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Bloody stool in infants with gastrointestinal manifestations of cow milk protein allergy, any significance?

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Abstract---Background: Cow milk protein (CMP) is the most common cause of food allergy in infants and young children. CMP allergy (CMPA) can affect more than one system, such as the skin, respiratory, or digestive systems. Gastrointestinal tract manifestations are nonspecific. One of the most important GI manifestations of CMPA is bloody stool. Purpose: This study aims to describe how many infants with GI manifestations of CMPA presented with bloody stool as it was a very annoying symptom to the family and describe how can be managed adequately. Methods: This study included 100 patients with gastrointestinal manifestations of CMPA,

their ages ranged from 8 weeks to 2 years. 52 males and 48 females. All study patients were subjected to complete history, thorough clinical examination, imaging necessary, and laboratory investigations. Results: bloody diarrhea was recorded in 23 patients, and 2 of them were diagnosed with food protein-induced enterocolitis syndrome (FPIES). Occult blood was detected in 11 patients in the diarrhea group (33.33%), 17 patients in the GER group (47.2%), and was detected in 5 patients (83.33%) who presented constipation associated with massive abdominal distension. Conclusions Lower GI bleeding is not rare in infants with cow milk protein allergy, clearer lower GI bleeding was observed in 25% of patients in this study and can be a manifestation of severe FPIES. Proper adequate management should be started as soon as possible to avoid complications. More studies with a larger number of patients are needed for a proper confirmation of the incidence.

Keywords---Bloody stool - Cow milk allergy- Allergic colitis

Introduction

Cow milk protein allergy (CMPA) can affect different systems, the skin, the gastrointestinal tract (GI), and the respiratory tract. Gastrointestinal presentations of CMPA are variable and occurred when infants were exposed to cow milk protein (CMP) via the maternal diet in breast milk-fed infants, or via the standard cow milk formula in bottle-fed infants. (1)

The World Health Organization (WHO) reported in 2007 that allergy has become the first environmental epidemic disease facing children in the developed world. While the World Allergy Organization reported that 1.9% to 4.9% of children had cow's milk protein allergy (CMA). (2)

Bloody stool in infants can be occurred most commonly due to different etiologies such as infectious colitis, necrotizing enterocolitis, ischemic colitis, vascular malformation, malrotation, and cow milk allergy, in addition to other causes. (3)

The signs of CMPA are nonspecific, including oral and perioral swelling; dysphagia, vomiting, regurgitation, anorexia, diarrhea (with or without malabsorption or protein loss due to enteropathy), rectal bleeding, failure to thrive, abdominal pain, and severe colic. (4)

Aim: This study aims to describe how many infants with GI manifestations CMPA presented with bloody stool as it was a very annoying symptom to the family and describe how can be managed adequately.

Patients and methods

This study included 100 newborns and babies with manifestations of GI disease diagnosed as CMPA, their age ranges from 3 weeks to 2 years. 52 males and 48 females. The study started in 2018 till July 2022 and included patients from Al Qassimi Women and Children Hospital, Sharjah, UAE.

Inclusion criteria: Infant with GI manifestations of CMPA

Exclusion criteria: bloody stool due to an identified cause other than CMPA, bloody stool in children over 2 years of age, infants under 2 weeks of age, infants with a known blood disease that causes bloody stool, and infants presented only with skin or respiratory manifestations of CMPA without presentation of GI.

All study patients were subjected to complete history, thorough clinical examination, Laboratory investigations included full blood count (FBC), liver function tests, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), stool culture and sensitivity, Prothrombin time, time and concentration, partial thromboplastin time (PTT), international normalized ratio (INR), ferritin level, iron studies, occult blood in stool, fecal calprotectin, fecal anti trypsin alpha one, total Ig E and radioallergosorbent test measurements (RAST) for milk.

