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Hypoalbuminemia and Malnutrition Associated With Cow's Milk Allergy: A Case Report

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Abstract

Introduction: Cow's milk allergy is the most common food allergy in children. Symptoms usually involve the skin and the gastrointestinal and respiratory tracts. Gastrointestinal tract manifestations of cow's milk allergy are nonspecific, and are the only type that can be diagnosed in all age groups. Here, we report a rare case of cow's milk allergy in an infant with hypoalbuminemia and malnutrition.

Case Presentation: A nine-month-old girl was admitted to Dr. Sami Ulus maternity and children's health and diseases training and research hospital, Ankara, Turkey, in September 2013, for weakness and swelling of the legs that had endured for two days. She had bilateral pretibial pitting (+2) edema. Laboratory data revealed albumin at 1.7 g/dL; serum Na, K, urea, creatinin, and alanine-aspartate aminotransferase levels were normal. Her urinary analysis did not reveal proteinuria. Stool samples were normal, and stool steatocrite was negative. Anti-gliadin, anti-endomysium, and anti-tissue transglutaminase antibodies were negative. Cow's milk allergy was diagnosed due to cow's milk-specific IgE and skin prick test results.

Conclusions: On rare occasions, cow's milk allergy presents with hypoalbuminemia. When diagnosis is delayed, this allergy may impair the growth and quality of life and may even be life-threatening.

Keywords: Cow's Milk Allergy, Malnutrition, Hypoalbuminemia, Infant

1. Introduction

Cow's milk allergy (CMA) is the most common food allergy in infants and young children, with a prevalence of 2% - 3% in the general population. Allergic reactions to cow's milk may be categorized as IgE-mediated, non-IgE-mediated, and mixed types (1, 2). In infancy, there is no definitive means of differentiating IgE- and non-IgE-mediated CMA, owing to significantly overlapping presentations; however, quick onset symptoms are almost always IgE-mediated (1).

Symptoms and signs of CMA usually involve the skin and the gastrointestinal and respiratory tracts. Gastrointestinal tract manifestations of CMA are nonspecific and the only type that can be diagnosed in all age groups (1). When diagnosis is delayed, the allergy may impair the growth and quality of life and even be life-threatening (3). Rarely, CMA may also present with hypoalbuminemia (4, 5). Here, we report a rare case of CMA in an infant with hypoalbuminemia and malnutrition.

2. Case Presentation

A nine-month-old girl was admitted to Dr. Sami Ulus maternity and children's health and diseases training and research hospital, Ankara, Turkey, in September 2013, after having suffered weakness and swelling of the legs for two days. She had diarrhea four times, and was vomiting three times daily, for two months. Her stool was non-bloody and watery; however, these complaints were resolved one week before hospital admission. She had only been breastfed for a week before admission. Milk formula and complementary feeding was started at six months of age, but the patient usually avoided this combination and ultimately vomited. The interval between intake of cow's milk and onset of symptoms could not be determined by her mother, whose prenatal, natal, and postnatal history was not significant; neither was her family history.

The patient was agitated and pale, with bilateral pretibial pitting (+2) edema. Vital functions were in normal ranges. Her weight was 7 kg (3% - 10% percentile) and her height was 66 cm (3% percentile). Her weight gain had been < 10 gr/day for the previous month. The re-

mainder of the physical examination was normal. Laboratory data revealed a white blood cell count of 10.000/mm^3, hemoglobin at 7.5 g/dL, MCV at 102 fL, platelets at 405 $\times$ 10^3/mm^3, and albumin at 1.7 g/dL. Serum Na, K, urea, creatinin, and alanine-aspartate aminotransferase levels were normal. Her urinary analysis did not reveal proteinuria, and the reticulocyte count was normal. Her serum vitamin B12 level was < 45 pg/mL (200 - 1510 pg/mL), indicating severe vitamin B12 deficiency. The maternal hemoglobin level was 11 g/dL, MCV was 100 fL, and the maternal serum vitamin B12 level was 167 pg/mL. The patient's serum folic acid and ferritin levels were normal; anti-gliadin, anti-endomysium, and anti-tissue transglutaminase antibodies were negative. Serum IgA, IgM, and IgG were normal, but IgE concentration was 250 IU/mL (normal level is 0 - 15 IU/mL). There was no peripheral eosinophilia. Stool samples were normal, and stool steatocrite was negative. Cow's milk-specific IgE was 7.98 ku/L (normal level: < 0.35 ku/L) and caseine-specific IgE level was 0.35 ku/L (normal: < 0.35 ku/L). The skin prick test for cow's milk protein was 4 $\times$ 5 mm (negative control 0 mm, positive control 6 $\times$ 7 mm) and positive (Table 1). The patient was diagnosed with CMA.

