ภาวะถ่ายเหลวเรื้อรังและขาดสารอาหารเฉียบพลันรุนแรงในเด็กอายุ 1 เดือนที่แพ้โปรตีนนมวัว: รายงานผู้ป่วย

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บทคัดย่อ

บริบท ปัจจุบันโรคแพ้โปรตีนนมวัวพบได้บ่อย มีอาการแสดงได้หลายรูปแบบคล้ายอาการนำของโรคอื่น ซึ่งยากในการวินิจฉัย

วัตถุประสงค์ เพื่อศึกษาอาการทางคลินิกของเด็กอายุ 1 เดือน ที่มีภาวะถ่ายเหลวเรื้อรังและขาดสารอาหารเฉียบพลันรุนแรงจากการแพ้โปรตีนนมวัว ซึ่งเป็นลักษณะที่พบได้น้อยในรายงานวารสารทางการแพทย์

กรณีศึกษา ผู้ป่วยเด็กชายอายุ 1 เดือน ทานนมมารดาตั้งแต่แรกเกิด เข้ารับการรักษาที่โรงพยาบาลมหาวิทยาลัยบูรพาในช่วงเดือนสิงหาคม พ.ศ. 2563 หลังได้รับนมผสมตอนอายุ 1 สัปดาห์ มีอาการถ่ายเหลวเรื้อรังนาน 3 สัปดาห์ น้ำหนักลด ขาดสารอาหารเฉียบพลันรุนแรง มีความผิดปกติของระดับเกลือแร่ในเลือด โซเดียมในเลือดต่ำ เลือดเป็นกรด มีภาวะ Refeeding syndrome หลังจากปรับเพิ่มปริมาณนมผสมและสารน้ำทางเส้นเลือด มีการคั่งของน้ำดีและค่าการทำงานของตับผิดปกติในช่วงแรก ซึ่งเป็นผลจากภาวะขาดสารอาหารเฉียบพลันรุนแรง ส่งตรวจวินิจฉัยแยกโรคนึกถึงโรคแพ้โปรตีนนมวัวและทำการรักษา โดยให้อาหารทางการแพทย์สูตรเปปไทด์สายสั้น อาการดังกล่าวหายไปอย่างมีนัยสำคัญ รวมถึงน้ำหนักตัวเพิ่มขึ้น และกลับมาทานนมสูตรปกติได้ เมื่ออายุ 19 เดือน

สรุป ภาวะถ่ายเหลวเรื้อรังและขาดสารอาหารเฉียบพลันรุนแรงจากการแพ้โปรตีนนมวัว พบได้น้อยในรายงานวารสารทางการแพทย์ หากไม่ได้นึกถึงอาจทำให้การวินิจฉัยล่าช้าออกไป ซึ่งอาจมีผลกับคุณภาพชีวิตและอาจถึงแก่ชีวิตได้

คำสำคัญ ภาวะถ่ายเหลวเรื้อรัง ขาดสารอาหารเฉียบพลันรุนแรง แพ้โปรตีนนมวัว การดูดซึมสารอาหารผิดปกติจากภาวะแพ้โปรตีนในอาหาร

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Food protein induced enteropathy in a 1-month-old child presenting chronic diarrhea and severe acute malnutrition: A case report

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Abstract

Introduction: Cow's milk protein allergy (CMPA) is the most common food allergy in young children, and can result in various manifestations that are difficult to diagnose.

Objective: To describe the rare case of a 1-month-old male infant with food protein-induced enteropathy (FPE).

Case presentation: A retrospective descriptive study collected data from the medical records of patients admitted to Burapha University Hospital throughout August, 2020. A 1-month-old male infant with food protein-induced enteropathy (FPE) was presented with chronic diarrhea. A fecal test found fat globules, electrolyte disturbance, hyponatremia, metabolic acidosis and severe acute malnutrition, after a few days on a formula milk intake. Refeeding syndrome occurred in the third day of hospitalization, after an increase in elemental formula. Severe acute malnutrition was thought to be the primary cause of the liver parenchymal disease, cholestatic jaundice and elevated liver enzymes. Ultimately, the patient's symptoms stabilized with the introduction of an elemental formula, confirming the diagnosis of severe CMPA. By 19 months, he was thriving on a regular diet, which included a whole milk formula. He had normal growth and no symptoms of diarrhea.

