A Child with a Rare Cause of Chronic Diarrhea, Weight Loss and Seizures

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Abstract

Etiology of Chronic Diarrhea, implying diarrhea of > 2 weeks is exhaustive and diagnostic evaluation needs to be step-by-step with good history taking and clinical examination, followed by investigations depending on the individual merits of the case. Inflammatory Bowel Disease (IBD) represents one of the rare causes of chronic diarrhea in children.

Keywords: Chronic Diarrhea; IBD; Crohn’s Disease (CD); Ulcerative Colitis (UC)

Introduction

Inflammatory Bowel Disease (IBD) is used to represent 2 distinctive disorders of idiopathic chronic intestinal inflammation: Crohn's Disease and Ulcerative Colitis.

Both of which are characterized by unpredictable exacerbations and remissions. The most common time of onset of IBD is during the preadolescent/adolescent era and young adulthood.

A bimodal distribution, one is early onset at 10 - 20 years old of age and second small peak at 50 - 80 years of age.

IBD may begin as early as the 1st year of life and an increased incidence among children has been observed since the turn of the century.

Case Presentation

A boy aged 11.5 years old, complains of Gastrointestinal Symptoms (excessive vomiting, abdominal pain and fever) for several days, and later on he develop diarrhea.

The child is a known epileptic case and is on Sodium Valproate, with the dose increased one week before, due to an episode of convulsions while he is on a treatment.

The clinical examination of the boy is within normal limits.

Weight: 30 Kg (on 5th centile), Height: 144.5 cm (on 25th centile).

Except for signs of severe malaise, fatigability and anorexia, laboratory investigations showed mild Hypokalemia (S.K + - 3.2 meq/L), Hyponatremia (S.Na + - 126 mEq/L), stool analysis showed Pus Cells > 100 per field and Stool and Urine Culture has No Growth.

So, we manage the case as Acute GE, with fluid and electrolyte replacement, antibiotics and antiemetics.

Due to slow improvement in terms of vomiting and anorexia and fatigability, the patient went to another hospital where he is also admitted and many investigations had done. The important positive results are high CRP 31.5 (Normal: < 5), numerous Pus Cells in Stool Analysis and negative for Rotavirus. And after around 10 days, the patient readmitted in our hospital with complain of watery diarrhea, anorexia, fatigue, weight loss and with marked abdominal distention. Our positive results was Hypoalbuminemia with S.Albumin of 27g/L (N: 39 - 40 g/L). S.Potassium of 2.6 mEq/L (N: 3.5-5 mEq/L) (treated with suitable replacement of Potassium) and abdominal X-ray showed Multiple Air Fluid Level.

So due to a prolonged course of symptoms around 4 - 5 weeks, we collect all the information and the following impressions were made:

- Chronic Diarrhea and other GI Symptoms.
- Weight loss from 30 kg to 27 kg over 4 - 5 weeks, this means a 10% loss of body weight.
- Hypoalbuminemia.
- High CRP “Inflammatory Marker”.
- Strong positive family history of IBD.

We consider the diagnosis of IBD (Chon’s Disease) and we refer the patient to a tertiary hospital for definitive diagnosis.

The tertiary hospital did Upper and Lower GI Endoscopy with multiple Biopsies and result showed:

- Upper GIT: Revealed pangastritis with severe panduodenitis and duodenal erosions and non-specific antral gastritis. *Helicobacter pylori* is negative.

- Colonoscopy: Normal findings.

- Biopsy revealed picture suggestive early picture of IBD, showing crypt abscess and cryptitis with crypt distortion in the terminal ileum, colon is normal.

- CT Enterography: No CT findings suggest active inflammatory bowel disease.

- Some important laboratory investigations to rule out celiac disease: (Tissue endomesium AB-IgG: negative, tissue transglutaminase AB-IgA: negative - Total IgA within normal limits). TB negative, CMV negative, ANCA = negative ASCA = pending.

*Figure 1*
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So, the patient diagnosed as having Crohn's disease and seizure disorder and treated with:

- Methalazine
- Modulen IBD powdered feed with diet modification

The patient discharged from the tertiary hospital on 26/2/2019 with a stable general condition, good activity, no fever and no diarrhea with weight gain of 2 kgs (BW = 29 kg).

Discussion

Inflammatory bowel disease

Genetically susceptible host

- 100 Loci associated with Chron's and UC both of which involve the innate and adaptive immune system.

