Common Mucosal and Luminal Disorders

Dr. Kadakkal Radhakrishnan, MD
MRCP (UK), MRCPCH, FAAP

Objective

- Discuss the etiology and pathophysiology of common mucosal and luminal gastrointestinal disorders
- Discuss briefly their clinical features and workup
- Discuss the various treatment options

Case 1- 19 month Caucasian female with poor weight gain

Her weight has dropped from the 50th percentile to the 5th since 10 months of age.
Her appetite is decreased, she is more irritable lately and her BMs are loose, 3-4 /day.
Her exam is remarkable for a protuberant abdomen and loose folds of skin in her arms and thighs.
CBC shows microcytic, hypochromic anemia, normal WSR, CRP, CMP, UA and stool hemoccult is negative
Likely cause here would be?

- A- Cow milk protein allergy
- B- Celiac disease
- C- Ulcerative colitis
- D- Immune deficiency
- E- Ascariasis
- F- All of the above

Celiac disease

- Otherwise called gluten sensitive enteropathy
- Permanent intestinal intolerance to dietary wheat protein gliadin and related protein
- Occurs only in genetically susceptible individuals

Epidemiology

- In US
  - By persistent IgA transglutaminase positivity was 1/104
  - 1/105 IgA anti-endomysial
- Sweden- 1/77- 1/285
- Finland-1/99 (biopsy)
- Rare in Asia and Africa (very rare)
  - Highest by serology in sub-Saharan Africa, 1/60

NIH consensus on celiac disease, Gastroenterology 2005
**Pathogenesis**

- Genetic susceptibility
  - HLA DQ-2 and DQ-8: > 90% of celiacs but seen in 30% of Caucasians
- Exposure to incriminating proteins
- Other susceptibility genes?
- Incites T cell mediated response
- Inflammation and mucosal change

---

**Dietary factor**

- Three main cereals
  - Wheat (Gliadin)
  - Barley (Hordeins)
  - Rye (Secalins)
- All fall under the tribe Triticeae
- Oats rarely activates celiac disease—plays a role in a small fraction of patients
  - Separate tribe - Avineae
- All above proteins are structurally similar and the last 33 amino acids are resistant to digestion

---

**Overall pathogenesis of CD**
**Clinical features**

- **Classic presentation**
  - FTT
  - Loose stools/diarrhea
- **Common presentation**
  - Most patients are asymptomatic
  - Incidentally diagnosed by serology
- **Refractory iron deficiency in adults**

**Uncommon presentations**

- Constipation
- Osteoporosis
- Fat soluble vitamin deficiency
- Elevation in transaminases
- Depression
- Dermatitis Herpatiformis

**Clinical spectrum of CD**

[Diagram showing the clinical spectrum of CD with classic or atypical symptoms, Abnormal serology, Histological disease, Normal Mucosa, Genetic susceptibility, DD and/or IBD.]
**Diagnosis- serology**

- **Screening tests**
  - Tissue transglutaminase- TTG-IgA
    - Sensitivity > 90% Specificity > 95%
  - Anti-endomysial antibody –IgA
    - Sensitivity > 95% Specificity > 98%
  - Total IgA
  - Gliadin
    - Relatively higher false positivity

---

**Genetic testing- HLAs**

- Negative HLA DQ2 and DR8 essentially rules out celiac disease
- Positive testing for either gene or for both does not rule in celiac disease
  - HLA DQ2 homozygous- 30 times higher risk for celiac than general population
  - HLA DR8 homozygous- 10 times higher risk for celiac
  - HLA DQ2/ HLA DR8- 14 times higher risk

---

**Definitive diagnosis**

- By endoscopy and small bowel biopsy
- Changes
  - Subtotal to total villous atrophy
  - Increased round cell infiltration
Normal duodenal histology

