**INTRODUCTION**

Food protein-induced enterocolitis syndrome (FPIES) is a gastrointestinal, non-IgE mediated, and food hypersensitivity syndrome, and particularly occurs in infants during the introduction of new foods. There is no specific diagnostic test for FPIES, and therefore, diagnosis relies on medical records, symptoms presented, oral food challenges, and symptomatic relief after dietary avoidance. Contrarily, necrotizing enterocolitis (NEC) is a life-threatening emergency of the gastrointestinal tract that almost exclusively affects newborns, with 70% of these cases occurring in preterm infants (<36 weeks of gestation). This condition warrants treatment with broad-spectrum antibiotics, bowel rests, inotropes, and fluid support.

The diagnosis of FPIES can be challenging, as its clinical manifestations may mimic other diseases such as NEC, leading to misdiagnosis. Symptoms that arise in both conditions include vomiting, abdominal distention, diarrhea, bloody stools, feeding difficulties, lethargy, apnea, and shock. Additionally, in both conditions, diagnostic tests, such as abdominal radiography, may show intestinal dilatation, pneumatosis intestinalis (PI), and portal venous gas.

We present a case of FPIES in a 1-month-old, exclusively breastfed male, initially diagnosed with NEC. However, after suspecting food protein-induced enterocolitis syndrome (FPIES), oral feeding was resumed using an exclusive elemental formula, and the biochemical and radiological findings were resolved.
and was exclusively breastfed since birth. No maternal dietary restrictions were in place.

Twenty-four hours prior to admission, he presented with two vomiting episodes, three stools with blood and mucus (Figure 1), and poor feeding afterward. During the initial assessment in the emergency room, vital signs fell within the normal range (temperature, 37.5°C; heart rate, 120 beats per minute; blood pressure, 70/50 mmHg; respiratory rate, 40 breaths per minute; and oxygen saturation, 95%), and his weight was 4905 g. Upon physical examination, he was alert and active, but irritable with a normal tone. The anterior fontanelles were found to be normotensive. He presented with other signs of dehydration, such as dry mucous membranes, decreased skin turgor, sunken eyes, and mildly prolonged capillary refill (3 s). Cardiopulmonary auscultation was normal with no signs of respiratory distress. His abdomen was soft but distended, with normal bowel sounds in tone and frequency and no organomegaly.

Laboratory analyses revealed metabolic acidosis in the venous blood gas test (pH: 7.26; HCO₃⁻: 15.4; BE: −11.5) and normal complete blood cell count, renal function, and electrolyte levels. The C-reactive protein levels were also within normal range. Abdominal radiography showed left flank PI (Figure 2), while abdominal ultrasound and upper GI series were normal, which helped rule out other surgical etiologies. These findings raised concerns regarding non-surgical necrotizing enterocolitis.

The patient was started on standard NEC therapy with intravenous fluids, empiric antibiotics, and bowel rest for 36h. Despite adequate therapy, metabolic acidosis and pneumatosis intestinalis persisted in subsequent X-rays. The blood culture obtained at admission was negative, and other inflammatory markers continued to be negative as well.

Pediatric gastroenterology was involved in this patient’s care after reviewing the patient’s clinical details. As a term infant with no risk factors for necrotizing enterocolitis, the patient continued to present biochemical and radiological findings, despite the ceasing of his bloody stools.

Additional diagnostic tests, including fecal calprotectin and eosinophil counts, were performed and showed normal results, leading us to suspect FPIES. Antibiotics were discontinued, and feeding was resumed exclusively using an elemental formula. In less than 24h, the patient’s metabolic acidosis improved, with no additional vomiting, blood, or mucus in stools, despite resuming oral feeding. The patient was discharged after 4 days. An abdominal X-ray after a week showed resolution of PI. An oral food challenge was suggested to confirm the diagnosis; however, the parents did not provide their consent.

Currently, the patient is 4 months old and is exclusively fed an elemental formula. He did not present with any other episodes of bloody stools or vomiting after switching to an elemental formula. His weight gain was normal and remained in the 70th percentile of the weight-for-age curve.

3 | DISCUSSION

FPIES is a poorly understood, non-IgE, and cell-mediated gastrointestinal food allergy that primarily affects children under 2 years of age. Males and females are equally affected, and it is more common in infants with a personal and family history of allergic diseases. In this case, the patient was a 1-month-old infant without a history of allergic diseases.5,6 The incidence of FPIES may vary between regions. In a population-based survey that took place in Australia over 2 years, the prevalence of acute FPIES in infants under 24 months was approximately 15 per 100,000 infants per year.7 Contrastingly, in Israel, a prospective two-year study was done in which FPIES was reported at a higher rate of 3 per 1000 infants per year who took cow milk.8 Additionally, FPIES may be underdiagnosed or underreported. In
Ecuador, only one case of FPIES has been reported,9 and no epidemiological studies have further assessed this condition.