Conclusion: On rare occasions, cow's milk allergy presents itself with chronic diarrhea, electrolyte disturbance and severe acute malnutrition. When diagnosis is delayed, this allergy may impair growth and quality of life, and may even be life-threatening.

Keywords: Chronic diarrhea, Severe acute malnutrition, Cow's milk protein allergy, CMPA, Food protein induced enteropathy, FPE

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Received: March 5, 2023 Revised: March 23, 2023 Accepted: March 24, 2023

อ้างอิง

เบญจารัตน์ ทรรทรานนท์, วิภาวี สุวรรณบริบูรณ์, กีรติ อยู่เย็น, กันติชา ฉัตรเพิ่มพร, วิชชุวรรณ อ่อนสร้อย และวรรณธิดา ชื่นจิต. ภาวะถ่ายเหลวเรื้อรังและขาดสารอาหารเฉียบพลันรุนแรงในเด็กอายุ 1 เดือนที่แพ้โปรตีนนมวัว: รายงานผู้ป่วย. บูรพาเวชสาร. 2566; 10(1): 61-69.

Citation

Dardaranonda B, Suwanboriboon W, Yooyen K, Onsoi W, Chatpermporn K, and Chuenjit W. Food protein induced enteropathy in a 1-month-old child presenting with chronic diarrhea and severe acute malnutrition: A case report. Bu J Med. 2023; 10(1): 61-69.

Introduction

Cow's Milk Protein Allergy (CMPA) is the most common food allergy in infants and young children, resulting from an abnormal immunologic response against bovine milk protein. It has a prevalence in the general population from 1.8% to 7.5%[1] in infants, and 1% to 3%[2] in young children. Allergic reactions to cow's milk may be categorized as IgE-mediated, non-IgE-mediated and mixed types.[2] Non-IgE gastrointestinal food allergies are classified as the following: food protein-induced enterocolitis syndrome (FPIES), food protein-induced allergic proctocolitis (FPIAP), and food protein-induced enteropathy (FPE). FPIES can be subclassified into classical and chronic types.[3]

There have been several studies on the prevalence of CMPA in Thailand. Incidences just from the Department of Pediatrics at King Chulalongkorn Memorial Hospital over a bracket of 10 years (1998 to 2007)[4] included 382 children. The average age at the time of CMPA diagnosis was 14.8 months (7 days-13 years). The most common symptoms were respiratory (43.2%), followed by gastrointestinal (22.5%) as well as skin manifestations (20.1%). Less common symptoms included failure to thrive (10.9%), anemia (2.8%) and anaphylactic shock (0.2%). Gastrointestinal manifestations varied from diarrhea (33.3%), GI bleeding (15.1%), enterocolitis (9.1%), gastroesophageal reflux (8.0%), colic (7.0%), constipation (2.7%), protein-losing enteropathy (1.1%), steatorrhea (1.1%) and gastroparesis (0.5%).

From 1997-2001, the incidences of CMPA patients observed by the Gastrointestinal Unit at King Chulalongkorn Memorial Hospital[5] included gastrointestinal manifestations of hematemesis (n = 6), mucous bloody diarrhea (n = 3) and chronic watery diarrhea (n = 2).

