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Case Report

Food Protein Induced Allergic Proctocolitis with Pneumatosis Intestinalis in SARS-Cov-2 Positive Infant

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Abstract

Pneumatosis Intestinalis (PI), characterized by the presence of submucosal air in the intestinal wall, is an uncommon finding in the pediatric population. Food Protein Induced Allergic Proctocolitis (FPIAP) is a prevalent manifestation of food allergy in children, presenting with bloody stools in otherwise healthy infants. We present a case report of a 5-week-old boy with PI, diagnosed in the course of FPIAP and concurrent COVID-19 infection.

The patient was admitted to the hospital due to the occurrence of bright blood in the stool. Subsequent abdominal USG revealed an increasing pneumatosis intestinalis in the ileum and ascending colon. During hospitalization, the patient developed cough, rhinitis, and was tested positive for SARS-CoV-2. The main therapeutic intervention involved a change in feeding from a milk-containing diet to extensively hydrolysed formula, which was followed by a remission of the symptoms and improvement in patient's clinical condition.

Pneumatosis Intestinalis still remains an unexplored phenomenon in pediatric patients. Recent observations suggesting an association with common diseases definitely require further investigations to explore its characteristics and proceeding in allergy and viral infections.

Keywords: Food Protein Induced Allergic Proctocolitis; Pneumatosis Intestinalis; COVID-19; Pediatric Allergy; Food Allergy

Introduction

Pneumatosis Intestinalis (PI) is characterized by a presence of submucosal air in the intestinal wall. It affects approximately 0.03% of the general population, although the prevalence is less frequent in children [1]. Food Protein Induced Allergic Proctocolitis (FPIAP) is a commonly recognized non-IgE-mediated food allergy [2,3]. The diagnosis is based on clinical recognition of the intermittent bloody stool in otherwise healthy infants that resolve with dietary restriction. Causes of the Pneumatosis Intestinalis can vary widely, but it was described in accompany of FPIAP only once [4]. The objectives of this article are to describe a case of a 5-week old boy that developed Pneumatosis Intestinalis in the course of allergic proctocolitis while he was tested positive for SARS-CoV-2.

Case Presentation

A 5-week-old boy was admitted to the Clinic due to the increasing amount of bright blood in the stool and a poor weight gain, observed over the past week. He was born at the 38 weeks, delivered by cesarean section with 3760 g of weight and 10 Apgar points. The pregnancy was complicated by

gestational diabetes and hypertension. During the perinatal period the baby experienced jaundice, requiring a phototherapy treatment, and underwent a right-sided inguinal hernia surgery on the seventh day of life. Initially he was breast-fed since birth, but for two weeks preceding admission he had been given the first infant formula due to an insufficient breast milk supply. In physical examination, he was in good general condition, with a seborrheic rash on the face, hair scalp and upper chest skin. On the day of admission, the mother tested positive for SARS-CoV-2, presenting with mild cough and rhinitis, but initially the baby tested negative and remained asymptomatic. The patient's laboratory tests revealed low WBC count with inflammatory markers values within the normal range and negative stool culture and stool virus tests. The first abdominal USG revealed the presence of gas bubbles within the portal venous system, shown in the Figure 1. Subsequent follow-up USG conducted after three days exposed the indications of Pneumatosis Intestinalis within the walls of the ileum and ascending colon, shown in the Figure 2. The mother started a dairy-free diet, but with no significant change both in the baby's clinical condition and the USG imaging. Therefore, on the 6th day of hospitalization when the boy began to be fed exclusively with a protein hydrolysate diet, the gradual improvement in his clinical picture was observed. Within the following days a seborrheic rush decreased and the daily weight gain enhanced. It was followed by a reduction of the bright blood observed in the stools. Due to the characteristic clinical features the boy was diagnosed with FPIAP, although the mother declined proceeding with a cow's milk oral food challenge. On the 10th day of hospitalization the patient developed a cough, rhinitis, and tested positive for SARS-CoV-2. However, after a brief observation period, he was discharged home in a good clinical condition.

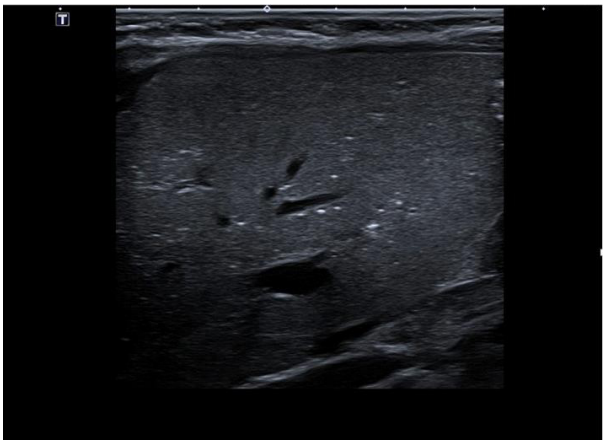

Figure 1: Gas bubbles in the portal venous system.

