Gastrointestinal, Liver and Nutritional Problems in Fanconi Anemia

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GI problems in FA

- 7% have gastrointestinal tract abnormalities
- GI symptoms common
  - Poor oral intake in some; overweight in others
  - Nausea
  - Abdominal pain
  - Diarrhea
- Liver adenomas associated with androgen treatment
- Complications of HSCT

Some conditions causing GI symptoms

- Complications of anatomic gastrointestinal abnormalities
  - Strictures
  - Obstructions
- Chronic inflammation/infection
  - Diarrheal disease
  - Small bowel overgrowth
- Medication side effects
- Neurologic/behavioral problems

Gastroesophageal reflux

- Commonly associated with esophageal atresia
- Reflux may become more common with age
- Medical management is essential to reduce complications
- Many require anti-reflux surgery

Symptoms of GER

- Heartburn
- Abdominal pain
- Excessive burping, hiccuping
- Poor appetite, vomiting
- Poor sleep, nightmares

Small bowel overgrowth

- Proliferation of bacteria in the small intestine
- Bacteria in small intestine may be changed by antibiotic therapy
- Associated with stasis
  - Impaired peristalsis
  - Abnormal anatomy
  - Blind loop

Symptoms of SBO

- Excessive bowel gas
- Diarrhea
- Steatorrhea
- Bloating
- Abdominal pain

- Anemia
- B12 deficiency
- Malabsorption
- Weight loss/Failure to gain weight

Rome II criteria

- "Abdominal pain for at least 12 wk, *which need not be consecutive*, in the preceding 12 mo."
- Applies to:
  - Functional dyspepsia
  - Irritable bowel syndrome
  - Functional abdominal pain
  - Abdominal migraine

Functional dyspepsia

- Persistent or recurring upper abdominal pain
- No evidence of organic disease
- No relief with defecation
- No change in stool frequency or form

IBS

- Abdominal pain characterized by 2 of the following 3:
  - Relieved with defecation
  - Onset associated with change in stool frequency
  - Onset associated with change in stool form
- No structural/metabolic cause
- Supported by:
  - Abnormal stool frequency
  - Abnormal stool form
  - Abnormal stool passage
  - Mucus passed in stool
  - Bloating or feeling of abdominal distention

Functional abdominal pain

- Nearly continuous pain in school age child
- Rare relief of pain with physiologic events
- Some loss of daily functioning
- Pain that is not feigned
- No evidence of other GI disorder to explain pain

Evaluation of gastrointestinal symptoms

- Good history and physical exam
- Blood for CRP, ESR, zinc level
- Stool for ova and parasites, giardia, cryptosporidium
- Urine culture
- Hydrogen breath tests
- Endoscopy with biopsy
- Avoid radiographic imaging, if possible

Alarm symptoms and signs

- Involuntary weight loss
- Deceleration of linear growth
- Gastrointestinal blood loss
- Significant vomiting
- Chronic severe diarrhea
- Unexplained fever
- Persistent right upper or right lower quadrant pain
- Family history of inflammatory bowel disease

Suggested treatment options

- Acid suppression: Proton pump inhibitor
- Gastric motility-promoting agents
  - Erythromycin
- Antinausea agents
  - Ondansetron (Zofran)
- Treatment of small bowel overgrowth
  - Metronidazole (Flagyl)
- Supplemental nutrition

Treatment of chronic abdominal pain

- Effective
  - Cognitive behavioral therapy for recurrent abdominal pain
  - Famotidine for dyspepsia
  - Peppermint oil for IBS
- No evidence for benefit: Added dietary fiber, lactose-free diet, lactobacillus GG, analgesics, antispasmodics, sedatives, antidepressants

Poor growth in FA

- Short stature associated with genetic defect: >50% have shorter than average height
- Multiple endocrine abnormalities
- Inflammatory disease
- Poor oral intake

Malnutrition

- 22% children underweight for height
- Measure height and weight at each visit
- Failure to thrive
  - Weight for height persistently less than 85%
  - BMI persistently < 3 d percentile for age
  - Persistent decline in either measurement

Appetite stimulants

- None tested directly in FA patients
- Must evaluate first for treatable causes of poor intake
- Weight gained is usually lost when drug is stopped

Appetite Stimulants

- Cyproheptadine (Periactin)
  - Minimal weight gain
  - Well tolerated
  - Initial sleepiness
- Megestrol acetate (Megace)
  - Minimal weight gain
  - Adrenal insufficiency, glucose intolerance

Plan for supplemental feeds

- Nutritional goals
  - Normal growth for genetic potential
  - Energy to meet demands of daily living
  - Adequate reserve to face short-term malnourishment during acute illness
- Lasting benefits may require long-term therapy.
- Supplementation through GI tract is preferable to supplementation by IV

Overweight

- 27% FA patients overweight or obese
- Associated with abnormal lipids
- Associated with diabetes
- Although failure to thrive has been a significant problem in FA, over-nutrition and metabolic syndrome are now being seen.

Giri, et al. J Clin Endocrinol Metab 2007

Managing OW/OB

- 6-day diet diary to initiate dietary intervention
- Explore potential for exercise
- Try to explore the family eating habits

5-2-1-0

- "5 a day" fruits and vegetables
- Less than 2 hr/day of screen time
- At least 1 hour of moderate activity each day
- No sweet drinks-0 pop, juice, Kool-ade, sports drinks, ect

GI conditions to consider before HSCT

- Previous use of androgens: US/CT/MRI liver
- Chronic abdominal pain: consider endoscopy to detect potential bleeding or infectious risks
- Chronic diarrhea: screen for infections
- Established liver disease

Long-term concerns after HSCT

- Liver
  - Chronic GVHD
  - Chronic viral hepatitis
  - Iron overload
- Intestine
  - Chronic GVHD with diarrhea and weight loss

Gastrointestinal graft-versus-host disease

- Complication of HSCT
- Mild to very severe damage to lining of GI tract
- Severe, watery diarrhea and/or nausea and vomiting
- Liver may also be involved with jaundice and reduced function

Gastrointestinal GVHD in FA patients

- Incidence
  - Early data suggested increased incidence of GVHD in FA patients
  - Risk and severity have decreased as HCT has improved
- May increase risk of squamous cell carcinoma

Hepatic complications of androgens

- Hepatic adenoma 6-7%
- Peliosis
- Potential complications
  - Intrahepatic bleeding
  - Hepatoma
- Screening/Management

Screening for androgen-related liver disease

- Liver enzymes every 3 months
- Ultrasound every 6 months

Secondary iron overload

- May lead to organ damage: liver, heart, pancreas
- Screening
  - Serum iron
  - Transferrin saturation
  - Ferritin
- Must confirm iron overload with liver biopsy or MRI

Vitamins for cancer prevention

- Speculation that FA is an oxidant stress disease
- Diets high in vegetables and fruits may reduce the risk of some cancers
- Individual vitamin preparations do not show similar results
- Some vitamins are toxic in excess
  - Vitamin A
  - Vitamin D
  - Vitamin C
  - Niacin
- Controlled clinical trials are essential to avoid unnecessary toxicity

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