Due to the various presentations of CMPA, it can mimic several other disease processes. We reviewed a case of a 40-day-old male from Saudi Arabia, on regular formula, and was presented with generalized edema and chronic watery diarrhea since birth. Laboratory data revealed serum albumin at 0.9 g/dL. CMPA was diagnosed based on history and a rapid response to an amino-acid-based infant formula. At the patient's last follow-up examination at 24 months, he was thriving on a regular diet.[6]

A seven-month-old, breastfed male from Florida, USA, presented with severe atopic dermatitis, emesis, oily diarrhea, failure to thrive, electrolyte disturbance and hemodynamic instability. Following stabilization, the patient's symptoms resolved with the introduction of an elemental formula. However, the patient's symptoms returned after reinitiating cow's milk protein, confirming the diagnosis of severe CMPA.[7]

Here below, we describe a 1-month-old male from Burapha University Hospital, who was presented with severe CMPA at the first month of life. The patient's diagnosis was obscured by the clinical features of chronic diarrhea, electrolyte disturbance and severe acute malnutrition. An improvement was

observed of the gastrointestinal symptoms after eliminating the causative food.

Objective

To describe the case of a 1-month-old male with FPE that was difficult to diagnose. He was presented with chronic diarrhea, electrolyte disturbance and severe acute malnutrition after a few days intake of formula milk.

Case presentation

A retrospective descriptive study collected the data from the medical records of patients admitted to Burapha University Hospital in August 2020.

From the university hospital's records, we reviewed the case of a 1-month-old male born at 38 weeks gestation, with a 3-week history of non-bloody diarrhea, six to eight times per day. His mother noticed that his weight was progressively decreasing. His prenatal, natal, and postnatal history revealed a full-term gestation period, normal vaginal delivery, no neonatal intensive care admission and with no other significant issues in his medical history. His mother's diet during pregnancy was regular, with no history of allergy.

He was fed exclusively breast milk from birth, switching to formula milk after 1 week. He did not develop anaphylactic symptoms with the formula milk intake. There were no accompanying signs and symptoms related to other organs, such as mild eczema, skin dryness or frequent upper respiratory tract infection due to a cows' milk allergy. Neither he nor anyone in his family had allergic diseases such as atopic dermatitis or asthma.

At 1 month of age, he developed diarrhea and weight loss. Upon admission to our hospital his physical examination revealed the following: height, 50.0 cm (less than 3 percentile); body weight, 2510 grams (less than 3 percentile) (170 grams below the weight measured at birth); head circumference, 36 cm (25-50 percentile) and a mid-upper arm circumference of 75 mm. Regarding his anthropometry: Weight-for-age (WA), 52.3 (severely underweight), weight-for-height (WH), 76.1 (moderate wasting) and height-for-age (HA) 90.9 (mild stunting). Further, his body temperature was 37.2 °C, heart rate at 124 beats per minute and blood pressure at 103/58 mmHg. He was a cachectic, drowsy appearing infant with sunken eyeballs. Additionally, he had a depressed anterior fontanelle, dry and red lips, had a loss of buccal fat pads, non-pale conjunctival and no sign of jaundice. His chest wall showed costochondral beading. His skin showed fine whitish scaling at the neck, was loose and wrinkled with no flaky paint dermatosis, poor skin turgor, perianal redness, but with no skin hyperpigmentation.

Initial laboratory studies were significant for low serum sodium along with metabolic acidosis (Table 1). Serum lactate, blood glucose, serum cortisol and ammonia were normal. Blood tests showed high levels of liver enzymes. Serological testing identified his HIV antibody was negative.

Table 1 Initial complete blood count panel and comprehensive metabolic panel obtained upon presentation to the hospital, as well as subsequent lab evaluations collected throughout the hospitalization period.

Serum	Patient value	Reference range and units[8]
WBC	10,440	6,000-14,000/mm^3
Hemoglobin	13.2 g	10.5-14.0/dL
Hematocrit	40	32-42%
Platelet count	373×10^3	$150\text{-}400\times10^3$ cells/mL
Sodium	120	137–147 mmol/L
Potassium	5.5	3.6–5.2 mmol/L
Bicarbonate	8.0	21.0–27.0 mmol/L
Serum lactate	2.46	1.1-3.5 mmol/L,
Blood glucose	76.0	50-90 mg/dL
Cortisol	46.5	1-24 µg/dL
Ammonia	33.0	11-35 µmol/L
Total protein	4.6	4.6-7.4 g/dL
Albumin	2.3	1.9-4.9 g/dL
Aspartate aminotransferase	316	22–63 IU/L
Alanine aminotransferase	364	12-45 IU/L
Total bilirubin	3.9	<1.0 mg/dL
Direct bilirubin	3.2	<0.2 mg/dL
Blood urea nitrogen	8.8	3-12 mg/dL
Creatinine	0.17	0.03-0.50 mg/dL
C-reactive protein	0.47	0.08-1.58 mg/dL