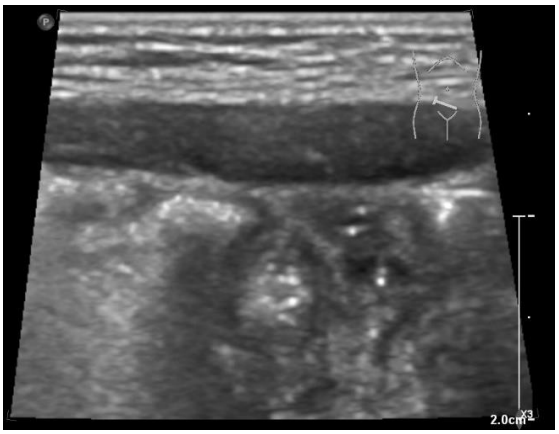

Figure 2: Gas infiltration in the intestinal wall.

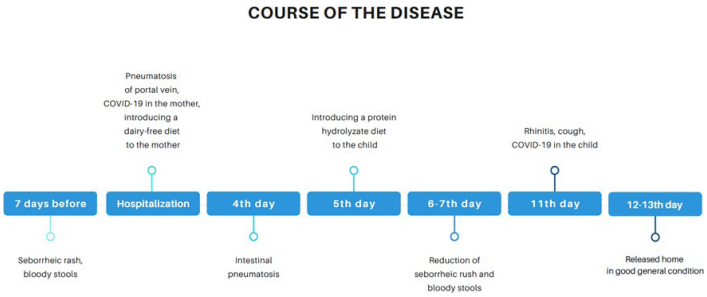

Figure 3: Timeline.

Discussion

Food Protein Induced Allergic Proctocolitis (FPIAP) is a commonly recognized in children non-IgE-mediated food allergy, which is characterized by mild clinical features and a self-limiting character. The prevalence of FPIAP is estimated between 18% and 64% of the infants with rectal bleeding [4]. In prospective cohort study by Martin, a prevalence was 17% in the otherwise healthy infant population [5]. The clinical picture includes intermittent, bloody, mucus-laden stools, colic behavior and increased bowel movement in otherwise healthy infants, without growth failure. It presents between 2-8 weeks of life, more often in breastfed infants, than in infants fed with formula. The beginning is usually insidious, with a latent occurrence of symptoms relative to introduction of inciting food. The most common triggers are cow milk, soy, egg and wheat in maternal diet or formula. Dietary restriction results in a resolution of bleeding within 72-96 hours with a recurrence after re-exposure [6]. No failure to thrive was observed in affected infants, even without food restriction [7]. There are no characteristic markers that could be useful to support diagnosis of FPIAP [5].

Laboratory test may reveal periodic mild anemia, elevated IgE antibody levels and peripheral eosinophilia [8,9]. The diagnostic process is based on the recognition of specific syndrome pattern and the exclusion of other potential causes, preferably confirmed by oral food challenge with the probable inciting dietary factor 4-8 weeks after a resolution of the symptoms.

Based on the available literature there are no specific or characteristic radiological features described in the course of typical FPIAP, therefore some radiological abnormalities in the course of cow's milk allergic colitis were reported. In a study by Masumoto two patients with allergic enterocolitis exhibited distinct radiological findings, including an abnormal bowel gas pattern - suggestive of obstruction, on abdominal plain X-Ray, thickening of the intestinal wall in USG and CT, and thickened intestinal folds in the contrast studies of the upper and lower gastrointestinal tract [10]. Only one case study has described the occurrence of PI in the context of allergic colitis. Liu reported a case involving a 5-week-old premature infant with allergic colitis, which was subsequently followed by the presence of diffused PI observed in X-Ray imaging [11].

Pneumatosis Intestinalis is a sign of intestinal distress that may represent severe intestinal insufficiency or be a benign phenomenon. It is defined as a presence of submucosal air in the intestinal wall, usually revealed in imaging studies. The exact pathophysiology of PI remains elusive; however, suggested theories point to a mechanical origin where gas dissects from the intestinal lumen into the intestinal wall. It may also be associated with the intestinal dysmotility, causing inadequate peristalsis that fosters bacterial overgrowth, leading to heightened gas production and increased intraluminal and transmural pressure. The potential etiology of PI comprises a wide spectrum of underlying conditions, including infection, trauma, congenital abnormalities and autoimmune process [12-14]. PI is associated with intestinal failure, although in the study by Reppucci they observed that it is not combined with a specific etiology of the intestinal compromise or anatomical abnormalities. The authors also noted that PI development could be attributed to the increased intestinal stress resulting from providing an enteric feeding in conditions of impaired bowel function [15] that may potentially stem from intestinal malfunction, caused by non-IgE mediated food allergies and subsequent allergic reactions. The majority of PI cases may be managed conservatively, especially in children that are able to be fed enterally [16].

