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Case report

Necrotizing enterocolitis associated with food protein-induced enterocolitis syndrome: A case report

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ABSTRACT

Introduction: Food protein-induced enterocolitis syndrome (FPIES) is a T-cell-mediated allergy that can occur in newborns and infants who are introduced to milk protein. Some of the serious complications of FPIES include necrotizing enterocolitis (NEC), massive bloody stools, and disseminated intravascular coagulation. Here we report a case of NEC caused by FPIES.

Presentation of case: A 28-day-old girl born at full term suddenly developed marked abdominal distention and shock a few hours after being fed highly regulated milk protein. Emergency laparotomy was performed, and extensive small-intestinal necrosis was found. The histological examination showed chronic inflammation with typical ghost crypts, hemorrhage, and extensive pneumatosis intestinalis, a presentation consistent with NEC.

Discussion: In this case, the fragile intestinal mucosa associated with FPIES was stimulated by milk protein, leading to NEC. The greatest diagnostic difficulty is the lack of a definitive method for distinguishing between NEC and FPIES. The allergen-specific lymphocyte stimulation test with lactotransferrin was positive, indicating that the primary condition was FPIES. However, no eosinophilic infiltrate was found in the histological examination, but there was chronic inflammation with typical ghost crypts, hemorrhage, and extensive pneumatosis intestinalis. Consequently, the final histological diagnosis in our case was NEC rather than FPIES.

Conclusion: FPIES has a variable clinical course, and severe FPIES may become exacerbated even after ingestion of highly regulated milk protein. Taking appropriate actions after correct diagnosis can prevent progression to surgical emergency and secondary NEC.

1. Introduction

Food protein-induced enterocolitis syndrome (FPIES) is a non-immunoglobulin E (IgE)-mediated food allergy that can cause not only digestive symptoms, including abdominal distention, vomiting, diarrhea, constipation, and bloody stools, but FPIES can also cause nonspecific symptoms, including poor weight gain, fever, and apnea [1,2]. Although FPIES currently can only be diagnosed clinically, acute FPIES manifests within 1–4 h after ingestion of the causative food and is accompanied by repetitive emesis, pallor, and lethargy progressing to dehydration and hypovolemic shock in 15 % of cases [3]. Early recognition of FPEIS is important because some patients can exhibit serious complications, including necrotizing enterocolitis (NEC), massive bloody stools, and disseminated intravascular coagulation. Here, we report a case of NEC caused by FPIES. The reporting of this case followed the SCARE criteria [4].

2. Case presentation

A 28-day-old girl born at full term weighing 2.86 kg and who had no family history of food allergies developed diarrhea at age 2 weeks. She had been feeding on breast milk and formula milk since birth; however, her weight gain was poor. She soon became hypoactive and developed dehydration and metabolic acidosis. She was admitted to the pediatric emergency department of our hospital because of her deteriorating general condition. She was fasting to improve her intestinal condition and was treated for dehydration and metabolic acidosis. Feeding with Elemental formula®, an amino acid-based formula milk, was started as her general condition improved, and she remained stable during her feeding. However, a few hours after feeding her with the highly

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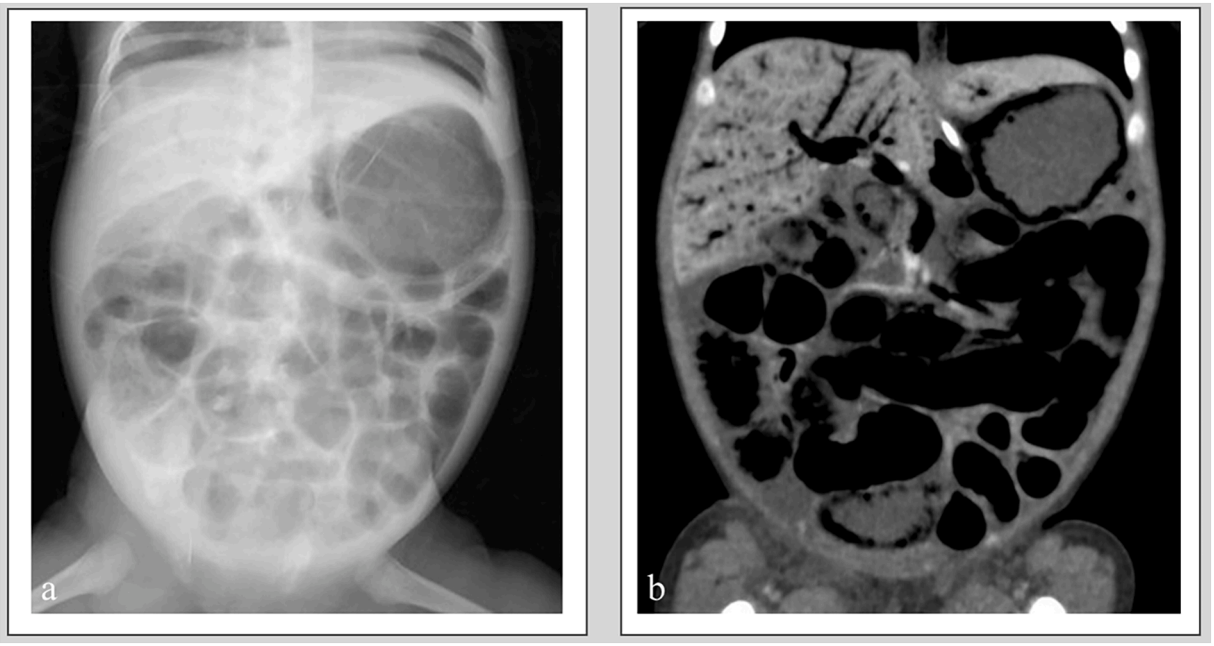