No detection of stool abnormalities or intestinal problems were present with the microscopic examination of the stool, and no infection was detected in stool culture tests. Stool rotavirus antigen tests were negative. A stool test for Clostridioides difficile was negative. A stool reducing sugar test was negative. Both urinary and cerebrospinal fluid analyses and cultures were normal. Imaging was performed to determine the cause of the prolonged diarrhea. Abdominal radiography and ultrasound examinations revealed no abnormalities in the small intestine. Finally, internal hyperechoic contents in the gallbladder indicated a possible bile sludge.

During hospitalization, after withholding oral ingestion of milk for 24 hours, the patient still had diarrhea two to three times per day. Feeds were initiated with lactose free formula milk. Upon further investigation, a fecal test found fat globules. An elemental formula containing high medium-chain triglycerides

(MCTs) oil was started, due to signs of fat malabsorption, indicating concern for possible CMPA.

After the initial stabilization and rehabilitation, the general treatment for severe acute malnutrition involves 10 steps in two phases. In the initial phase he had neither hypoglycemia nor hypothermia. His dehydration and electrolyte derangements were corrected. A sufficient number of volume and calories were being administered intravenously. Empiric antimicrobial therapy, as well as intravenous cefotaxime and metronidazole were started. To correct micronutrient deficiencies, vitamin A, folic acid, multivitamins and zinc supplements were administered. Cautious feeding to prevent refeeding syndrome was begun. Plasma electrolytes (in particular potassium, phosphate and magnesium) were monitored during refeeding. The hallmark of refeeding syndrome is hypophosphatemia. The patient's phosphate levels were 3.6 mg/dL (the normal range (NR) being 3.8-6.5). Likewise, potassium levels were at 3.6 mg/dL (NR 3.5-5.6) and magnesium levels were 1.8 mg/dL (NR 1.6-2.6). Therefore, the patient's potassium and magnesium were normal. Refeeding syndrome occurred in the third day of hospitalization, after increasing the elemental formula intake. The syndrome was corrected by electrolyte and thiamine supplements.

The causes of cholestatic jaundice and elevated liver enzymes were evaluated. Gamma glutamyl transferase (GGT) was found to be high 556 U/L (NR 12-123), though the patient had normal coagulogram. Likewise, hepatitis B surface antigens (HBsAg) and hepatitis B surface antibodies (HBsAb) were both negative. Severe acute malnutrition was thought to be the primary cause of the liver parenchymal disease. After treating the severe acute malnutrition and a follow up blood test, liver enzymes were found to have returned to the normal range at three months of age.

After starting the elemental formula containing high medium-chain triglycerides (MCTs) oil, the patient showed significant clinical improvement in his weight and diarrhea. Diarrhea was not seen during hospitalization. The patient was discharged after two weeks with improvement in weight by an average of 25 grams per day – for a total of 320 grams. An oral cow's milk challenge test was planned, but neither parent wanted to go through with the challenge. He demonstrated good weight gain on an elemental formula and a diet of nondairy solid food. After a follow-up examination at 19 months, he was thriving on a regular diet, including whole milk formula, and exhibited normal growth with no symptoms of diarrhea. (Figure A1, A2)