In the neonatal population PI is most often present in the course of Necrotizing Enterocolitis (NEC), which is a severe, potentially fatal disease of the gastrointestinal tract, affecting primarily premature infants or full-term infants with significant comorbidities [1]. It is induced by bacterial invasion into the intestinal wall, followed by inflammation and destruction that may lead to intestinal perforation. The diagnosis is based on the overall clinical picture, laboratory tests and radiological signs. Symptoms of NEC are variable and nonspecific. It can present with decreased activity and appetite, vomiting, diarrhea and bloody stools, which may progress to respiratory and circulatory failure [17,18]. The characteristic radiological signs include PI and less often-portal venous gas appearance [19].

Among all of the Non-IgE-Mediated Food Allergies in infants Food Protein-Induced Enterocolitis Syndrome (FPIES) requires particular attention. Starting out with repetitive, profuse vomiting and watery diarrhea after incorporating triggering food, may lead to dehydration, pallor, lethargy, hypovolemic shock and failure to thrive [2]. No specific radiographic features for FPIES were described. However, signs of PI were reported in FPIES [20]. There are several studies documenting a concomitance of NEC, FPIES and PI [21-23]. In the research by Kim 6.7% of preterm and 44.7% of term infants with presumed NEC were confirmed to have FPIES [23]. Clinical features and course of a disease of FPIES and NEC overlap, which may lead to misdiagnosing, especially when PI is present. Hu focused on comparison of the clinical features and identification of either NEC or FPIES in-patient with PI in order to achieve the best possible management and avoid the unnecessary interventions [22].

In this case report, the diagnosis was based on the characteristic symptoms pattern, a typical course of a disease and exclusion of other potential causes. Our patient presented Pneumatosis Intestinalis visualized in USG although he didn't meet the clinical criteria of FPIES and NEC so both of them were excluded during the diagnostic process [24]. The diagnostic limitation of the presented case report is that the oral food challenge with the most probable inciting factor – cow milk, was not proceeded due to the mother's disapproval so it is not possible to definitely determine the inciting factor that induced the allergic reaction. Oral food challenge is perceived as a golden standard in FPIAP diagnosis. Furthermore, this approach can be employed to assess the development of tolerance to the offending food, providing a potential avenue for evaluating the presented case in the future.

On the 10th day of hospitalization, the patient developed a mild SARS-CoV-2 infection with cough and rhinitis. In infants, SARS-CoV-2 is described as a rather rare disease with only 0,27% of neonatal patients in the total affected population. The time of incubation is approximately 2 weeks [25]. The symptoms of FPIAP started a week before a mother was diagnosed with COVID-19, therefore it suggests that the patient might also have been infected - yet not positive, because of the incubation period when the symptoms occurred and PI developed. Mehl described a case of NEC-like intestinal pneumatosis in a 7-week old, full-term SARS-CoV-2 positive infant with no comorbidities. The patient initially presented with low-grade fever, fussiness, poor oral intake and mild congestion, to proceed with emesis, large volume bloody stools, lethargy and exacerbating PI, although the allergic background was eventually excluded [26]. There is also a case of NEC with PI in premature infant with COVID-19, described by Mannix [27]. Both patients, due to serious clinical abnormalities,

were treated with broad-spectrum antibiotics, but there was no need for surgical intervention. What distinguishes our patient is that he didn't require antibiotics or surgery. The key intervention that led to a significant clinical improvement was the change in feeding from a diet containing cow's milk protein to an extensively hydrolysed formula, free of that allergen.

There are a few cases documenting Pneumatosis Intestinalis in SARS-CoV-2 positive patients [28-31]. The authors suggest a role of a virus in the development of PI. Rohani described a protein losing enteropathy and PI in a child with COVID-19 infection [32]. The patient presented with fever, vomiting, diarrhea, abdominal pain, loss of protein in the stool exam, and was initially diagnosed with acute abdomen due to appendicitis. In the article by Rousset [33] coronavirus-like, particles were observed in specimens from intestinal mucosa of intestine, appendix, and colon in infants with PI in the course of NEC. Currently, there are no cases of triggering or exacerbation of allergic colitis by SARS-CoV-2 infection in the accompany of PI described in the literature, therefore a potential correlation between them requires further investigations.

Conclusions

This case highlights the importance of considering allergic proctocolitis as a potential cause of Pneumatosis Intestinalis in infants and underscores the significance of individualized nutritional management in such cases. Further research is needed to better understand the pathophysiological mechanisms linking FPIAP and SARS-CoV-2 infection with PI and to optimize diagnostic and therapeutic approaches for affected patients.

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Ethical Considerations: Written informed consent was obtained from the patients's parent for publication of this case report and any accompanying images

Conflict of Interest Statement: Authors have no conflicts of interest to declare

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