Leads to abnormal immune response

- The intestinal immune system role is to:
  - Tolerate commensal Microorganism
  - Protect against potential pathogen in IBD, there is an imbalance between these two functions.
  - The innate immune system (Neutrophils, Macrophages, etc.) infiltrate into the Lamina Propria of the Intestines.
  - Also, the adaptive immune system (T and B lymphocytes) has an exaggerated response by activation of certain CD4+ T-Helper cells (Th1-Th2-Th17) leads to poorly regulated secretion of pro-inflammatory cytokines: TNFα, IL1β, Interferon γ - IL23.

To environmental factors mostly intestinal bacteria

- It is thought that the normal bacteria in the gut activate the immune response to provide constant immune system stimulation.

When to consider IBD in children?

- Abdominal pain and bloody diarrhea, unexplained Fever and/or weight loss.
- Hypoalbuminemia, Anemia, Thrombocytosis and/or Inflammatory Markers

![Figure 2](image)
### Crohn's Disease

**Clinically**
- Oral Aphthous Ulcers
- Upper GI complaints “vomiting”
- Persistent unexplained fever
- Poor growth + Fatigue +
- Anorexia
- Delayed puberty

**Extra-intestinal Manifestations**
- Perianal Disease
- Joint Disease
- Erythema Nodosum

**Laboratory Investigations**
- Hypoalbuminemia
- ESR
- CRP
- ASCA: Antisaccharomyces cerevisiae Antibody with
- isolated small bowel disease

**Endoscopy**

**Extent of Inflammation**
- Anywhere in the GI Tract

**Pattern of Inflammation**
- Patchy with normal mucosa in between diseased tissue (skip lesions) associated with rectal sparing

**Appearance of Inflammation**
- Discrete aphthous ulcers
- Linear ulcers causing cobblestoning deep ulcers

**Pathologically**
- Granulomas Formation

**Best Type of Endoscopy**
- Colonoscopy with Ileal Intubation
- Esophagogastroduodenoscopy “EGD”

**Imaging**
- Upper GI with small bowel follow through
- Identifies ulcers – narrowing and fistula in the small bowel

**CT**
- Identifies small bowel wall edema mesenteric/creeping fat
- Fluid collections
- Stricture, fistula and perianal disease

**MRI**
- Identifies small bowel wall edema mesenteric/creeping fat
- Fluid collections
- Stricture, fistula and perianal disease
- Without radiation

**Video Capsule Endoscopy (VCE)**
- Documents presence and extent of inflammation and ulceration in the small bowel
- 2% risk of pill retention

**Small Bowel Enteroscopy**
- Need a special equipment and training

### UC

**Clinically**
- Diarrhea
- Bleeding
- Anemia

**Extra-intestinal Manifestations**
- Primary Sclerosing
- Cholangitis
- Pyoderma Gangrenosum

**Laboratory Investigations**
- CRP
- Anemia
- pANCA

**Endoscopy**

**Extent of Inflammation**
- Limited to Colon

**Pattern of Inflammation**
- Diffuse, generally begins at the rectum and spreads proximally often with abrupt transition from diseased to normal appearing tissue

**Appearance of Inflammation**
- Erythema
- Loss of vascular pattern
- Friability superficial ulcers
- ± Inflammatory Polyps

**Pathologically**

**Imaging**
- Normal small bowel

**CT**
- Thickening of the colon with lead pipe appearance

**MRI**
- Thickening of the colon with lead pipe appearance

**Video Capsule Endoscopy (VCE)**
- Limited role in UC

**Small Bowel Enteroscopy**
- Limited role in UC
Treatment of CD

1. The current goals of treatment is:
   - Induce remission.
   - Maintain a prolonged remission.
   - Minimizing Drug toxicity.

2. At long time:
   - Preventing relapses.
   - Optimizing growth and pubertal development.
   - Improving quality of life.

Conventional therapy

- Aminosalicylate
- 5-ASA, the use isn’t supported.
- Only for mild terminal ileal or mild chronic disease of the colon.
- Mesalamine
- 50-100 mg/kg.
- Maximum: 3 - 4g (divided by TID or BID).
- How does it work: inhibits synthesis of Leukotriene, a potent chemotactic agent. Also inhibit the activation of NF-kappa B which is a potent mediator in inflammatory response.
- Steroids
- To induce remission that quickly weaned
- A special controlled ileal - release formulation of Budesonide with local anti-inflammatory activity.
- Immnomodulators:
  - Azathioprine
  - 6 mercaptopurine Thiopurines
  - Methotrexate

Nonconventional Therapy

Nutrition:

- EEN (Exclusive Enteral Nutrition): elemental, semi-elemental, polymeric.
- Used for induction and maintenance of remission, when used as exclusive or predominant form of nutrition.
- Mechanism of action: by modification the microbiota of the gut lumen → reduction of the antigenic load → bowel rest.
- The main drawback is the poor compliance, "need therapy for 6-8 weeks" and require NGT.
- Probiotics are the friendly bacteria that usually are beneficial to the host when available in adequate quantity.
- The best studied probiotics are:
  - Lactobacillus rhamnosus (LGG)
  - Bifidobacterium lactis

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- *Streptococcus thermophilus*
- There is an increasing evidence of their usefulness in IBD especially for prevention of recurrent pouchitis in patient who have undergone ileal pouch - anal anastomosis.