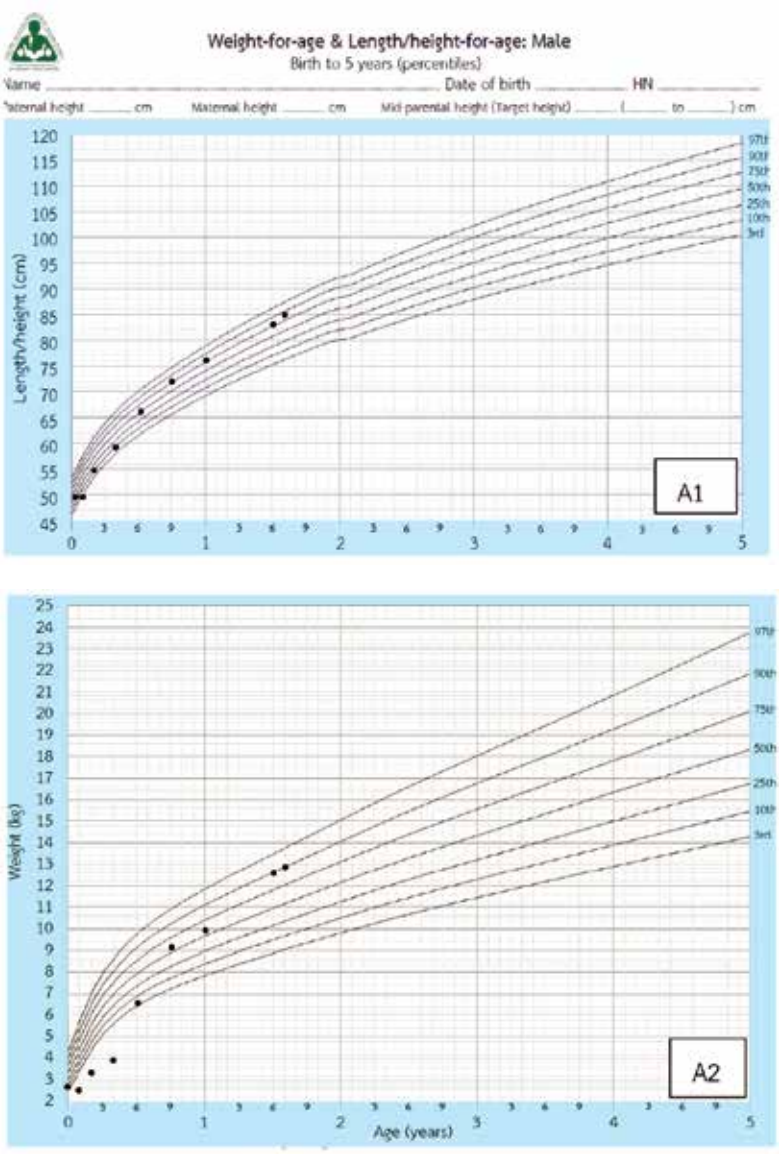

Figure A1, A2 A picture of our patient's growth chart designed by the Pediatric Nutrition Association of Thailand, demonstrating failure to thrive. His weight and height declined until he was admitted to the hospital at 1 month of age. He demonstrated normal weight gain at 9 months of age.

Discussion

Comparative literature:[6,7] A forty-day-old male and a 7-month-old male were presented with chronic diarrhea, generalized edema, hypoalbuminemia and protein losing enteropathy. The patient's symptoms resolved with the introduction of an elemental formula.

On rare occasions, our patient (the 1-month-old male discussed above), presented with very early onset of chronic diarrhea,[9] electrolyte disturbance and severe acute malnutrition, after a few days of formula milk intake, and no sign of hypoalbuminemia or protein losing enteropathy, such as

generalized edema. Laboratory abnormalities suggestive of fat malabsorption challenged us to consider a variety of differential diagnoses, including inflammatory states, protein-losing enteropathy, congenital diarrheal disorders, inborn errors of metabolism, immunodeficiency and CMPA. His diagnosis of severe CMPA was ultimately confirmed, and his symptoms resolved with the introduction of an elemental formula.

Conclusion

On rare occasions, a cow's milk allergy can present itself with chronic diarrhea, electrolyte disturbance and severe acute malnutrition. When diagnosis is delayed, this allergy may impair the patient's growth, quality of life and may even be life-threatening.

Acknowledgement

We would like to thank the Faculty of Medicine at Burapha University for their support.

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