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 < 3rd 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.

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, etc
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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