A positive elimination food test was used to confirm the diagnosis. Patients were classified into 5 groups according to GI presentations: 1- the first group of patients who presented diarrhea, 2- a group of patients who presented gastroesophageal reflux (GER), 3- *a group* of patients who presented constipation associated with dilated bowel loops, 4- *a group* of patients presented bloody stool and finally 5- *a group* of patients presented with food protein-induced enterocolitis syndrome (FPIES).

Ethical Points

During the interview, the respondent of the children were simply informed about the aims of this study and the fact that it is done to improve the health status and education of all populations. Written consent was obtained from the respondent who accompanied the child. The study followed the ethical standards of Al Qassimi Women and Children Hospital- Sharjah - MOHAP- UAE

Statistical analysis

Data were fed to the computer and analyzed using the IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using numbers and percentages. The Kolmogorov- Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, and median. The significance of the results obtained was judged at the 5% level.

The used tests were:

Chi-square test: For categorical variables, to compare different groups,

Mann-Whitney test: For abnormally distributed quantitative variables, to compare two studied groups,

Results

There were 100 neonates and infants enrolled in the study presented with GI manifestations of CMPA as, gastroesophageal reflux, vomiting, diarrhea, constipation associated with abnormal bowel distension detected by X-ray, and bloody stool.

Gross blood in stool was seen in 25 patients (23 patients with bloody diarrhea + 2 patients with FPIES), while occult blood in stool detected in 24 patients

Gastrointestinal presentations were as follows:

Diarrhea was seen in 33 patients, gastrointestinal reflux (GER) in 36 patients, constipation with massive abdominal distention (not constipated only) in 6 patients (*Fig. 1*), bloody diarrhea (characteristics of Colitis) in 23, and two patients presented food protein-induced enterocolitis (FPIEC). (Table 1)

Occult blood was detected in 32% of the patients enrolled in this study with gastrointestinal manifestations of CMPA ($n = 75$) (patients with gross blood in the stool were excluded, they constitute 25 patients of all cases enrolled in this study), 11 patients in the diarrhea group (33.33%) (table 2), 17 patients in the GER group (47.2%) and detected in 5 patients (83.33%) with constipation associated with massive abdominal distension. Patients with bloody diarrhea and FPIE were excluded as they already presented with obvious bloody stool.

Male distribution was 52% of patients in this study and 48% female (table 3), while the mean age was 4.1 ± 8.2 months (table 4). Hemoglobin level was dropped in the bloody diarrhea group at 8.8 ± 2.4 gm/dL, then followed by FIPES, Constipation with abdominal distention, GER, and diarrhea groups respectively. (Table 5)

Table (1): distribution of cases of CMPA presented with manifestations of the GI

	No and %	Bottle-fed infants	Breastfed infants
Diarrhea	33	26	7
GER	36	22	14
Bloody diarrhea	23	16	7
Constipation + marked abdominal distention	6	4	2
FPIES	2	2	0
Total	100	70	30

Table (2): Distribution of positive occult blood with GI symptoms in infants with CMPA

	Occult blood in the stool		<i>P</i> -value
	<i>n</i>	%	
<i>Diarrhea (n = 33)</i>	9	(27.27)	< 0.01
<i>GER (n = 36)</i>	10	(27.77)	
<i>Constipation + marked abdominal distention (n= 6)</i>	5	(83.33%)	< 0.001

Table: (3): Comparison between the cases included in the study regarding the sex of the patients

Sex	Patients included in the study <i>n</i> = 100	
	<i>N</i>	%
Male	52	(57.77)
Female	48	(42.23)

Table (4): Age distribution of the studied group

Studied variables	Infants with GI presentations of CMPA <i>n</i> =100
mean of age (months)	4.1 ± 8.2

Table (5): Hb level in different studied groups before and after elimination of CMP.