Fig. 1. a. Abdominal X-ray radiography showing intestinal dilatation and intestinal emphysema as well as portal vein gas.
b. Abdominal computed tomography showing extensive intestinal dilatation and intestinal emphysema as well as massive portal vein gas.

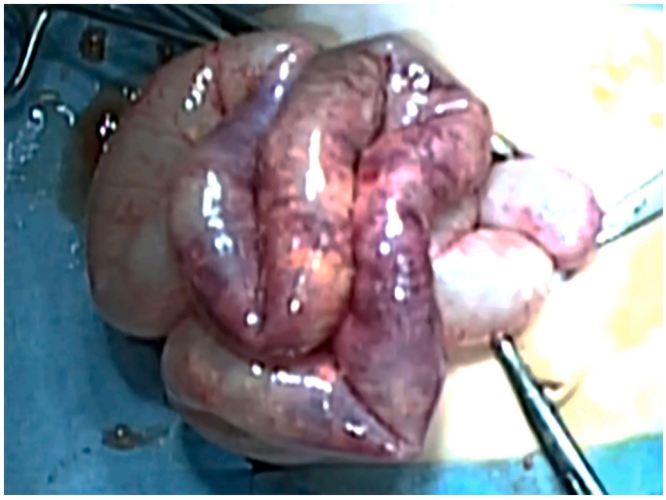

Fig. 2. Extensive necrosis of the small intestine and intestinal emphysema are shown. We resected the necrotic intestine from 3 cm to 80 cm and from 181 cm to 201 cm from the ligament of Treitz.

hydrolyzed formula, New MA-1®, which is highly regulated milk protein, she suddenly developed marked abdominal distention and shock. Abdominal X-ray and abdominal computed tomography showed extensive intestinal dilatation and emphysema with massive portal vein gas (Fig. 1a, b). An emergency laparotomy was performed, and extensive small-intestinal necrosis was found (Fig. 2). Hence, the necrotic intestinal region was resected, and ileostomy was performed for decompression. The histological examination showed chronic inflammation with typical ghost crypts, hemorrhage, and extensive pneumatosis intestinalis; the eosinophilic infiltrate was not observed (Fig. 3a, b), a presentation consistent with NEC. The results of the allergen-specific IgE were as follows: milk, 2.2 UA/mL; α-lactalbumin, 0.57 UA/mL; β-lactalbumin, 2.13 UA/mL; and casein, 1.54 UA/mL. Her thymus and activation-regulated chemokine level was 2226 pg/mL, and the results of the allergen-specific lymphocyte stimulation test using lactotransferrin were positive. She was able to feed normally on Elemental formula® 8 days after the ileostomy, and her general condition improved without any recurrence of NEC. Ileostomy closure was performed 3 months postoperatively and oral feeding was started 6 days later. She was discharged 17 days after the ileostomy closure and had a good postoperative course.

3. Discussion

NEC is a severe complication of preterm birth that occurs in 5 %–10 % of very-low-birth-weight infants and is associated with high mortality [5], and the typical characteristics of the disease include intestinal inflammation, hypoxia/ischemia, and necrosis. Although NEC is primarily observed in preterm infants, it has also been reported in full term infants [6].

FPIES is a T-cell-mediated allergy that occurs in newborns and infants [2]. The pathophysiology of FPIES is not well known, but it has been hypothesized that an abnormal cell-mediated immunological disorder of gastrointestinal mucositis after ingestion of a trigger food, which is often cow's milk or soybean formula but can potentially be any food (fish, egg, wheat, rice, meat, fruit, and vegetables) [7–9]. The condition can present with variable symptoms, including abdominal distention, vomiting, diarrhea, constipation, and bloody stools, whereas the nonspecific symptoms include poor weight gain, fever, and apnea. Some of the serious complications of FPIES include NEC, massive bloody stools, and disseminated intravascular coagulation. Recently, there has been an increase in the reports of this condition, with some patients requiring surgical intervention for the consequent intestinal perforation and NEC [10]. The onset of FPIES and a history of surgery are correlated, and the underlying pathology is thought to possibly be associated with deterioration of gastrointestinal function and damage to the intestinal mucosa [5]. Although our patient had no history of surgery, the fragile intestinal mucosa caused by FPIES was stimulated by milk protein, leading to NEC. However the greatest diagnostic difficulty is the lack of a definitive method for distinguishing between NEC and FPIES. Both conditions will result in progressive changes in intestinal structure, and in extreme cases, surgical intervention.

