Pediatric Allergic Proctocolitis

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Pediatric allergic proctocolitis is considered an IgE-mediated allergic reaction to dietary proteins; most commonly is Cow’s milk protein, which represents about 50-65% of the cases. It’s a frequent, significant cause of infant colitis. This article explains the main clinic-patho-physiological aspects of the disease.

Definition

Pediatric allergic proctocolitis (PAP) is a part of non-IgE mediated food allergic disorders, where cell-mediated immunity plays the key role. It’s one of the causes of hematochezia in infancy around the age of 1 day to 3 months. It’s considered a frequent and a significant cause of colitis in infants, which usually resolves by the age of 1 year.

Non-IgE cell-mediated food allergy disorder types

Non-IgE, cell-mediated food allergic disorders comprises of different disorders, namely:

1. Food protein-induced enterocolitis syndrome (FPIES)
2. Food protein-induced enteropathy
3. Heiner’s syndrome (pulmonary hemosiderosis)
4. Celiac disease
5. Cow’s milk (CM) protein-induced iron deficiency anemia

Food protein-induced enterocolitis syndrome (FPIES)
Seen in infants from day 1 to about 12 months of age, FPIES involves severe vomiting, explosive \textit{diarrhea}, severe bloody stools and acute severe \textit{edema}. Incriminated food proteins are CM, soy, rice, fish, pea, turkey and barley. \textit{CM and soy} account for about 40\% of cases.

\textbf{Significant positive personal and family history} for atopies and allergies is often documented. The child is often sick with about 15\% being in \textit{shock}, and a significant subset presenting with \textbf{moderate failure to thrive and anemia}. Methemoglobinemia, academia and acute hypoalbuminemia mark FPIES.

The standard evaluation for IgE-mediated allergic disorders comprises of various tests, such as the food prick skin test, peripheral blood eosinophil titer, total IgE and serum food allergen IgE levels are normal.

Treatment typically resorts to the elimination of the trigger protein from a diet with the often addition of casein hydrolysate. Symptoms resolve within 3-10 days of elimination of the culprit molecule. CM allergies naturally regress by about 2 years of age.

\textbf{Food protein-induced enteropathy}

Enteropathy presents up to 2 years of age with most commonly implicated protein molecules being CM and soy. \textit{Breast milk} is the source of these culprit compounds. The clinical picture involves moderate diarrhea with seldom rectal bleeding, intermittent vomiting and moderate edema. \textit{Moderate hypoalbuminemia} is the only laboratory marker. Allergy evaluation is remarkable for being normal. The treatment involves the elimination of the culprit protein.

\textbf{Celiac disease}

With allergic reaction to wheat protein, celiac disease etio-pathogenesis is well documented in literature.

\textbf{Heiner's syndrome (pulmonary hemosiderosis)}

This is often rarely diagnosed.

\textbf{Cow's milk (CM) protein-induced iron deficiency anemia}

This presents until the age of about 20 months. \textit{CM-based formula feeds} lead to this entity. Symptoms are minimal with often normal laboratory and allergic evaluation results. Treatment comprises of the elimination of whole CM protein and use of humanized CM-based formulas. Most children are in remission by 3 years of age.

\textbf{Epidemiology of Pediatric Allergic Proctocolitis}

PAP is estimated to be responsible for about 15-60\% of infants with rectal bleeding. It is surprisingly cited in breastfed infants in areas of the relatively lower prevalence of food allergies. Associated \textit{eczema} is seen in about 22\% of patients, while a positive family history of allergies is present in up to 25\% of children.

\textbf{Pathogenesis and Clinical Features of Pediatric Allergic Proctocolitis}

\textit{Maternal ingestion of the food allergen}, commonly CM, subsequently transferred in babies through breast milk as immunologically prone form, \textit{breast CM} is the
hypothesized theory. Formula-fed infants demonstrate an allergy to CM and soy proteins.

**Prominent eosinophilic aggregations** are appreciated on intestinal mucosal biopsy in PAP. Degradation of eosinophils around the nerves leads to a release of eosinophilic mediators.

These immunomodulator molecules cause a subsequent induction of **mast cell degranulation, vagal muscarinic M2 receptor dysregulation, smooth muscle contraction** and **stimulation of chloride secretion** from the colonic epithelium. They also culminate in **gastric dysmotility**. These mechanisms are thought to contribute to the role of **mucosal eosinophilic infiltration** in the pathogenesis of PAP.

**Signs and symptoms** of PAP are summarized as follows:

<table>
<thead>
<tr>
<th>Symptom/Sign</th>
<th>Explanation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intermittent vomiting</td>
<td>Rare</td>
</tr>
<tr>
<td>Intermittent blood streaked stools</td>
<td>Most frequent complaint</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>Mild</td>
</tr>
<tr>
<td>Pain on defecation</td>
<td>Occasional</td>
</tr>
<tr>
<td>Flatulence</td>
<td>Occasional</td>
</tr>
<tr>
<td>Occasional abdominal colic</td>
<td>Mild</td>
</tr>
<tr>
<td>Failure to thrive</td>
<td>No</td>
</tr>
<tr>
<td>Family history of atopy</td>
<td>In about 25% of patients</td>
</tr>
</tbody>
</table>

**Diagnosis and Differential Diagnosis of Pediatric Allergic Proctocolitis**

Diagnosis is based on the following salient features of PAP:

- History of blood-streaked stools.
- Relatively preserved child.
- Exclusion of other infections and etiologies behind rectal bleeding.
- Response to elimination diet serves as a concluding proof. It leads to resolution of symptoms within 3 to 4 days.