	<i>Before CMP elimination gm/dL</i>	<i>6 months after CMP elimination gm/dL</i>	<i>P-value</i>
<i>Diarrhea</i>	<i>12.4 ± 1.9</i>	<i>13.4 ± 1.7</i>	<i>> 0.5</i>
<i>GER</i>	<i>11.3 ± 2.1</i>	<i>12.3 ± 2.4</i>	<i>> 0.5</i>
<i>Bloody diarrhea</i>	<i>8.8 ± 2.4</i>	<i>11.6 ± 3.5</i>	<i>< 0.01</i>
<i>Constipation + abdominal distention</i>	<i>9.7 ± 2.5</i>	<i>12.2 ± 2.5</i>	<i>< 0.01</i>
<i>FPIES</i>	<i>8.9 ± 1.5</i>	<i>12.7 ± 1.5</i>	<i>< 0.01</i>

Discussion

This study aimed to detect how common bloody stool is in infants with GI manifestations of cow milk protein allergy, how are the sequelae, and how to manage it.

Cow's milk protein allergy (CMA) is an immune-mediated response to proteins in cow's milk. It is considered one of the most common food allergies in early life, with an estimated prevalence in developed countries ranging from 0.5% to 3% at age 1 year. The incidence is lower in breastfed babies. (5)

The mean age of the babies in this studied group was 4.1±8.2 months while 52% of the babies enrolled in this study were males (table 3 and 4), other studies had nearly similar findings. (6)

The main milk allergens are whey proteins (β-lactoglobulin is the most abundant) and caseins. Caseins consist of several isoforms: α s-1casein, α s-2 casein, β-casein, and k-casein. The diagnosis of CMA must be confirmed or excluded with an elimination diet, which can last between 2 and 4 weeks. (7)

CMPA may be immunoglobulin E (IgE)- or non-IgE-mediated. In immediately occurring Ig E mediated CMPA, the Symptoms can occur immediately within minutes to 1 or 2 hours of ingestion, while in delayed non-IgE mediated the symptoms can occur days to weeks after ingestion.

Many children with CMPA develop symptoms in at least two of the following organ systems: gastrointestinal (50–60%), skin (50–60%), and respiratory tract (20–30%). (8) The amount of cow's milk needed for an immediate reaction varies from one drop to more than 150 ml (9)

Lower gastrointestinal bleeding (LGIB) in infants is an annoying and frightening symptom for the family and alarming for pediatricians and pediatric

gastroenterologists. LGIB can be occult or overt or gross and can be seen by the inspector's eyes. Occult bleeding can be detected when stool is tested, and can be presented with iron-deficiency anemia.

In this study lower GI bleeding in the form of overt bleeding was documented in 25 patients (25%), 23 infants presented with bloody stool and mucus, and the other 2 were infants diagnosed with FPIES. (*Table 1*), the incidence in this study may be higher than in other studies, this can be explained because this study was done in a tertiary center, maybe a pediatrician outside our center managed other nonbloody cases while referred cases with overt bloody stool.

Occult blood was detected in 27.27 % of infants with CMPA who presented diarrhea, 27.77 % of infants who presented GER, and 83.33% of patients with constipation associated with marked abdominal distension. Occult blood was detected in a total of 33% of patients with gastrointestinal presentations, not presented with overt bleeding (*Table 2*)

The low level of hemoglobin was statistically significant in the group of patients with visible blood in the stool (bloody diarrhea group and FPIES (P value <0.01) followed by the group with occult blood in the stool, the group had constipation associated with dilated bowel loops. (*Table 5*)

Other Studies (10) showed the diagnosis of proctitis based on rectal biopsy which reverted to normal after milk elimination. But some studies were unable to correlate occult blood loss in the stool and iron status in infants.

