There has been a recent insurgence in pertinent knowledge regarding cell-mediated non-IGE food allergic disorders. Pediatric allergic proctocolitis is a frequent, significant cause of infant colitis. This article expatiates on clinic-patho-physiological aspects of the same.

Definition of Pediatric Allergic Proctocolitis

First attested in literature by Lake et al. in 1982, pediatric allergic proctocolitis (PAP) comprises of hematochezia in infancy around the age of 1 day to 3 months. Blood-streaked stools in an otherwise healthy baby are typically described. Lake et al. described this entity in about 6 exclusively breastfed infants with rectal bleeding that manifested within the first month of life.

Often a common, frequent and significant cause of colitis in infants, PAP is benign and transient. It usually resolves by 1 year of age. It is a part of non-IgE mediated food allergic disorders, where cell-mediated immunity plays the key role. A current review establishes an incidence of almost 40% of milk protein allergies for these pathologies.

Non-IgE cell-mediated food allergy disorder types

Food protein-induced enterocolitis syndrome (FPIES)

Seen in infants from day 1 to about 12 months of age, FPIES involves severe vomiting, explosive diarrhea, severe bloody stools and acute severe edema. Incriminated food proteins are CM, soy, rice, fish, pea, turkey and barley. CM and soy account for about
40% of cases.

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

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

**Food protein-induced enteropathy**

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

**Celiac disease**

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

**Heiner's syndrome (pulmonary hemosiderosis)**

This is often rarely diagnosed.

**Cow's milk (CM) protein-induced iron deficiency anemia**

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

**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 **eczema** is seen in about 22% of patients, while a **positive family history of allergies** is present in up to 25% of children.

**Pathogenesis and Clinical Features of Pediatric Allergic Proctocolitis**

**Maternal ingestion of the food allergen**, commonly CM, subsequently transferred in babies through breast milk as immunologically prone form, **breast CM** is the hypothesized theory. Formula fed infants demonstrate 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 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 |
| Intestinal mucosa biopsy findings | • Total IgE: normal or elevated |
|                                   | • Peripheral blood eosinophilia: occasional |
| Fecal mucus smear                 | Increased polymorphonuclear neutrophils |
| Endoscopy                         | No anatomic abnormalities appreciated. Lymphoid nodular hyperplasia and focal erythema are commonly documented. |
| Stool culture                     | Negative                 |

**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:

<table>
<thead>
<tr>
<th>Extent of rectal bleeding</th>
<th>Implicit diagnosis</th>
</tr>
</thead>
</table>
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 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.

**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.

Though 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 on Pediatric Allergic Proctocolitis

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 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*.


Morita H, Nomura I, Matsuda A, Saito H, Matsumoto K. *Gastrointestinal food allergy in*

Correct answers: 1A, 2D, 3A

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