**Biologics**

1. **Infliximab**: It is a monoclonal anti TNFα antibodies IgG1, given IV effective in inducing and maintaining remission. We give 3 doses induction 5 mg/Kg/IV at 0,2,6 weeks followed by 5 mg/kg every 8 weeks.
   - **Side Effects**:
     - Blood Dyscrasias
     - Serious infection like reactivation of Hepatitis B, or tuberculosis
     - Lymphoma or solid tissue cancer
     - Drug induced lupus
     - Demyelinating CNS Disorder
     - Liver injury
     - Hepatosplenic T-cell Lymphoma especially when combined with thiopurines.

3. Certolizumab.

**Antibiotics**

- Used especially in CD with perianal involvement used as adjunctive intermittent therapy.
- Metronidazole 500 mg BID + Ciprofloxacin 500 mg BID (For 8 weeks) or Metronidazole 250 mg TID + Ciprofloxacin 500 mg BID (For 10 weeks) (Adult Protocols).

**Surgery**

- The main indications are complications especially stricture, fistula or perforation
- Or a failed medical therapy
- Weight and height catch up are markedly significant in patient undergoing surgery within 3 years from CD Diagnosis.

**Disease activity**

Figure 3

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### How do I know if my patient with IBD is Truly in Remission and doing well??

#### Clinical remission

<table>
<thead>
<tr>
<th>Pedicatric Chron's Disease Activity Index (PCDAI)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Abdominal Pain</strong></td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Mild: doesn’t interfere with activities</td>
</tr>
<tr>
<td></td>
<td>Moderate/Severe: daily, longer lasting, affects activities, Nocturnal</td>
</tr>
<tr>
<td><strong>Number of Stool / Day</strong></td>
<td>0 - 1 Liquid Stools No Blood</td>
</tr>
<tr>
<td></td>
<td>2 - 5 Liquid or ≤ 2 Semi formed with small blood</td>
</tr>
<tr>
<td></td>
<td>≥ 6 liquid, gross blood or nocturnal diarrhea</td>
</tr>
<tr>
<td><strong>General Well-Being</strong></td>
<td>Well</td>
</tr>
<tr>
<td></td>
<td>Below Par</td>
</tr>
<tr>
<td></td>
<td>Very Poor</td>
</tr>
<tr>
<td><strong>Weight</strong></td>
<td>Weight gain</td>
</tr>
<tr>
<td></td>
<td>Weight loss 1 - 9%</td>
</tr>
<tr>
<td></td>
<td>Weight loss ≥ 10%</td>
</tr>
<tr>
<td><strong>Height</strong></td>
<td>Height velocity ≥ - ISD</td>
</tr>
<tr>
<td></td>
<td>Height velocity between – ISD and -2SD</td>
</tr>
<tr>
<td></td>
<td>Height velocity ≤ -2SD</td>
</tr>
<tr>
<td><strong>Abdomen</strong></td>
<td>No tenderness, No mass</td>
</tr>
<tr>
<td></td>
<td>Tenderness or mass without tenderness</td>
</tr>
<tr>
<td></td>
<td>Tenderness or definite mass</td>
</tr>
<tr>
<td><strong>Peri-rectal Disease</strong></td>
<td>None or asymptomatic tags</td>
</tr>
<tr>
<td></td>
<td>1-2 indolent fistula Scant drainage and no tenderness</td>
</tr>
<tr>
<td></td>
<td>Active fistula or abscess</td>
</tr>
<tr>
<td><strong>Extra-intestinal Manifestations</strong></td>
<td>Non</td>
</tr>
<tr>
<td>• Fever ≥ 38.5 °C for 3 days over past week</td>
<td>1</td>
</tr>
<tr>
<td>• Arthritis</td>
<td>≥ 2</td>
</tr>
<tr>
<td>• Uveitis</td>
<td></td>
</tr>
<tr>
<td>• Erythema Nodosum</td>
<td></td>
</tr>
<tr>
<td>• Pyoderma</td>
<td></td>
</tr>
<tr>
<td>• Gangrenosum</td>
<td></td>
</tr>
<tr>
<td><strong>HCT</strong></td>
<td>Normal: 36-51</td>
</tr>
<tr>
<td><strong>ESR</strong></td>
<td>Normal: 0-20</td>
</tr>
</tbody>
</table>

