CASE REPORT

Protein-Losing Enteropathy Associated With Egg Allergy in a 5-Month-Old Boy

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Abstract

Protein-losing enteropathy (PLE), the manifestation of a diverse set of disorders, is characterized by excessive loss of plasma proteins into the affected portions of the gastrointestinal tract, and this results in hypoalbuminemia. A 5-month-old breastfed boy presented severe PLE with hypogammaglobulinemia, hypocalcemia, and hypomagnesemia induced by an egg allergy. He developed hypocalcemic convulsions. The diagnosis of PLE was confirmed by elevated fecal $_1$-antitrypsin clearance and a positive finding on a protein-losing scintigram. His allergy to egg delivered through maternal milk was confirmed as the cause of PLE, since the mother's elimination of egg from her diet improved his condition and maternal egg challenge provoked symptoms of diarrhea, vomiting, and elevated $_1$-antitrypsin clearance. At the time of writing, he is 22 months old and has experienced no further episodes after the elimination of egg-containing food.

Key words: Protein-losing enteropathy (PLE). Hypocalcemia. Egg allergy. Food challenge.

Resumen

La enteropatía de pérdida de proteínas (EPP), la manifestación de varios conjuntos de trastornos, se caracteriza por la pérdida excesiva de proteínas séricas en los tramos afectados del aparato gastrointestinal, dando lugar a la hipoalbuminemia. Un niño de 5 meses alimentado con lactancia materna presentó EPP grave con hipogammaglobulinemia, hipocalcemia e hipomagnesemia inducidas por una alergia al huevo. El niño presentó convulsiones por hipocalcemia. El diagnóstico de EPP se confirmó mediante la elevada eliminación de $_1$-antitripsina en las heces y el resultado positivo en una gammagrafia de pérdida de proteínas. La alergia al huevo, que procedía de la ingesta de la leche materna, se confirmó como la causa de la EPP, ya que cuando la madre eliminó el huevo de su dieta el estado del niño mejoró, pero la prueba de provocación con huevo de la madre ocasionaba la aparición de los síntomas de diarrea, vómitos y una elevada eliminación de $_1$-antitripsina . En el momento en que se escribe este documento, el niño tiene 22 meses y no ha experimentado ningún otro episodio después de la eliminación de alimentos que contuvieran huevo.

Palabras clave: Enteropatía de pérdida de proteínas (EPP). Hipocalcemia. Alergia al huevo. Prueba de provocación alimentaria.

Introduction

Protein-losing enteropathy (PLE) has been associated with many disorders occurring at different anatomic sites in the gastrointestinal tract. Any process that leads to a profound leakage of proteins from the gastrointestinal tract can lead to PLE but there are 3 main mechanisms that are responsible: 1) lymphatic obstruction, such as primary intestinal lymphangiectasia, cardiac diseases, and lymphoma; 2) erosions and ulcerations, such as erosion of the esophagus and ulcerative colitis; and 3) intestinal permeability (leakage), such as is found in celiac disease and Henoch-Schönlein purpura, [1-3]. Food-allergies are attributable to the adverse immune response to dietary proteins and account for numerous gastrointestinal disorders of childhood [3]. Eosinophilic gastroenteritis and dietary protein enteropathy have been reported to cause PLE [3].

We report on a 5-month-old boy who had PLE caused by allergy to egg proteins that had arrived through maternal milk. He developed hypocalcemic convulsions.

Case Description

A 5-month-old boy was hospitalized with the chief complaint of afebrile convulsions 3 times a day. He had been exclusively breastfed until he started eating rice porridge 10 days earlier. His grandmother had pointed out his loose stools 2 weeks before hospitalization and his mother reported that he had had diarrhea (3 times per day) and regurgitated milk (several times per day) for 3 days prior to admission. He drank well and had been cheerful. His parents did not recognize his change, which included edema. His developmental milestones were within the normal range. His height was 69.5 cm and body weight was 7.8 kg. On admission, he was conscious, slightly edematous with pretibial pitting edema, periorbital edema, and was mildly hypotonic. He had no apparent dermatitis. Laboratory data on admission (table) showed remarkable hypoproteinemia including hypogammaglobulinemia (total protein, 2.8 g/dL; albumin, 1.9 g/dL; immunoglobulin [Ig] G, 31 mg/dL; IgM, 19 mg/dL; IgA 7 mg/dL). In addition, serum calcium (3.8 mg/dL; corrected for serum albumin, 5.4 mg/dL) and magnesium (0.8 mg/dL) levels were very low; serum sodium, potassium, and chloride levels were within normal ranges. Lymphocytopenia (<1000/ L) was noted. The C-reactive protein level was within the normal range. Urine analysis showed neither proteinuria nor hematuria.