Celiac disease histology

Other causes of Villous Atrophy

- Severe Crohn's disease
- Immune deficiency
  - Cell mediated- congenital or acquired
- Radiation enteritis
- Severe Cow Milk Protein Allergy
- Giardial infection
### Treatment

- Complete gluten free diet
  - Life long
- No sharing of cooking utensils
- Follow up with endomysial antibody
- Oats may be introduced after 6 months
- Follow up
  - labs once every year- CBC, CMP and serology
  - Bone density every 2-3 years

### Associations with other diseases

- Type 1 diabetes
  - 7% of patients have CD
- Down syndrome
  - Up to 7% have CD
- Hypothyroidism
  - 20% of CD may have hypothyroidism
- T cell lymphoma of the gut
  - Relative risk is 3 in CD patients

### Case 2- 6 week old male infant

- Irritable for < 1 day, later develops seizure-generalized
- Treatment started for sepsis
- CT scan of head showed Rt- parietal lobe hemorrhage
- Required surgery on day 3 of life for meconium ileus
- Patient had mild conjugated hyper bilirubinemia- 4.8/2.7
- AST- 202 ALT 313 PT- 39 sec PTT 42 sec
What simple test can you order to diagnose?

- A-Factor V assay
- B-HIDA scan
- C-Sweat chloride
- D-USS of abdomen
- E-Stool 72 hr fat estimation

Cystic fibrosis

- One of the common genetic disease of the pancreas
- Prevalence
  - Caucasian - 1/2500
  - African Americans - 1/15000
  - Asians 1/100000

Mutations

- Over 1400 mutations
- Homozygous delta 508 the most common
- 99% of children with homozygous delta 508 mutation are pancreatic insufficient
- 70% of compound delta 508 mutation are pancreatic insufficient
Pancreatic insufficiency

- Untreated patients often have greasy stools
- Severe malabsorption may lead to failure to thrive and hypoalbuminemia
- Fat soluble vitamin deficiency
  - Vitamin E: hemolysis
  - Vitamin K: coagulopathy
- Patients may compensate with increased intake
  - Decompensate when oral intake decreases with intercurrent infections

Other GI manifestations

- Meconium ileus
  - 10-20% of CF neonates
- Distal Intestinal Obstruction Syndrome
- GERD and gastric acid hypersecretion
- Rectal prolapse
- Fibrosing colonopathy
  - Seen with lipase supplementation more than 20,000 IU/kg

CF liver disease

- Hepatic steatosis is the most common finding
  - ~ 60% patients
- Neonatal cholestasis
  - Jaundice
  - Late onset hemorrhagic disease
**CF liver disease**

- **Focal biliary cirrhosis**
  - 10% at 3 months of age to 70% of young adults
  - No clinical findings
- **Multilobular biliary cirrhosis**
  - 5% of CF patients
  - Evolves into PHT

**GI work up for CF**

- Sweat chloride and mutation analysis
- 72 fecal fat estimation (and yearly)
- Fat soluble estimation (and yearly)
- USS of abdomen (yearly)
- Nutritional evaluation (every 6 months)

**GI Management**

- Close follow up
- Ensure adequate intake
  - Energy 120% RDA with 40% as long chain fatty acid
  - Protein 100% RDA
- Enzyme supplementation- 5000 – 10,000/kg for lipase
- Fat soluble supplementation
  - 5-10 times the RDA
Case 3

During teaching rounds you come across a patient with Rota virus diarrhea. Patient continues to have diarrhea day 10 after onset. You tell the residents that the diarrhea is secondary to malabsorption due to loss of cells lining the villi. One smart resident asks you how long it would take for intestinal cell to turn over!!

