The role of the gastroenterologist in non-IgE mediated gastrointestinal food allergy

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Abstract

The prevalence of food allergy has been on the rise in the UK over the last 30 years. Food allergy can be classified as Immunoglobulin E (IgE)-mediated, non-IgE mediated or mixed IgE and non-IgE mediated food allergy. Whilst the management of IgE-mediated food allergy is relatively well established with regards to investigations and treatment options, non-IgE mediated food allergy management is emerging. The role of the gastroenterologist in food allergy is in the management of non-IgE mediated gastrointestinal food allergy, which is performed closely alongside allergologists.

The aim of this review is to discuss the common presentations of non-IgE mediated food allergy (i.e. cow's milk protein allergy, food protein-induced enterocolitis, eosinophilic gastrointestinal disorders) and describe current investigation and treatment options for these conditions. It focuses on the main management options available such as elimination diets, drug therapies, as well as gastroenterology-specific tests such as endoscopy. It also highlights the importance of both allergy and gastroenterology multi-disciplinary team support in order to ensure the best management of these children.

Keywords gastrointestinal; non-IgE mediated allergy; paediatrics

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Background

Food allergy is defined as the adverse immunological reaction to a specific food that is reproducible on repeat exposure to the same food. The prevalence of food allergy has increased globally over the last 30 years and in the UK, the prevalence of food allergy in children is approximately 6–8%. Food allergy is currently classified as Immunoglobulin E (IgE)-mediated, non-IgE mediated or mixed IgE and non-IgE mediated food allergy. IgE-mediated food allergy tends to have a quick onset, presenting with skin, respiratory and gastrointestinal symptoms compared to non-IgE mediated food allergy, which has a delayed onset of symptoms which are often gastrointestinal or cutaneous in nature and can masquerade as common disorders such as infantile colic, gastro-oesophageal reflux, feeding problems and abdominal pain.

The natural progression of allergic disease, which comprises atopic dermatitis/eczema, food allergy, asthma and allergic rhinitis, has been well described and is commonly called 'the allergic or atopic march'. Skin and gastrointestinal symptoms are common in the presentation of non-IgE mediated food allergy, with eczema being one of the first manifestations of the food allergic march appearing in the first few weeks of life. However, gastrointestinal food allergies can also present very early and in some cases such as in cow's milk protein allergic proctocolitis, it can be the first presentation of the food allergic march.

The role of the gastroenterologist in managing non-IgE mediated gastrointestinal food allergy is emerging and increasingly being utilised to differentiate common gastrointestinal disorders from ones in which food may play an important role in symptom control. Non-IgE mediated food allergies are being increasingly recognised as being associated with certain functional disorders in the future (i.e. functional abdominal pain, functional dyspepsia and irritable bowel syndrome).

Presentation of gastrointestinal food allergy

Symptoms and signs may overlap with many non-allergic conditions

Gastrointestinal symptoms are common, particularly during infancy and in many children are benign in nature and not related to non-IgE mediated food allergy or other conditions. The diagnosis of gastrointestinal food allergy is challenging because the differential diagnosis is often extensive. For example rectal bleeding in childhood can be caused by an anal fissure from constipation, can be indicative of cow's milk protein allergy (CMPA) or could be the onset of inflammatory bowel disease (IBD). As important as it is to identify non-IgE mediated food allergy, it is necessary for gastroenterologists to have a high clinical suspicion for common non-allergic gastrointestinal diseases such as IBD and coeliac disease. Some of the most common gastrointestinal symptoms that can be the manifestation of non-IgE mediated food allergy are summarised

Common gastrointestinal symptoms of non-IgE mediated food allergy

Gastrointestinal symptoms
Infantile colic
Reflux
Irritability
Vomiting
Food aversion/refusal
Diarrhoea
Blood and/or mucus in stools
Abdominal discomfort/pain
(Soft stool) Constipation
Perianal redness
Faltering growth
Flatus

Table 1

in Table 1. Early diagnosis of children results in better control of any gastrointestinal diseases, prevention of long term complications i.e feeding issues and can have a significant impact on disease progression as well as quality of life for the child and their families.

