

Review Article

Systemic manifestations and treatment algorithm of food allergy

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ABSTRACT

Food allergy or hypersensitivity can be defined as the presence of an observable immune secondary reaction to the administration of certain proteins that are present within the ingested foods. It has been previously estimated that around 2-10% of the general population suffer from IgE-mediated food allergy. Furthermore, identification of the manifestations is a key point to achieve appropriate evaluation and management of this condition. In this literature review, we aim to discuss the systemic manifestations and treatment algorithm for patients who suffer from a food allergy, according to the current evidence from studies in the literature. Gastrointestinal and skin-related manifestations have been reported to be the most common symptom. However, respiratory tract symptoms are also common and might severely deteriorate the affected patients. The development of severe anaphylaxis is also life-threatening with multiple organ affection. The appropriate management of food hypersensitivity is mainly based on the proper intervention from exposure to the related allergens. In addition, another appropriate management is early sensitization during the first few months of infancy to manage the symptoms of affected patients. Additionally, it should also be noted that most children usually develop tolerance, and the reported allergy to certain types of foods during childhood usually fades away by the age from 8 to 12 years old and also during the period of adolescence. Future studies are needed to develop adequate management modalities with favorable safety and efficacy outcomes.

Keywords: Allergy, Pediatrics, Hypersensitivity, Management, Manifestations

INTRODUCTION

Food allergy or hypersensitivity can be defined as the presence of an observable immune reaction secondary to the administration of certain proteins that are present

within the ingested foods. Food allergy has been reported as a natural sequence of atopic profiles in children, as atopic dermatitis usually occurs the earliest before food allergy and asthma, which are then followed by allergic rhinitis.¹ It has been demonstrated that such reactions

might be immunoglobulin mediated (IgE-mediated), cell-mediated, or induced secondary to mixed reactions of both mechanisms. In addition, It has been demonstrated that occurrence of food reactions mostly occur secondary to IgE-mediated mechanisms, being the most common one. Moreover, it has been previously estimated that around 2-10% of the general population suffer from IgE-mediated food allergy.² In 2008, a statistical report by the National Center for Health Statistics assessment reported that around three million children (3.9%) have developed a food allergy, which has been reported to be 18% more than the previously reported rates within the previous estimates of older decades.³ In the same context, previous reports have also demonstrated that the prevalence of peanuts-allergy has tripled as compared to the 1990s.²⁻⁴ Identification of the manifestations is a key point to achieve appropriate evaluation and management of the condition.

The aim of the study was to discuss the systemic manifestations and treatment algorithm for patients who suffer from a food allergy, according to the current evidence from studies in the literature.

METHODS

This literature review was based on an extensive literature search in Medline, Cochrane, and Embase databases which was performed on 5th June 2021 using the medical subject headings (MeSH) or a combination of all possible related terms. This was followed by the manual search for papers in Google scholar while the reference lists of the initially included papers.^{5,6} Papers discussing the systemic manifestations and treatment algorithm for patients who suffer from a food allergy were screened for relevant information, with no limitation on date, language, age of participants, or publication type.

DISCUSSION

Systemic manifestations

Many adverse events have been associated with food intolerance, which are summarized and presented in Figure 1. Evidence in the literature shows that food allergy can be associated with many manifestations of different systems that can even be severe sometimes and lead to the death of the affected patients. Most food allergies and reactions, which are usually IgE-mediated, have been previously observed to be associated with many cutaneous manifestations, including rash, pruritis and angioedema or urticaria. However, it was previously demonstrated that these manifestations are not specific as many anaphylactic reactions are usually diagnosed in the presence of other findings, which may or may not include these cutaneous manifestations as reported in 20% of the patients that did not develop any apparent cutaneous manifestations.⁷ The systemic manifestations that have been previously reported that diarrhea, vomiting, abdominal pain and other gastrointestinal manifestations are common among patients with food allergies.

Other manifestations might also include edema of the tongue, perioral area, or the lips, in addition to the potential development of pruritis in the tips and palate, which has been previously reported to occur in milder forms in patients that were previously diagnosed with the pollen-allergy syndrome. Moreover, the latter is probably attributable to the presence of plant proteins that are usually located in raw vegetables and fruits. It usually has significant cross-reaction activities with the proteins that are present in pollens, leading to the activation of mast cells when they are in direct contact with the oral mucosa, stimulating a local allergic reaction.⁸