There are various **ancillary tests** that one may use to supplement the clinical diagnosis and rule out other closely associated differentials. A summary of the same is presented as below:

| Laboratory tests | • Hypobuminea: infrequent  
|                 | • Anemia: mild            
|                 | • Methemoglobinemia: absent  
|                 | • Acidemia: occasional     |
| Allergy evaluation | • Food prick skin test: negative  
|                  | • Serum food allergen IgE: negative  
|                  | • Total IgE: normal or elevated  
|                  | • Peripheral blood eosinophilia: occasional  |
| Intestinal mucosa biopsy findings | Focal colitis with mild linear mucosal erosions without evidence of villous injury is seen. Eosinophilic infiltration is appreciated in abundance.  |
| Fecal mucus smear | Increased polymorphonuclear neutrophils.  |
| Endoscopy | No anatomic abnormalities appreciated. Lymphoid nodular hyperplasia and focal erythema are commonly documented.  |

**Differential diagnosis for rectal bleeding**

Rectal bleeding is the most prominent symptom of PAP. Consequently, one needs to be wary of other crucial etiologies behind bleeding per rectum. The same can be segregated as per the degree of rectal bleeding as follows:
### Extent of rectal bleeding

<table>
<thead>
<tr>
<th>Significant</th>
<th>Implicit diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Sepsis</td>
<td>• Food protein induced enterocolitis syndrome (FPIES)</td>
</tr>
<tr>
<td>• Necrotizing enterocolitis</td>
<td>• Volvulus</td>
</tr>
<tr>
<td>• Hirschsprung’s disease</td>
<td>• Gastrointestinal infection (Campylobacter, Shigella, Salmonella, parasites) causing dysentery</td>
</tr>
<tr>
<td></td>
<td>• Vitamin K deficiency</td>
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<tr>
<td></td>
<td>• Perianal dermatitis</td>
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<tr>
<td></td>
<td>• Coagulation disorders</td>
</tr>
<tr>
<td></td>
<td>• Anal fissure</td>
</tr>
</tbody>
</table>

### Intermediate to minimal rectal bleeding

- Gastrointestinal infection (Campylobacter, Shigella, Salmonella, parasites) causing dysentery
- Vitamin K deficiency
- Perianal dermatitis
- Coagulation disorders
- Anal fissure

## Treatment and Prognosis of Pediatric Allergic Proctocolitis

Pediatric allergic proctocolitis is deceptively alarming and seemingly an annihilating disease of infants with rectal bleeding. It is a benign, transient disease and has a very manageable course.

**Dietary restriction** and *elimination of the offending protein molecule* from the maternal diet for breastfeeding mothers is definitive, curative and a complete treatment for PAP. Lake proposed the discontinuation of breast milk and the use of casein hydrolysate formula for about 72 hours or until resolution of bleeding, whichever occurs earlier.

**Soy proteins** are better avoided as there is a cross reaction to soy in about 40% of children with allergy to CM. Few children require amino acid-based formulas.

Once remission sets in, food introduction is done at home in a progressively increasingly graded manner. Full feeds are typically reached at the end of two weeks.

Excellent long-term prognosis prevails. Almost one-fifth of babies demonstrate spontaneous regression of rectal bleeding. Many develop a tolerance to the offending protein by one year of age. These children essentially are normal adults with no increased predisposition to future grave gastro-intestinal diseases.

## Prognosis

Prognosis is considered excellent, with most of the infants being able to tolerate the soy products and cow’s milk by the age of 1 year.

## Summary

Pediatric allergic proctocolitis belongs to the family of **cell-mediated non-IgE mediated food allergic disorders** which are being increasingly appreciated in recent times. Cow protein allergy, soy protein allergy and allergy to unidentified potential breast milk triggers in breast milk fed babies are the inciting factors.

PAP is an important cause of rectal bleeding and frequent etiology behind colitis in infants below one year of age.

Although seemingly alarming with streaks of blood accompanying stools, PAP has a benign and transient course.
The child is well preserved and has no signs of failure to thrive. Food allergy tests are negative. Diagnosis is based on clinical acumen, often supplemented by tests meant to rule out close differentials.

Treatment consists of the elimination of the offending molecule and from the maternal diet for breastfed infants. Casein hydrolysate, hypoallergenic formula feeds and amino acid based formulas may also be used. Reintroduction of foods is typically done in an insidious, graded manner, reaching full feeds at about 2 weeks.

Excellent prognosis is implied for these patients with many undergoing spontaneous resolution. Long-term increased predisposition to chronic, inflammatory gastro-intestinal disorders is a myth.

Review Questions

The correct answers can be found below the references.

1. Which of the following is true?
   A. Pediatric allergic proctocolitis can occur in breast fed infants.
   B. Breast milk protects against pediatric allergic proctocolitis.
   C. Pediatric allergic proctocolitis is an IgE mediated allergic reaction.
   D. Pediatric allergic proctocolitis is diagnosed only on the basis of intestinal mucosal biopsy findings.

2. Which of the following statements is false?
   A. Pediatric allergic proctocolitis shows an allergic reaction to cow milk protein and occasionally to soy protein.
   B. Casein hydrolysate and amino acid formulas are helpful in the treatment of pediatric allergic proctocolitis.
   C. Pediatric allergic proctocolitis does not make the child prone to future gastro-intestinal allergic disorders.
   D. Pediatric allergic colitis has a stormy course with the majority of children developing shock if not resuscitated at the right time.

3. Allergic proctocolitis is seen in which pediatric population?
   A. Infants
   B. Toddlers
   C. Adolescents
   D. Neonates

References


Nelson’s textbook of Pediatrics.


Correct answers: 1A, 2D, 3A

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