Children with non-IgE mediated food allergy can also present with extra-intestinal manifestations including mouth ulcers, headaches, hypermobility/joint pain or fatigue, which may not be the most obvious symptoms of a diagnosis of food allergy. Recurrent mouth ulcers are common in gastrointestinal diseases such as IBD and coeliac disease but there is also evidence to suggest an association between mouth ulcers and sensitivity to food components (i.e. benzoic acid and cinnamaldehyde). Recently, there has been increasing recognition of the link between hypermobility and gastrointestinal disease in children. More specifically, patients with Ehlers–Danlos Type 3 Syndrome have been found to have a higher prevalence of food allergies and eosinophilic disorders and it is hypothesised that gastrointestinal complications in these patients could be due to dysregulation of gut-related immune function.

There can also be more generic symptoms such as headache, irritability, poor sleep and fatigue that can be associated with gastrointestinal food allergy and atopic disease. For example, the association between atopic disease and increased number of headaches in children is well described, with children who have more than one atopic condition (such as eczema or allergic rhinitis) having a significantly higher chance of experiencing headaches. However, children with these symptoms may often be seen by other professionals such as General Practitioners, Paediatricians or other Paediatric specialists who perform investigations to try and identify the cause, of which gastrointestinal food allergy is not usually a differential. Non-IgE-mediated allergy can also present in more acute ways as seen in food protein induced enterocolitis syndrome (FPIES), where the child may present with diarrhoea and vomiting to Emergency Departments where they may be misdiagnosed and treated for infection or sepsis.

Allergy-focused history

History is the key to identifying a possible allergic disorder

Obtaining a good clinical history is paramount to working towards a diagnosis of non-IgE mediated food allergy. A general paediatric history about the child's birth and medical history are important but more specific allergy related questions are required. These include a focused, detailed feeding and diet history – was the child breast fed or formula fed; when were solids introduced; are there any symptoms attributable to certain foods? More specific questions about gastrointestinal symptoms (Table 1), bowel habits and extra-intestinal manifestations (i.e. joint pain, fatigue, headaches, mouth ulcers, prolonged respiratory infections) should also be considered. In addition, questions about atopic disease, family atopic disease, medications trialled and their efficacy should be asked. Another important area to ask about is the quality of life of the child and family (i.e. quality of sleep, social interactions, time off school or work for parents) which can provide vital information of the impact allergic disease has on a family, as research has shown that allergic diseases can place significant psychological and emotional burdens on families.

Tests and investigations

Diagnosis can be delayed because of a lack of non-invasive specific diagnostic tests

There are currently no specific investigations that are diagnostic of non-IgE mediated food allergy. The National Institute for Health and Care Excellence (NICE) recommend referral for specialist care if a child has faltering growth combined with one or more gastrointestinal symptoms that have not responded to a single-allergen elimination diet, had one or more severe delayed reactions, or has significant atopic eczema where multiple or cross-reactive food allergies are suspected by the parents/carer. Once it is suspected, food skin prick tests (SPT), specific IgE (sp-IgE) tests, and patch testing may be used to help identify potential allergenic foods; however, they are most often negative. Patch testing has been shown to be effective in identifying allergy of some foods e.g. wheat and diary; however, there are conflicting reports on its diagnostic accuracy, standardisation and consistency in interpretation of results making it less reliable. General blood tests may be performed for specific allergic presentations (i.e. FPIES) but are usually normal although they may occasionally show signs of anaemia, hypoalbuminaemia, hypoproteinaemia or leucocytosis. The main challenge in investigating these children is that they often present with non-specific gastrointestinal symptoms and multiple suspected food allergens and with the absence of accurate tests, the diagnostic process can be long and frustrating.

Gastroenterologists can use endoscopy in the investigative process to identify if there are any other macroscopic or microscopic features such as the presence of on-going inflammation, eosinophils or lymphonodular hyperplasia, that may suggest non-IgE mediated food allergy. There are no specific indications that warrant an endoscopy in non-IgE mediated allergy but children who present with rectal bleeding or