The GI clinical findings in CMPA can be explained by inflammation, dysmotility, or a combination of both. FPIES is non-Ig E mediated, characterized by vomiting associated with pallor or/and lethargy, bloody diarrhea with mucus, abdominal distension, and dehydration. Elevated white blood count with high C reactive protein, low albumin, high fecal calprotectin and high fecal alpha one anti-trypsin level was reported in our patients, who developed shock and metabolic acidosis. It may develop as soon as half an hour or as late as 6 hours after ingestion. Acute FIPES is more common than the chronic form with shock and metabolic acidosis. Cow milk and soy-based formulas are the most frequently implicated foods. (11)

Management of CMPA depended mainly on the feeding of the infant, in artificially fed infants, amino acid formula or extensively hydrolyzed formula was used in severe cases, while in breastfed infants, the treatment depends on the severity of the presentation if bleeding is severe or FPIES, amino acid formula used (12) as it can progress to metabolic acidosis and shock. (13) In case of mild bleeding that does not affect the patient's general condition, and does not cause a rapid drop in the patient hemoglobin level, feeding baby breast milk can start with the elimination of cow milk protein from the mother's diet.

Conclusions

Lower GI bleeding is not rare in infants with GI manifestations of cow-milk protein allergy. Overt lower GI bleeding was seen in 25% of patients in this study, while occult blood in stool was reported in 32%. The bloody stool could be a

manifestation of serious FPIES. Proper adequate management should be started as soon as possible to avoid complications. More studies with a larger number of patients are needed for a proper confirmation of the incidence.

References

- 1- Venter C, Pereira B, Voigt K, Grundy J, Clayton CB, Higgins B, et al: Prevalence and cumulative incidence of food hypersensitivity in the first 3 years of life. *Allergy* 2008, 63(3):354–359.
- 2- Fiocchi A, Brozek J, Schunemann H, Bahna SL, von BA, Beyer K, et al: World Allergy Organization (WAO) diagnosis and rationale for action against Cow's milk allergy (DRACMA) guidelines. *World Allergy Organ J* 2010, 3(4):57–161.
- 3- Bhanu Pillai R and Vasundhara Tolia. Gastrointestinal bleeding in infants and children. *Therapy* (2008) 5(4), 465–473
- 4- Arvola T, Ruuska T, Keranen J, et al. Rectal bleeding in infancy: clinical, allergological, and microbiological examination. *Pediatrics* 2006;117:e760–8.
- 5- Savage, J.; Johns, C.B. Food allergy: Epidemiology and natural history. *Immunol. Allergy Clin. N. Am.* 2015, 35, 45–59.
- 6- Jarungchit Ngamphaiboon, Pantipa Chatchatee and Thaneya Thongkaew. Cow's Milk Allergy in Thai Children. *ASIAN PACIFIC JOURNAL OF ALLERGY AND IMMUNOLOGY* (2008) 26: 199-204
- 7- Boettcher, E.; Crowe, S.E. Dietary proteins and functional gastrointestinal disorders. *Am. J. Gastroenterol.* 2013, 108, 728–736.
- 8- Host A. Frequency of cow's milk allergy in childhood. *Ann Allergy Immunol* 2002;89(Suppl 1):33–7.
- 9- Vanto T, Juntunen-Backman K, Kalimo K, Klemola T, Koivikko A, Koskinen P, Syvanen P, Valovirta E, Varjonen E. The patch test, skin prick test, and serum milk-specific IgE as diagnostic tools in cow's milk allergy in infants. *Allergy*. 1999 Aug;54:837-42.
- 10- Morton RE, Nysenbaum A, Price K. Iron status in the first year of life. *J Pediatr Gastroenterol Nutr* 1988;7:707-12.
- 11- Mehr S, Frith K, Barnes E, Campbell D; FPIES Study Group. Food protein-induced enterocolitis syndrome in Australia: a population-based study, 2012-2014. *J Allergy Clin Immunol.* 2017;140(5):1323-30.
- 12- Koletzko S., Niggemann B., Arato A. , Vandenplas Y. Diagnostic Approach and Management of Cow's-Milk Protein Allergy in Infants and Children: ESPGHAN GI Committee Practical Guidelines. *JPGN* 2012;55: 221–229.
- 13- Ahrens B, Lopes de Oliveira LC, Schulz G, Borres MP, Niggemann B, Wahn U, et al. The role of hen's egg-specific IgE, IgG and IgG4 in the diagnostic procedure of hen's egg allergy. *Allergy* 2010;65:1554e7.

Fig (No) 1

