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CASE REPORT

A rare cause of methemoglobinemia; food protein-induced enterocolitis syndrome

Methemoglobineminin nadir bir nedeni; besin proteini ile ilişkili enterokolit sendromu

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ABSTRACT • Food protein-induced enterocolitis syndrome, an uncommon non-immunoglobuline-E mediated food hypersensitivity, is characterized by profuse vomiting, diarrhea and acute dehydration. There are no specific laboratory findings, however leukocytosis, metabolic acidosis and rarely methemoglobinemia may be observed. The primary treatment involves elimination of the food that causes the allergic reaction. Here we report the case of a 45-day-old female infant diagnosed acute food protein-induced enterocolitis syndrome co-existing with methemoglobinemia.

Key words: Allergy, infant, methemoglobinemia

ÖZET • Nadir görülen immünglobulin-E aracılı olmayan bir gıda aşırı duyarlılığı olan besin proteini ile ilişkili enterokolit sendromu, aşırı kusma, ishal ve akut dehidratasyon ile karakterizedir. Spesifik bir laboratuvar bulgusu yoktur, ancak lökositoz, metabolik asidoz ve nadiren methemoglobinemi görülebilir. Birincil tedavi, alerjik reaksiyona neden olan gıdanın ortadan kaldırılmasını içerir. Burada methemoglobineminin eşlik ettiği akut besin proteini ile ilişkili enterokolit sendromu tanısı konulan 45 günlük bir kız infant olgusu sunulmuştur.

Anahtar kelimeler: Alerji, infant, methemoglobinemi

INTRODUCTION

Food protein-induced enterocolitis syndrome (FPIES) is an allergic disorder that occurs in the gastrointestinal system due to a reaction to food proteins, mediated by non-immunoglobuline-E (IgE) mechanisms. In community-based studies, the incidence has been reported to vary between 0.015% and 0.7%. It is characterized by episodes of severe vomiting, lethargy, hypothermia and subsequent diarrhea within a few hours following food intake (1-4). Consumption of cow's milk and/or soy-based formulas may lead to growth retardation and hypoalbuminemia in affected infants (5,6). Metabolic acidosis, methemoglobinemia and neutrophilia could be observed in some infants (7-9). Due to the absence of a confirmed and universally accepted diagnostic test, diagnosis is primarily based on medical history, clinical responses to elimination diets, and the exclusion of causes such as infections (10,11).

Methemoglobinemia is rare in childhood, but differential diagnosis should consider hemoglobin-M (HbM) disease, hereditary causes such as enzymatic and erythrocyte metabolism disorders, as well as acquired causes like FPIES and the using of local anesthetics. In this case report, we presented an infant with acute FPIES who had metabolic acidosis and methemoglobinemia.

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CASE REPORT

A 45-day-old female infant was admitted to the emergency department with complaints of diarrhea and vomiting 8-10 times a day for a week, without blood and mucus. The patient, born at 3100 grams and 50 cm via normal spontaneous vaginal delivery, had no significant past medical or family history. The infant's parents have been living as refugees in Turkey since 2021. The infant's height, weight and head circumference at the time of admission to the hospital were 50 cm (< 3 p) 3400 gram (3-10 p) and 35 cm (3-10 p) respectively. The physical examination of the infant, who had poor general condition due to severe dehydration, revealed sunken anterior fontanelle, dry mucous membranes, tachycardia, and hyperactive bowel sounds, but no other significant findings. Laboratory tests revealed metabolic acidosis and methemoglobinemia in blood gases [pH: 7.1, pressure of carbon dioxide (PCO2): 27.8 mmHg, bicarbonate (HCO3): 8.4, methemoglobin (MetHb): 11.9%]; leukocytosis and anemia in complete blood count [white blood cells (WBC): 20800 µL, neutrophils (NEU)%: 46.4, lymphocytes (LYM) %: 39.3, hemoglobin (Hb): 9.2 mg/dL); hypernatremia and elevated C-reactive protein (CRP) level (Sodium: 152 mEq/L, CRP: 11.7 mg/L) (Table 1). Total protein level at admission: 5.3 g/dL (5.7-8.2 g/dL) and albumin level was 3.1 g/dL (3.2-4.8 g/dL). Stool and urine tests were unremarkable. The infant, who had been fed a milk-based formula since birth, was started on bicarbonate fluid therapy due to metabolic acidosis. Since there was no known history of anesthesia or disease to explain methemoglobinemia, HbM level was demanded from the infant. After recovery of metabolic acidosis, the infant was put on a well-tolerated amino acid based formula. With the change in formula, the infant's vomiting and diarrhea decreased and eventually resolved. Thereupon, food allergy was suspected. After the formula change, daily control blood gases revealed improved acidosis and decreased methemoglobinemia. The clinical response to the amino acid based formula and the regression of methemoglobinemia confirmed the diagnosis of acute FPIES. During the two-month post-treatment period, the infant put on weight by an average of 30 grams per day. The infant, whose general condition improved and gained weight, is being followed up in the paediatric gastroenterology clinic.

