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Research Article

Gastrointestinal Presentations of Cow's Milk Protein Allergy in Infants and Young Children: Clinical Practice

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Abstract

Background/Aim: Cow's milk protein allergy (CMPA) is considered the most common food allergy in infants and children. Symptoms developed after few months of birth. However gastrointestinal presentations of CMPA can be presented in all age groups. The aim of this study is to categorize the gastrointestinal presentation of CMP allergy in infants and children.

Methods: The study included 60 infants and young children (38 male and 22 female) who presented with gastrointestinal manifestations and diagnosed as cow milk allergy from September 2017 till January 2019, all children were presented with gastrointestinal symptoms, and diagnosis of cow milk protein allergy was confirmed by investigations and confirmation of improvement after elimination of cow milk products. Other patients with same gastrointestinal presentations were excluded as inflammatory bowel diseases, Celiac and infectious gastrointestinal diseases.

Results: Exclusive gastrointestinal manifestations in thirty nine, while six patients presented with mixed gastrointestinal and dermatological, fifteen patients presented with gastrointestinal and respiratory manifestations.

Conclusion: Diarrhea and constipation are the most common gastrointestinal presentations while food protein induced enterocolitis is the most severe.

Keywords: *Cow Milk; Allergy; Diarrhea; Constipation and Enterocolitis*

Introduction and Aim

Food allergy is common in children; Cow's milk protein allergy (CMPA) is considered the most common food allergy in infants and children [1]. Symptoms developed after few months of birth [2]. However gastrointestinal presentations of CMPA can be presented in all age groups.

Infants fed by breastfed (BF) and cow's milk formula (CMF) can be affected by Cow's milk protein allergy (CMPA). No single clinical presentation is considered specific for CMPA [3].

Immediate and delayed reactions are the main two types of CMPA; based on onset of clinical presentation after ingestion of cow's milk protein (CMP) [2]. The reactions occurring within minutes (e.g. anaphylaxis, angioedema, urticaria and vomiting), mostly, these immediate reactions were Ig E mediated, while syndromes with delayed reactions that occur within hours to days (e.g. food protein-induced

enteropathy, proctocolitis or eosinophilic oesophagitis), mostly non Ig E mediated. Certain presentations carry the features of both immediate and delayed reactions [4]. So CMPA can be classified as a) immunoglobulin E (IgE)-mediated, b) non-IgE-mediated, c) Mixed [5].

Thorough clinical history, including family history of atopy, and a careful clinical examination, detailed dietetic history are still the corner stone in the diagnosis of CMPA. Confirmation of the diagnosis of CMPA can be determined by clinical improvement after complete elimination of CMP. Skin Prick test (SPT), determination of specific IgE, or patch tests, indicate sensitization to the substrate and are not necessarily proof of an allergic reaction [6].

Sometimes the clinical symptoms persist after complete elimination of CMP, The cause for that is the presence of unrecognized associated other food allergies (e.g. egg, peanut, wheat) or a condition affecting the diagnosis of CMPA (e.g. lactose malabsorption, idiopathic urticaria). Tolerance development can be detected by effects after accidental exposure, skin prick test (SPT), measurement serum immunoglobulin E (IgE) of cow's milk-specific [7].

Aim of the Study

The aim of this study is to study the different gastrointestinal clinical presentation of cow milk allergy in infants and young children.

Patients and Methods

The study included 60 infants and young children (38 male and 22 female) who presented with gastrointestinal manifestations and diagnosed as cow milk allergy according to Diagnostic Approach and Management of Cow's Milk Protein Allergy in Infants and Children: ESPGHAN GI Committee Practical Guidelines 2012.

All children were presented with gastrointestinal symptoms; diagnosis of cow milk protein allergy was confirmed by improvement after elimination of cow milk products. Exclusion criteria: patients with inflammatory bowel diseases, Celiac and infectious gastrointestinal diseases.

Forty nine of our patients presented with exclusive gastrointestinal manifestations, six patients presented with mixed gastrointestinal and dermatological manifestations. Five patients presented with mixed gastrointestinal and respiratory manifestations.

