [38]. Food allergy is not, as previously thought, a disease of the first two years of life only, but might well continue to affect 25% of children over 5–7 years after onset [53,54] and may even persist into adulthood. The time to clinical recovery is related to the sensitizing antigen [49,52,55,56].

Estimates of incidence of food-allergic gastrointestinal symptoms

Currently the incidence of food-allergic (gastrointestinal disease) in a non-selected population of children ranges between 1.5 and 4% with reported milk allergy incidence at approximately 2–3% [57]. The overall prevalence of food-allergic symptoms in the general population is not well documented. A prevalence of 0.2% in adults has been quoted [58] but this seems inappropriately low when compared with other studies and prevalences in childhood. Based on careful studies in children and adolescents [50,59,60] a prevalence of about 5–6% for food-induced (mainly) atopic and gastrointestinal symptoms seems to be an appropriate figure [61].

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