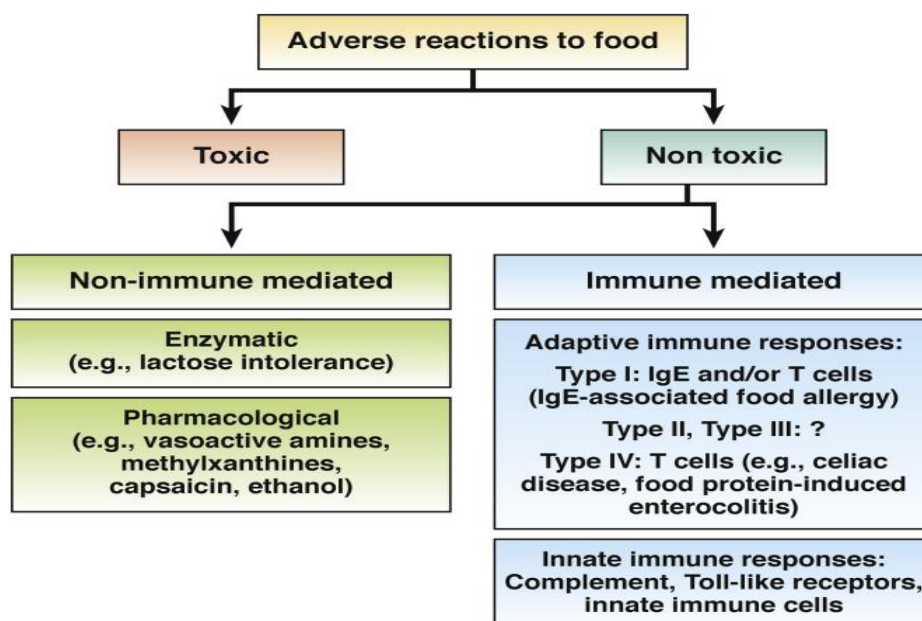


Figure 1: Food intolerance and classification of the related common adverse events.²⁴

Wheezing and bronchoconstriction were also previously reported as separate lower respiratory tract allergy-induced symptoms. However, they are not common with such disorders, and are not specific and may be attributable to other anaphylactic systemic reactions. Other symptoms as rhinorrhea, sneezing, and nasal pruritis was also reported among studies in the literature. Nevertheless, these are not also common symptoms in cases of food allergy, and are usually attributable to other disorders when they are solely observed. In the emergency departments, generalized anaphylaxis that is owing to food allergy has been marked as the most common type of allergy among other etiologies of anaphylaxis.⁸ It has been previously estimated that the ingestion of tree nuts and peanuts is the most common cause of anaphylaxis-induced mortality within the United States.⁹

It was also reported that the symptoms of such reactions usually develop within minutes following the ingestion of these types of foods, and the symptoms might also re-develop even after management by 2-4 hours. Additionally, It has been estimated that the recurrence of these disorders has been noticed to be as severe as the initial attack, and it has been estimated to occur in around a third of the affected patients.^{8,9} On the other hand, it was reported in another investigation that only <1% of patients will only have a monophasic reaction.¹⁰ Accordingly, it should be noted that such reactions resulting from food-related allergies are serious disorders and can lead to death.¹¹ Many risk factors have been previously reported for such severe reactions and death, including the delayed use of epinephrine injections, the presence of underlying asthma, symptoms denial by the patient, having a previous history of severe allergic reactions following food ingestion, and being young or adolescent.⁹

It was previously reported that although the IgE-related anaphylactic reactions usually develop in an acute pattern, other chronic and subacute aberrancies were also reported to be significant clinical markings that might affect the skin and gastrointestinal tract of the affected patients, especially in children. In this context, it was previously reported that food allergy might act as a trigger for some systemic symptoms as atopic dermatitis. Furthermore, it has been reported that around 35% of the children that suffer from moderate and severe atopic dermatitis were observed to have a prior food allergy which has been considered to be the main trigger for such conditions.^{2,4,12}

Previous reports have also previously demonstrated that although eosinophilic gastroenteropathies usually develop secondary to IgE and non-IgE-related mechanisms, food allergy was also previously observed to cause such conditions.¹³ These studies have also reported that the symptoms of such conditions are usually dependant on the site of the eosinophilic infiltration that occurs secondary to the ingestion of the food allergens, and might include gastroesophageal reflux, dysphagia, food impaction, postprandial emesis, obstruction of the gastric outlet, failure to thrive and weight loss. Allergic reactions that are

mediated by non-IgE mechanisms are also commonly reported in the literature. Additionally, it has been previously reported that the ingestion of proteins that are present in the soy and cow's milk usually leads to the development of cell-mediated gastrointestinal reactions, causing enterocolitis syndrome in infants, which might be a serious and challenging condition at this age.

In the same context, it has been reported that if the condition is delayed onset (with symptoms taking more than 2 hours to develop), the patient will eventually suffer from severe episodes of vomiting, diarrhea, and abdominal cramps which can significantly lead to metabolic acidosis, dehydration, and can even lead to hypotension and shock.¹⁴ On the other hand, it was also reported that weight loss and chronic diarrhea might also be the significant presentations for these patients. However, it should be noted that the development of such symptoms is timely depending on the ingestion of the allergens causing the systemic reaction and the symptoms usually resolve on eradicating the antigens. Another less severe condition is benign during infancy.