Analyses of cerebrospinal fluid, an electroencephalogram, computed tomography and magnetic resonance imaging of the brain showed no abnormalities. Thus, his recurrent convulsions were considered to be due to severely low calcium and magnesium levels. Convulsions occurred twice after admission. The patient was given intravenous calcium, magnesium, and albumin; after 7 days, calcium and magnesium levels became normal, after which convulsions did not recur.

Since proteinuria was not observed, a loss of proteins into the gastrointestinal tract was suspected as the cause of hypoproteinemia. Fecal occult blood was repeatedly positive and $_1$-antitrypsin clearance was 400 mL/d (normal range, below 13 mL/d). His stool culture was negative and a rotavirus antigen test was negative. May–Giemsa staining of the stool revealed no eosinophils. A protein-losing scintigram using technetium 99m (99mTc)-labeled human serum albumin demonstrated leakage into the small intestine. Based on these findings, we diagnosed PLE.

The infant's serum IgE level was slightly high (22 U/mL). The egg-white and egg-yolk–specific IgE levels measured by CAP system radioallergosorbent testing (RAST) (Phadia, Uppsala, Sweden) were 1.2 kU/L and 1.1 kU/L, respectively, whereas other allergen-specific IgE antibodies (to milk, wheat, rice, soybean, mites, house dust) were not detected. Prick tests for egg-white and egg-yolk were positive but tests for other foods (milk, soybean, rice, wheat) were negative. In intracellular interleukin (IL) 4 and interferon (IFN) staining of $CD4^+$ cells, the percentages of type 1 helper T cells (T_H1) (IFN- positive, IL-4 negative) and T_H2 cells (IFN- negative, IL-4 positive) were both highly elevated to 28.5% and 4.8%, respectively, on admission in comparison with age-matched controls (T_H1, 2.02% [SD, 1.12 %]; T_H2, 0.33% [SD, 0.18%]) [4]. The T_H1 and T_H2 percentages decreased gradually to 5.23% and 0.28%, respectively, on discharge.

After admission, oral food intake including breastfeeding was stopped and total parenteral nutrition was undertaken for 10 days. Four days before breastfeeding was restarted, elimination of egg-containing foods from his mother's diet was started. Then maternal milk and additional formula milk feeding was restarted. He had no vomiting or diarrhea, and his serum protein levels increased gradually (on the 50th hospital day: total proteins, 5.3 g/dL; albumin, 4.1 g/dL; IgG, 197 mg/dL; IgM, 71 mg/dL; and IgA 28, mg/dL). Fecal $_1$-antitrypsin clearance decreased to the normal range. The second protein-losing scintigram (1 month after the first scintigram) did not detect leakage of the labeled albumin into the intestine.

A food challenge test for egg through maternal milk was started on the 50th hospital day. His mother took 1 whole boiled egg every 2 days and continued to breastfeed. The boy was well until the second challenge when he vomited 3 times. Egg was again eliminated from the mother's diet. Positive occult blood in the stool was noted for 3 days after the second challenge. $_1$-antitrypsin clearance in the stool was elevated again to 360 mL/d; however the clearance became normal within 2 weeks after the challenge. He was discharged at 120 days.

At age 22 months, he thrives with egg-containing foods eliminated from his diet. No other food restriction has been necessary. He has experienced no further episodes of PLE and has had no apparent symptoms of gastrointestinal food allergy.

Discussion

We have presented a case of PLE caused by egg allergy. Diagnosis of PLE was confirmed by hypoalbuminemia, elevated $_1$-antitrypsin clearance in stool, and a positive protein-losing scintigram using 99mTc-labeled human serum albumin. Egg allergy was confirmed as the cause of PLE by 1) improvement of the boy's condition with the first period of elimination of eggs from the mother's diet; 2) diarrhea and vomiting, with elevated $_1$-antitrypsin clearance, provoked by the egg challenge through maternal milk; 3) further improvement with re-elimination of egg-containing foods from the mother's diet.