The most common trigger is cow milk protein, although there appears to be specific triggers that vary from country to country and are based on regional diets.3 Rice is the main trigger in Australia,7 while cow milk is the most common trigger in the United States and Europe.5 In our case, because the patient was exclusively breastfed, it was difficult to identify a specific trigger.

In most reports, FPIES in exclusively breastfed infants is uncommon. Monti et al. (2011) described the first case of FPIES diagnosed in an infant caused by cow milk proteins passing through breast milk after accidental maternal ingestion.10 Since then, only a few cases have been reported in breastfed children.11,12 In this report, the patient was exclusively breastfed and no formulas were used, which raised concerns regarding the severe early onset of FPIES with acute symptoms.

FPIES is frequently confused with sepsis, metabolic diseases, severe gastroenteritis, abdominal surgical emergencies,13 and metabolic crises5 before reaching a final diagnosis. It is particularly challenging to diagnose FPIES in exclusively breastfed infants because it could be misdiagnosed as NEC.14

NEC is a life-threatening illness that primarily affects premature infants and has been documented in full-term infants with hypoxic events, such as cyanotic congenital heart defects. It can have a slow and insidious onset, with signs and symptoms that are highly variable and nonspecific, such as decreased activity, fatigue, vomiting, diarrhea, increased abdominal girth, and blood in stools.2

Patients with FPIES may also present with a wide range of clinical manifestations, ranging from vomiting to shock. Acute FPIES usually manifests between 1 and 4 h after ingestion of the trigger food. The main symptoms include profuse repetitive vomiting, diarrhea, pallor, and lethargy5; bloody diarrhea and failure to thrive are more commonly present in infants under 2 months of age with cow milk or soy FPIES.1 Finally, the most severe manifestation, hypovolemic shock, may develop in 15% of the patients with acute FPIES.1

Although no laboratory tests are needed to diagnose acute FPIES, they can reveal neutrophilia, thrombocytosis, anemia, hypoalbuminemia, eosinophilia, metabolic acidosis, methemoglobinemia, and stool leukocytes or eosinophils.5,15,16,17,18

Imaging studies are not necessary to diagnose FPIES, although findings of intestinal dilatation, PI, and PVG4 could be present on both radiography and in patients with NEC. It is essential to mention that PI is not a primary disease, but rather a clinical sign,19 nor is it a pathognomonic of any specific disease. PI has been reported as an incidental finding in some cases of cow milk protein allergies and FPIES.14,20,21,22

There are no specific tests to identify FPIES; however, there are international diagnostic criteria.23 In the case of our patient, one major criterion was evident (onset of vomiting usually 1–4 h after food exposure; considering that the patient was exclusively breastfed, and the mother did not follow a specific diet), as were three minor criteria (diarrhea, a visit to the emergency room, and intravenous fluid support) required for diagnosis. As the patient presented with a single episode, an oral food challenge (OFC) was strongly recommended to confirm the diagnosis.1 However, in this case, the parents did not consent to an OFC.

FPIES is initially treated with the elimination of the trigger food and through fluid replacement, either orally or intravenously, depending on the severity of the clinical manifestations.5 The use of corticosteroids has been reported, but there is scarce evidence to recommend their routine use.1 Contrastingly, the administration of ondansetron could be effective in shortening vomiting episodes.24 Complete recovery is expected within a few hours, in comparison with other diseases, such as sepsis, gastroenteritis, or surgical causes of acute abdominal pain.25 As explained previously, our initial diagnosis was of NEC, which was treated similarly with intravenous fluid therapy, antibiotic administration, and nil per os. However, after suspecting FPIES, antibiotics were discontinued and oral feeding was resumed using an elemental formula. Metabolic acidosis was resolved, and no more vomiting or blood or mucus in stools was observed despite resuming oral feeding.

4 CONCLUSION

FPIES in exclusively breastfed infants is an uncommon entity with potentially severe reactions that can be misdiagnosed as NEC in specific cases. PI can be found in both diseases, but is not a pathognomonic sign. Hence, it is important to increase the awareness of FPIES in this group of patients to avoid delaying adequate treatment.

AUTHOR CONTRIBUTIONS
PHA was involved in writing and study design. FVM was involved in study design and data collection. AVM was involved in data collection and literature review. RSM was involved in the literature review. GC edited and reviewed the manuscript. ECJ provided editing and review of the manuscript.

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CONFLICT OF INTEREST
None declared.
DATA AVAILABILITY STATEMENT

No data available.

CONSENT

Written informed consent was obtained from the parents of the patients to publish this report in accordance with the journal’s patient consent policy.

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