It is dietary protein-induced proctocolitis or proctitis which is characterized by bloody and mucous-containing stool, owing to the ingestion of cow's milk. However, it was also reported that the condition is self-limited and usually resolves within the first 12 months of life. The ingestion of cow's milk can also lead to the development of dietary-protein-related enteropathy that is characterized by the presence of malabsorption and patients usually present with significant weight loss and diarrhea. Nevertheless, it was also reported that the condition is benign and is usually self-limited with no medical interference or permanent dietary restrictions.

Treatment algorithm

The first step to appropriately manage a food allergy is a proper and early diagnosis of the subsequent hypersensitivity reactions to adequately prevent any potential adverse events and life-threatening complications. After the diagnosis of hypersensitivity following food administration was established, treatment and prevention should be adequately approached to carefully manage such cases. The current evidence from studies in the literature supports that the appropriate management of food allergies is to avoid the administration and exposure to the causative allergens. Other treatment modalities for acute reactions are based on the symptoms as signs of the reactions. For instance, cutaneous manifestations are treated by the administration of H₁ antihistaminics, while epinephrine might also be administered to manage acute anaphylaxis that involves multiple organs. It has been demonstrated that using autoinjectors that contain epinephrine is favorable and might enhance the outcomes of acute reactions. Therefore, should be prescribed for cases with the highest risk of developing such reactions until the arrival of the emergency medical services to adequately manage the case.

As some patients might develop biphasic reactions, it has been previously recommended that patients should be supervised even after the symptoms fade away by four hours.¹⁰ Moreover, monitoring of the cases with frequent observations from an immunologist with the continuous assessment of the IgE levels to decide whether tolerance has been reached or not and to determine when to recommend the start of the food challenge assessment.¹⁵ Previous studies have demonstrated that most children will eventually develop a food allergy to eggs or cow's milk until five years old. However, it has been demonstrated that tolerance will develop in these children shortly after this age, as reported that 42% will develop it by the age of 8 years old, while 79% of children have been reported to develop tolerance by the age of 16 years old.¹⁶ Similar prognostic pathways have also been previously reported with an allergy to eggs.¹⁶

On the other hand, higher tolerance rates have been previously reported with wheat and soy, as 65% will develop tolerance by the age of 12 years and 69% will develop it by 10 years for both types of food, respectively.^{17,18} On the other hand, it was also reported that food-allergy to certain foods are usually life-long and always need medical attention and avoidance of exposure to the relevant allergens, which include tree nuts, peanuts, and seafood.

Many clinical trials and research initiatives have tried to develop primary interventional approaches. The learning early about peanut allergy study previously demonstrated that introducing peanuts in the food of infants that are prone to develop an allergy to it has led to a significant reduction in the prevalence of food allergy in these children by the age of five years old, which has been estimated to be 86.1%.¹⁹ As per the addendum guidelines by the National Institute of Allergy and Infectious Diseases for preventing peanut allergy, introducing peanuts to infants should be inaugurated at an early age that is consistent with the family and their cultural beliefs, in case that the infant does not have a history with a food allergy or atopic dermatitis.²⁰ In cases of moderate and mild atopic dermatitis, the introduction of peanuts should be inaugurated at six months of age. In another context, evaluation of the skin-prick test (SPT), IgE levels, and food challenge tests should be considered for infants that develop a food allergy to eggs or severe eczema, and according to these assessments, peanuts should be introduced by the age of 4-6 months of age.²⁰ These recommendations were also similar to those published by the American Academy of Pediatrics, which required that patients should have a history of breastfeeding or administration of cow's milk within the previous 4-6 months.²¹ It is worth mentioning that no specific treatment has been approved for food allergy, and current trials are being conducted for this purpose. The future might be promising in these areas as the current investigations are focusing on the benefits, efficacy, and safety of desensitization by sublingual, epicutaneous, and oral

routes to determine the best treatment modality for these cases.^{22,23}

CONCLUSION

IgE-mediated allergy has been reported to be the most common type of food allergy. Gastrointestinal and skin-related manifestations have been reported to be the most common symptom. However, respiratory tract symptoms are also common and might severely deteriorate the affected patients. The development of severe anaphylaxis is also life-threatening with multiple organ affection. The appropriate management of food hypersensitivity is mainly based on the proper intervention from exposure to the related allergens, in addition to the early sensitization during the first few months of infancy to manage the symptoms of affected patients. Future studies are needed to develop adequate management modalities with favorable safety and efficacy outcomes.

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