Table 1 Daily laboratory values during follow-up.

	Day 1	Day 2	Day 3	Day 5
pH	7.1	7.23	7.36	7.37
PCO2 (mmHg)	27.8	34.4	35.2	41.6
HCO3	8.4	14.4	19.7	23.4
MetHb (%)	11.9	9.5	5.2	0.6
Hb (mg/dL)	9.2	8.9		9.3
WBC (µL)	20800			13200
Platelet (103/µL)	363	309		478
Neutrophil (103/µL)	9.6	3.5		4
Total protein (g/dL)	5.2			5,3
Albumin (g/dL)	3.1	3		3
CRP (mg/L)	11.7	45.6		7.9

PCO2: Pressure of carbon dioxide; HCO3: Bicarbonate; MetHb: Methemoglobin; Hb: Hemoglobin; WBC: White blood cells; CRP: C-reactive protein.

DISCUSSION

FPIES is a non-IgE mediated allergic disorder typically affecting infants and presenting with recurrent vomiting and diarrhea episodes, with malnutrition being prominent in chronic cases (12,13). Since affected infants often show signs of sepsis or severe dehydration, FPIES diagnosis is frequently delayed due to confusion with metabolic or infectious diseases (14). In our case, severe dehydration and shock symptoms were present, and food allergy was not initially considered. Despite fact that laboratory findings are not specific, anaemia, thrombocytopenia, leukocytosis with a left shift and hypoalbuminaemia might help to support the diagnosis of FPIES (15). In the present case, leukocytosis, anemia, increased CRP levels, and hypoalbuminemia were prominent in laboratory tests.

With increasing severity of the disease, metabolic acidosis and methemoglobinemia may be observed (16). In a study reported by Baldo et al., increased methemoglobinemia levels were detected in two infants with FPIES who were breastfed (17). Malin et al. started treatment with methylene blue in an infant with persistent vomiting, metabolic acidosis, and methemoglobinemia observed in laboratory tests. After ruling out sepsis and metabolic diseases, they diagnosed infant with FPIES (18). Similar to these two studies, our case was initially treated in the intensive care unit with a preliminary diagnosis of sepsis and metabolic diseases due to severe dehydration, acidosis, and methemoglobinemia. Once the general condition improved and the patient began feeding with a amino acid-based formula, methemoglobinemia levels quickly returned to normal values without the need for methylene blue or vitamin C supplementation.

The treatment of FPIES relies on the elimination of the responsible factor from the diet. The patient should be closely monitored for growth, development, and vitamin deficiencies following the dietary change. In cases of cow's milk-related FPIES, if the infant is formula-fed, the use of extensively hydrolyzed or amino acid-based formulas is recommended (11). Recently, Ribeiro et al. hypothesized that the early use of hypoallergenic formulas in suspected cases not only helps in the rapid remedy of FPIES but also assists in retrospective confirmation of the diagnosis (19). Following the initiation of a amino acid-based formula in our case, a rapid clinical improvement and normalization of laboratory tests were observed. The quick positive response to the elimination diet confirmed the diagnosis of acute FPIES, a non-IgE mediated allergic disorder.

In conclusion, the coexistence of methemoglobinemia and FPIES is a rare, life-threatening condition in infancy and should be detected as early as possible. Clinical suspicion and history can play a critical role in the diagnosis of acute FPIES.

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