Eosinophilia or eosinophils in stool as well as ALST are regarded as useful diagnostic markers for FPIES. Guo reported that abdominal

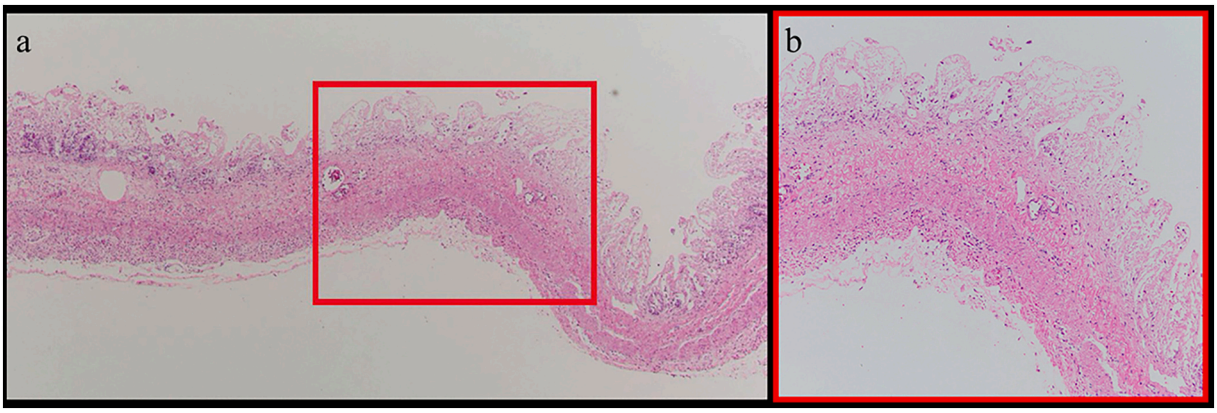

Fig. 3. a. Histological examination of the specimens showed mild chronic inflammation, with ghost crypts, hemorrhage, and pneumatosis intestinalis.
b. A high magnification view of (a); the eosinophilic infiltrate was not observed.

ultrasound can be used to differentiate between necrotizing enterocolitis and FPIES in the early stages [11]. Histopathological evaluation of the ileal mucosa, according to Kataoka, will be useful in clarifying the pathology of FPIES and its early diagnosis, particularly in surgical cases [2]. In our case, the allergen-specific lymphocyte stimulation test with lactotransferrin was positive, indicating that the primary condition was FPIES. However, although no eosinophilic infiltrate was found in the histological examination, chronic inflammation, with typical ghost crypts, hemorrhage, and extensive pneumatosis intestinalis, was observed. Therefore, the final histological diagnosis in our case was NEC rather than FPIES.

In the acute phase of FPIES treatment, urgent improvement in gastrointestinal symptoms and general condition are required. Since continuous administration of antigen induces further reactions, treatment must avoid ingestion of antigens. Especially in severe to fulminant cases involving massive hemorrhage and changes in vital signs, complete removal of the antigen for a few weeks is recommended to allow the entire mucosa to recover. Regarding the present case, the lesson is that we should have selected an amino acid-based elemental formula instead of highly regulated milk.

4. Conclusions

Although FPIES has a variable clinical course, we should consider the possibility of primary FPIES and avoid feeding milk protein. We should also consider that severe FPIES may become exacerbated even if highly regulated milk protein is ingested, especially in the acute phase. Taking these appropriate steps can prevent progression to surgical emergency and secondary NEC.

Abbreviations

FPIES	food protein-induced enterocolitis syndrome
NEC	necrotizing enterocolitis
IgE	immunoglobulin E

Consent

Written informed consent was obtained from the patient's guardian for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal upon request.

Ethical approval

This is a case report. The Human Research Ethics Committee of our institution did not require ethical approval to publish the manuscript.

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Guarantor

AF accepts full responsibility for the study and guarantee its accuracy.

Research registration number

1. Name of the registry: None
2. Unique identifying number or registration ID: None
3. Hyperlink to your specific registration (must be publicly accessible and will be checked): None.

CRediT authorship contribution statement

A.F., K.N., N.K., and T.M. treated this patient. A.T. performed the pathological evaluation. T.T. supervised manuscript writing. All authors contributed to the study design, data collection, and writing of the manuscript.

Declaration of competing interest

The authors declare they have no conflicts of interest.

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