Table 1. Description of Patient Characteristics

Characteristics	Results
Gender	Girl
Age, mo	9
Height, kg	7 (3% - 10%)
Weight, cm	66 (3%)
Body mass index	16
Systolic and diastolic pressure, mmHg	90/40
Family allergic history	None
Serious disease (patient and family)	None
Complaints	Weakness and swelling of legs
Albumin, g/dL	1.7
Alanine-aspartate aminotransferase	Normal
Urine protein	Negative
Stool steatocrite	Negative
Celiac autoantibodies	Negative
Cow's milk-specific IgE, ku/L	7.98 (normal: < 0.35)
Caseine-specific IgE, ku/L	0.35 (normal: < 0.35)
Skin prick test for cow's milk protein	Positive

Albumin was administered as an infusion twice and stopped when her serum albumin level reached 2.4 g/dL. Treatment with intramuscular vitamin B12 was commenced, and normalization of her vitamin B12 (1320 pg/mL) was seen. She had difficulty in oral feeding, so a nasogastric tube was inserted for feeding and an amino-acid-based infant formula was started. Cow milk products were eliminated from the diet of both mother and patient. The latter showed significant clinical improvement as her appetite and activity improved; she gained 1500 grams of body weight over the following 20 days. Diarrhea was not seen during hospitalization. After one month, the serum albumin reached a normal level (3.6 g/dL) spontaneously. An oral cow's milk challenge test was planned, but the patient did not attend the follow-up.

3. Discussion

Gastrointestinal symptoms and signs of CMA may be caused by inflammation, dysmotility, or a combination of both. The signs include dysphagia, vomiting, regurgitation, dyspepsia, early satiety, anorexia, diarrhea (with or without malabsorption or protein loss due to enteropathy), rectal bleeding, failure to thrive, abdominal pain, severe colic, and persistent constipation that is often accompanied by perianal abnormalities (1, 3). The state of inflammation may result in reduced bioavailability or an excessive loss of nutrients due to the increased intestinal permeability that causes poor growth in children with food allergies. Poor growth can have severe consequences for a child (6). Our patient had CMA accompanied by hypoalbuminemia; this is a rare condition. Hypoalbuminemia may be a consequence of gastrointestinal symptoms caused by CMA. We directed our patient to pay attention to uncommon different clinical presentations of CMA. Serum hypoalbuminemia on admission and a rapid decrease in serum albumin levels during follow-up are important clinical presentations of CMA. Hwang et al. (4) described a number of children with enterocolitis caused by cow's milk, and reported that a failure to gain weight (< 10 g/day) and serum hypoalbuminemia (< 3.5 g/dL) upon admission are the highest indices of suspicion for CMA. In addition, rapid reduction in the serum albumin level to < 3 g/dL, during follow-up or after admission, may be regarded as an important diagnostic clue (4). Harikul et al. reported that 4 of their 29 CMA patients had serum albumin of less than 2.5 g/dL. The nutritional status was normal in 38%, while first and second degrees of protein energy malnutrition were observed in 27.6% and 34.4% of patients, respectively (5). Upon admission, our patient presented a mild degree of protein energy malnutrition and severe hypoalbuminemia caused by the clinical manifestation of edema. The most common causes of edema and hypoalbuminemia were ruled out as she had no loss of protein in urine and stool.

Any diagnosis of CMA must be either confirmed or excluded through an allergen elimination and challenge procedure. Specific IgE and skin prick testing alone, although helpful in identifying patients who are more likely to have an immediate reaction to cow's milk protein, and those with a delayed reaction who are more likely to remain intolerant for a longer period, cannot diagnose all cases of CMA. The cutoff values for positivity of skin prick test results and sIgE determinations, as reported in most studies in the literature, are a wheal diameter greater than 3 mm and a kU/L sIgE level greater than 0.35, respectively (1). Our patient was diagnosed with IgE-mediated CMA from her sIgE and skin prick test results. An oral cow's milk challenge test was planned, but the patient did not attend the follow-up. As soon as the diagnosis was made, she started being fed with amino-acid-based infant formula and breast milk was not stopped, as the mother's diet was reconfigured as a cow's milk proteins-free diet. There was a significant clinical improvement in the patient after a period of one month, and an encouraging decrease in hypoalbuminemia was seen. As mentioned above, an oral cow's milk challenge test was planned, but the patient did not attend.

In our country, B12 deficiency has been found in nearly 50% - 70% of pregnant women and 40% of newborn babies (7). Our patient's low vitamin B12 level was attributed to low maternal levels.

The long-term prognosis for the majority of affected infants is generally good, with 80% - 90% naturally acquiring tolerance to cow milk proteins by the age of five. However, recent studies suggest that the natural history of CMA is changing, with an increasing persistence until later in life and increasing severity of illness (2). A multidisciplinary follow-up was recommended to our patient at pediatric allergy and pediatric nutrition units for three-month periods.

There are many causes of malnutrition and hypoalbuminemia in childhood and especially in infants. CMA should be kept in mind as a cause, although it is unclear whether in this case hypoalbuminemia is the result of persistent vomiting or a diet with low protein content.

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