Average rate of cell turn over in the intestine is?
- A-1 day
- B-2-3 weeks
- C-3-5 days
- D-1-2 months
- E-8-10 days

Lactose intolerance

- Prototype for malabsorption due to lack of brush border enzymes
- Due to deficiency or inactivity of lactase/phlorizin enzyme
- Almost all Asians and American Indians, 80% of African americans and 50% of Caucasians are lactose intolerant
Lactose intolerance

- Primary lactose intolerance is rare and mainly seen manifestation—gas, bloating, and diarrhea
- Women are more symptomatic than men.
- Symptoms become more evident as people become older

Diagnosis of lactose intolerance

- Breath test with lactose
  - Dose is 50 mg—equivalent to 4 cups of milk
  - Patients blow into the machine every 15 minutes
  - Rise in breath H2 over 20 PPM is diagnostic
  - Test positive in 90%, rest may have symptoms
- Patients to fast for 6 hours before test
- No antibiotics within 10 days of the test

Secondary lactose intolerance

- Primary hypolactasia never diagnosed before 5 yrs of age
- Seen after
  - Rota virus gastroenteritis or other post infective states
  - Celiac disease
  - Crohn’s disease
  - Immune deficiency
**Congenital lactase deficiency**

- Very, very rare
- Presents in the newborn period with profuse diarrhea in breast fed babies
- Reducing substances are positive in stool
- Mostly seen in the Scandinavian region
- Diagnosis is by elimination of lactose containing diet

**Other brush border enzymes in CHO metabolism**

- Sucrase / Isomaltase
  - Second common disaccharidase deficiency
  - Can present any time though most infants present soon after exposure to sucrose
  - Sucrose breath test for diagnosis or enzyme assay after biopsy
- Maltase/ Glucoamylase
- Trehalase

**Patient ‘X’**

- 14 year old Caucasian male
- Having trouble with swallowing for 2 years
- Today, having difficulty handling secretion after eating steak - “It is stuck”
- Previously - similar history in Buffalo a year ago
- Otherwise healthy except for mild seasonal allergy
- No heart burn
The likely possibility?

- A-Congenital anomaly of the esophagus
- B-Mediastinal mass
- C-Mitral stenosis
- D-Eosinophilic esophagitis
- E-GERD with stricture
- F-Functional

EGD for ? FB removal

Eosinophils and GI system

- Eosinophils home to GI tract in utero
  - Occurs even in germ free setting
- May have a role in GI development
  - Suggestions from its role in mammary glands
- Can present antigens to the T cells
- Can also stimulate T cells
- Anti-parasitic effect
### Eosinophilic Esophagitis

- **Primary**
  - Atopic
  - Nonatopic
  - Familial (10%)

- **Secondary**
  - Eosinophilic disorders
    - EGE
    - HIE
  - Non eosinophilic
    - Drugs
    - Infections
    - GERD
    - Esophageal leiomyomatosis
    - Vasculitis

### Primary EE

- Prevalence-
  - 3.5% of children with GERD, 7% with esophagitis
  - 20% with dysphagia and 50% with unexplained dysphagia
  - 70-95% of children unresponsive to PPI may have EE
  - Data in adults not clear

### Eosinophilic Gastrointestinal Disease - symptoms

- FTT
- Abdominal pain
- Irritability
- Gastric dysmotility
- Vomiting & diarrhea
- Dysphagia
- Microcytic anemia
- Protein loosing enteropathy
Workup for EGID

- H&P
- IgE
- ESR
- Skin testing, IgE RAST
- R/o parasites- stool studies, intestinal aspirates or antibodies
- EGD and colonoscopy
- ? Hyper IgE
  - Bone marrow
  - Serum tryptase
  - Vitamin B12
  - ECHO
  - Genetic analysis

Endoscopic findings

- Furrows
- Vertical lines
- Corrugations
- Rings- looks like trachea
- Adherent whitish plaques
- Crepe paper mucosa
- Strictures

Treatment

- Steroids
  - Oral steroids
  - Oral inhaled steroids- Fluticasone
- Montelukast
- Ketotifen
- Mepolizumab
Answers

- Case 1-B
- Case 2-C
- Case 3-C
- Case 4-D