**Score**

- < 10 → Remission
- 10-30 → Mild
- 35-65 → Moderate
- >65 → Severe Disease
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Deep remission

- Means actual healing of intestinal mucosa and surrounding tissue and this will be associated with better long-term outcomes.
- Serum biomarkers of disease activity
- CRP: correlates with endoscopic disease activity (but not always).
- ESR: slowly changed.
- Fecal Biomarkers:
  - Calprotectin- A protein that binds Ca and Zn and the most common protein present in granulocyte cytoplasm
  - Lactoferrin- An iron binding protein present within Neutrophils
- Both have more than 80% sensitivities and specificities and are superior to serum markers in reflecting intestinal inflammation.
- Imaging
  - MRE: Magnetic Resonance Enterography - for entire GI tract.

What routine health maintenance is needed for the Pediatric IBD patient

- 25% of patient with CD and UC present before the age of 18 years.
- The patient with IBD should routinely be seen by pediatric gastroenterologist every 3 - 6 months.

Monitoring growth and nutritional status

4. Pubertal stage.

Vaccinations

1. Live attenuated vaccines (MMR, VZV, Rota, Intranasal Influenza, BCG, Oral Typhoid)
   - Contraindicated in children on systemic corticosteroids ≥ 2 mg/kg/day defer for atleast one month after you stop steroids.
   - Contraindicated in children receiving biologics like infliximab.
   - Contraindicated in children receiving immunosuppressive medications like azathioprine.
   - Household or other close contacts of children on these immunosuppressive medications can safely receive Live Viruses Vaccines.
2. Inactive vaccines (DTP, TdP, Hib, IPV, HB A, B, etc.)
   - HPV which is important in males and females with IBD.
   - Safe.
   - Annual influenza vaccine is recommended.
3. Screening for latent tuberculosis with TST (Tuberculin Skin Test)
   - Should be done:
   - Routinely.
   - Before starting anti-TNF therapy.
   - Any TST ≥ 5 mm considered positive in an immunosuppressed patient.
Screening for extra-intestinal manifestations of IBD

- Anemia.
- Eyes: Uveitis, iritis, glaucoma, retinal vasculitis, optical neuritis - "Annual Evaluation".
- Oropharynx: Aphthous ulcers, aphthous stomatitis.
- GI: Perianal skin tag or fistulas, pancreatitis.
- Liver: Primary sclerosing cholangitis, autoimmune hepatitis.
- Renal: Kidney Stones.
- Endocrine: Amenorrhea (Primary or Secondary).
- Joints: Arthritis, arthralgias, ankylosing spondylitis.
- Skin: Erythema nodosum, pyoderma gangrenosum, psoriasis.
- Bone: Osteopenia, osteoporosis, compression fractures.
- Neurologic: Peripheral neuropathy, meningitis, Pseudo tumor cerebri, cerebral vasculitis, migraine.

Psychological well-being in IBD

- Depression and anxiety ≈ 31% more than healthy children (called internalizing symptoms).
- Irritable bowel syndrome can coexist with IBD.
- Also, patients with IBD has a more social problems (social phobia, panic attack) and these are more common in boys than in girls.
- No effect of IBD on the child academic performance and educational attainment.
- The overall impact of the disease on the one’s life which is also known as “Health Related Quality of Life (QOL)”.
- Refer to CAMH professionals, the best and most effective therapeutic modality is CBT (Cognitive Behavioral Therapy) [1-4].

Conclusion

- Chron’s Disease is a chronic disorder that is associated with high morbidity and low mortality.
- Symptoms tend to recur despite treatment and often without apparent explanation
- Weight loss and growth failure can usually be improved with treatment and attention to nutritional needs.
- Up to 15% of patients with early growth retardation secondary to Chron’s Disease have a permanent decrease in Linear growth.
- Osteopenia is particularly common in those with chronic poor nutrition and frequent exposure to high doses of corticosteroids.
- Some of the extraintestinal manifestation can, in themselves, be major causes of morbidity including sclerosing cholangitis, chronic active hepatitis, pyoderma gangrenosum, and ankylosing spondylitis.

Bibliography


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