All patients were subjected to thorough clinical history, with special interest of family history of atopic disease in parents or siblings, any personal history of early atopic disease, the infant's feeding history and the presenting symptoms and signs, details of previous management, including any medication and the perceived response to any management. Was there any attempt to change the diet and what was the outcome?

Thorough clinical examination was done with special interest on weight, height, and nutritional status and proper abdominal examination. Full blood count, Liver function tests, ESR, CRP, Stool culture and sensitivity, occult blood in stool, stool PH and reducing substances if needed, total Ig E and skin prick test when needed.

Clinical presentations and nutritional management of all patients were listed and followed.

Ethical points

The study followed the ethical standards of national liver institute- Menofiya university- Egypt, committee and international Review Board (IRB) of National Liver Institute. The study followed the ethical standards of National Liver Institute - Menofiya University - Egypt,

committee (IRB00003413). During the interview, the respondents (parents) of the children were simply informed about the aims of this study. Consent was taken from the Parents who accompanied the child during attending the mentioned hospitals before participating in the research.

Results

Sixty patients, thirty three males and twenty seven females, their ages ranges from 2 weeks till 5 years, presented with exclusive gastrointestinal manifestations in forty nine, while six patients presented with mixed gastrointestinal and dermatological symptoms in the form (eczema in 2 patients, some unspecified rashes in four patients)., the last five patients presented with gastrointestinal and different respiratory manifestations ranged from mild allergic rhinitis, to bronchospasm. No patient with anaphylaxis.

Gastrointestinal manifestations varied from mild symptoms to severe presentations needed pediatric intensive care unit admission (PICU) in one case.

The gastrointestinal presentations were as follow

- Diarrhea in 13 patients
- Constipation with abdominal distention in 11 patients
- Failure to thrive in 9 patients
- Features of gastrointestinal reflux in 8 patients
- Colitis with bloody diarrhea and abdominal distension in 8 patients
- Vomiting in 7 patients
- Two patients presented with food protein induced enterocolitis (FPIEC)
- Two patients with protein loosing enteropathy.

Inflammatory markers as high WBCs, CRP, ESR, low albumin and thrombocytosis found in some of our patient as follow:

- High WBCs count > 15,000 in 11 patients, low albumin level below 3 gm/dl in 12 patients, thrombocytosis in 7 patients, CRP and ESR was elevated in 8 patients, Hemoglobin below 8 g/dl in 5 patients.
- Total Ig E was elevated in 19 patients, skin prick test done in 23 patients and it was positive to milk in 21 patients.
- Nutritional management done in all patients according to the clinical condition of each patient, total parenteral nutrition for 1 week needed for one patient with FPIEC, while amino acids formula given to 24 patients, extensive hydrolyzed formula in 11 patients, partially hydrolyzed formula given to 5 patient as start of nutritional therapy and given to most of patient during withdrawal stage after improvement, infants who were on breast milk, resumed their breast milk feeding after discontinuation of diary product by lactating mothers.

Discussion

Cow milk protein allergy (CMPA) can be defined as an abnormal immunological response to one or more of the proteins in the cow milk. The immunological basis of CMP allergy differentiates it from other condition such as lactose intolerance. CMPA classified into Ig E and non-IgE associated [8].

Both breastfed (BF) and cow's milk formula (CMF) fed infants can be affected by CMPA which usually start within the first weeks after cow's milk introduction for gastrointestinal presentations. The digestive tract was affected in 50 - 60%, the skin was affected in 50 - 70% while the respiratory tract was affected in 20 - 30% [3].

Immediate or rapid onset reactions after cow milk ingestion characterizes Ig E mediated CMPA, which can be occurred within minutes up to 2 hours after exposure. Delayed reactions can be manifest 48 hours or even one week after exposure to CMP characterizes non-IgE-mediated CMPA. Combined immediate and delayed can be seen in the same patient [9].

In this study, food protein induced enterocolitis (FIPES) seen in two patients and it was the most serious gastrointestinal presentations among our patients.