A positive egg-white and egg-yolk IgE RAST and positive prick test for those foods indicated that the patient was sensitized to egg through maternal milk since he had never taken egg-containing food directly. Egg allergens, as well as cow's milk and wheat allergens, have been detected in breast milk as little as 2 to 6 hours after maternal intake and can be detected as long as 4 days later [5-7]. We therefore considered egg allergy as one of the causes of PLE. There are several gastrointestinal food-allergic disorders of infancy and childhood [3]. Our patient's PLE could have been dietary protein enteropathy [3], but an endoscopic examination and biopsy were not performed in this case. Usually, these gastrointestinal food-allergic disorders,

Table. Comparison of the Present Protein-Losing, Enteropathy Case With a Previously Reported Case [9]

	Present Case	Previous Case [9]
Onset	5 months	4 months
Feeding	breastfed	milk-formula–fed[a]
Diarrhea		
Onset	4.5 months	3 months
Frequency	3 times/d	5-6 times/d
Weight gain	good	good
General condition	good	good
Convulsions	present	present
Laboratory data on admission		
Total protein, g/dK	2.8	2.8
Albumin, g/dL	1.9	1.6
IgG, mg/dL	31	69
IgA, mg/dL	7	11.8
IgM, mg/dL	19	35
IgE, U/mL	22	220
Sodium, mEq/L	136	125
Potassium, mEq/L	3.9	3.2
Chloride, mEq/L	108	99
Calcium, mg/dL	3.8	4.6
Magnesium, mg/dL	0.8	0.7
White blood cells, per L	6440	NR
Lymphocytes, per L	943	NR
$CD3^+$, per L	366	1366
$CD4^+$, per L	134	528
$CD8^+$, per L	269	1157
$CD19^+$, per L	359	NR
T_H1, % in $CD4^+$ cells	28.5%	NR
T_H2, % in $CD4^+$ cells	4.8%	NR
IgE CAP-RAST		
Egg white, kU/L	1.4	markedly increased[b]
Egg yolk, kU/L	1.1	markedly increased[b]
Milk, kU/L	<0.34	markedly increased[b]
Histamine releasing test	no information	egg positive
Prick test	egg positive	NR
Protein-losing scintigram	positive	positive
Lymphoscintigram	not done	dilated
Egg elimination	effective	effective
Egg challenge	positive	not done

Abbreviations: Ig, immunoglobulin; T_H1 and T_H2, types 1 and 2 helper T cells; NR, not reported.
[a] This patient breastfed for the first few days.
[b] In their report, Hamada et al [9] did not report exact values; they used the phrase "RAST values for milk and egg were markedly increased" (p. 687).

except for immediate gastrointestinal hypersensitivity, are non-IgE-mediated but are associated with T cell responses [8]. We consider that the presence of a positive IgE antibody and prick test for egg protein does not exclude the presence of non-IgE-mediated enteropathy with T cell responses. In fact, activation of T_H1 and T_H2 cells were suspected by the fact that the percentages those cells in peripheral blood $CD4^+$ lymphocytes were very high on admission and were normalized on discharge from the hospital.

The boy presented not only hypoalbuminemia but also hypogammaglobulinemia, lymphocytopenia, and hypocalcemia/hypomagnesemia. In general, a low immunoglobulin level and lymphocytopenia are common in PLE that is caused by lymphatic obstruction but rare in PLE caused by other mechanisms. In this context, this patient was suspected of having PLE caused by lymphatic obstruction.

We located a case report of a 4-month-old boy whose clinical presentation was very similar to our patient's (table) [9]. That infant also had hypogammaglobulinemia, hypocalcemia, and hypomagnesemia with recurrent convulsions. He was diagnosed as having intestinal lymphangiectasia accompanying PLE by means of a protein-losing scintigram and lymphoscintigram.

However, although tests for IgE antibodies were positive for both egg and milk, a histamine-releasing test was positive only for egg. He was on hyperalimentation for the first month and thereafter elimination of egg from his diet was continued. His PLE condition, including laboratory findings, normalized completely 6 months later. A challenge test for egg was not performed in that case, but the elimination of egg as well as medium-chain triglyceride milk improved his condition. We did not perform a lymphoscintigram for our patient, but the laboratory data were consistent with those for lymphatic obstruction, and in general our case is consistent with the previous report. We speculate that some patients with dietary protein enteropathy may have lymphatic obstruction or a similar pathological condition which excretes gammaglobulin, calcium, and magnesium into the intestinal tract.

In summary, we report a rare case of infantile egg allergic enteropathy through maternal milk which caused severe PLE with hypocalcemia and hypomagnesemia resulting in afebrile convulsions in an infant.

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