One of our two patients was 10 months old female infant, She was spiking fever, with frequents vomiting and loose motions then distended abdomen, admitted as a cases of acute gastroenteritis, then started to have disturbed level of consciousness for that CT brain was done which reported normal. Lumbar puncture (LP) was done later and it was normal. Abdominal U/S reported normal. Abdomen X-ray showed pneumoperitoneum and CT abdomen was done, she went to diagnostic laparoscopy showed severely dilated terminal ileum, patient kept NPO and shifted to PICU.

Blood, stool, urine culture showed no growth, C-reactive protein showed continuous elevation reaching 378, hypoalbuminemia, prolonged prothrombin time and thrombocytosis.

Laboratory results showed High Ig E level 44.2 IU/ml (Normal results up to 1.5), fecal calprotectin > 600 Mg/g, negative ASCA, negative p ANCA, high fecal alpha one antitrypsin, positive occult blood in stool, negative CMV antibodies.

Patient admitted in PICU received total parenteral nutrition for 5 days then started gradually amino acid formula and showed gradual resolution of the symptoms and signs with improvement of inflammatory parameters.

Food protein- which proliferate activate T lymphocytes, then proinflammatory cytokines TNF-α and IFN-γ plus TGF-β were released, which decrease expressions of TGF-β receptor type I, leading to local intestinal inflammation and barrier permeability interruption [10].

It is non Ig E mediated and underdiagnosed, presented in acute and delayed forms, acute FPIES reaction lead to dehydration, hypotension, methemoglobinemia, shock and acidemia requiring emergency care. Vomiting Diarrhea, and poor weight gain or failure to thrive are the common presentations of chronic FIPES [11].

Constipation was seen in 11 patients in this study, some patients presented with severe constipation and severe abdominal distension went to pediatric surgery first to rule out Hirschsprung disease (HD) then pediatric gastroenterology to investigate for Hirschsprung like diseases. Two patients only had high titer of Ig E. Chin., *et al*. 1984 [12], was the first who described a case of constipation with CMA as the only symptom and well demonstrated the causal relationship between these two entities.

The cause of constipation induced by CMA could be explained by an increased anal sphincter pressure caused by allergic inflammation of the rectal mucosa [13].

This study described 13 patients with persistent diarrhea, severe diarrhea seen in 2 patients who needed urgent resuscitation while 9 with history of mild to moderate chronic diarrhea. The two patients with severe diarrhea were admitted to PICU because of dehydration with metabolic acidosis, the patients were drowsy, metabolic diseases were suspected, but with detailed clinical history and marvelous improvement on elemental formula, the diagnosis of CMPA was confirmed.

Features of gastrointestinal reflux (GER) seen in 8 patients, presented with feeding disturbance, regurgitation, recurrent chest infection, skin allergy in all 8 patients, positive milk reflux scan in 6 patients, with positive Ig E in 5 patients, patients improved dramatically on elemental formula. CMA has been reported in up to half of infants presenting with features of GER [14]. Other studies reported association between CMA and GER was reported in 15 - 42% of infants [15]. Gastric dysrhythmia delayed the gastric emptying and increased GER [16].

Hematochezia seen in 8 patients during this study, 3 of them were fed on breast feeding, 2 on goat milk formula, while the remaining 3 on cow milk formula. Five had high titer of Ig E. Cow's milk protein, can cause partial villous atrophy within the syndrome of food allergic enteropathy or an inflammatory colitis [17].

In this study, failure to thrive seen in 9 patients, no one of this group had diarrhea or vomiting, most of them has constipation. Cow's milk protein can cause partial villous atrophy, colitis, which can be manifested as vomiting and diarrhea with evidence of malabsorption and failure to thrive [18].

Conclusion

Gastrointestinal presentations of cow milk protein allergy can be presented with different gastrointestinal symptoms, ranging from mild to severe symptoms, management of such cases need high incidence of suspicion, cases presented with sever GI symptoms should be managed by pediatric gastroenterologists, diagnosis mainly depend on elimination tests, no other tests can confirm the diagnosis.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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