Extraintestinal Manifestations of IBD

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Why Other Organs Involved in IBD?
IBD - Extraintestinal Manifestations Related to Disease Activity

Aphthous stomatitis

Episcleritis and uveitis

Arthritis

Vascular complication

E. nodosum

P. gangrenosum
Organ Involvement

- Bones, Joints
- Eyes
- Skin
- Liver, Bile Ducts, Gallstones
- Kidney
- Pancreas
Peripheral Arthritis

- Seen in 25-40% of patients, more in CD
- Knees, ankles, wrists, elbows commonly affected – warm, tender
- Can be associated with arthralgia
- Can be associated with erythema nodosum, uveitis
- Rheumatoid factor negative; not erosive or deforming arthritis
- Treatments: Treat the bowel disease – mesalamine (sulfasalazine), steroid, pain medication
Peripheral Arthritis

- Monoarticular
- Asymmetrical
- Large > small joint
- No synovial destruction
- No subcutaneous nodules
- Seronegative
Axial Arthritis

- Ankylosing spondylitis, Sacroiliitis – low back pain, pelvic bone pain, spine pain
- HLA-B27 +
- Bone inflammation can lead to bone fusion and skeletal deformity
- Usually need aggressive treatment for IBD, including TNF Ab, pain management, steroid joint injection
- May not be associated with bowel inflammation
Ankylosing Spondylitis
Sacroiliitis
Osteoporosis

**Major complications from:**
1. Prolonged steroid treatment - dose, duration
2. Extensive small bowel inflammation - malabsorption
3. Small bowel resection (short bowel syndrome) – malabroption of Ca\(^{2+}\), Vit. D

- Important to get bone density scan every 1-2 years in active IBD
Site of Nutrient Absorption

- Esophagus
- Stomach
- Duodenum: fat-soluble vit. A & D, calcium, magnesium, iron
- Jejunum: disaccharides, sucrose, maltose, lactose
- Ileum: water-soluble vit.: thiamine, pyridoxine, riboflavin, folic acid, ascorbic acid
- Colon: potassium, short-chain fa & volatile fa from fiber digestion

- Ethyl alcohol
- Fat (i.e., short-chain fa, long-chain fa, partially split glycerides)
- Proteins & amino acids
- Vit. B_{12}
- Water
- Sodium chloride

Pipkin & Gadacz, p282, Nutrition Considerations in the ICU, 2002
Osteopenia Risk Factors

Baseline
- Ethnicity
- Family History
- Lifestyle and dietary habits
- Body habitus
- Reproductive history

Disease related
- Inflammation
  - Cytokines (CD > UC)
- IBD medication
  - Corticosteroids
Causes of Bone Mineral Loss

- Calcium and vitamin D malabsorption
- Coexisting conditions: menopause, inflammation
- Medications: steroids, cholestyramine
- Parenteral nutrition
Bone Health in IBD

Osteoporosis is associated with:

- Prior or current steroid use
- Family history of osteoporosis
- Tobacco & alcohol use
- Menstrual loss
- Extensive ileal disease or resection
- Inadequate calcium intake
- Prolonged active disease
- Liver disease
Treatment of Bone Loss

• Supplement Calcium, Vitamin D
• Exercise (weight bearing, walking)
• Treat underlying disease
• Don’t smoke, avoid excessive alcohol
• Eliminate offending medications
• Consider using estrogen, bisphosphonates
Crohn’s Disease

Treatment of Low Bone Mineral Density

Lumbar spine

Femoral neck

Mean % change in BMD

Alendronate 10mg/d

Placebo

Month

Haderslev KV et al., Gastroenterology, 2000; 119:639
Eye

- Ocular inflammation seen in 1.9% - 13% IBD
- More common in Crohn’s disease > UC
- Can see anterior uveitis, scleritis, keratitis, retinal vasculitis
- Anterior Uveitis – pain, redness, photophobia
  - More common in HLA-B27 + pts
  - Not reflect IBD activity
- Scleritis – discomfort, episcleral inflammation
- Treatment: Steroid eye drop, Ophthalmology evaluation.
UC - IBD Systemic Complications
Skin

- **Pyoderma gangrenosum** – painful ulceration with purple borders; induced by trauma
  - May not reflect that of bowel activity
- **Erythema nodosum** – painful nonulcerated nodules on lower extremity
  - Can also be seen in sarcoid, drugs, rheumatologic disease, streptococcal/viral infection
  - Skin lesion reflect that of bowel activity
- **Sweet’s syndrome** – painful plaques on the head, neck, upper extremities, can be vesicles
- **Aphthous stomatitis** – painful oral ulcers; associated with active IBD
- **Vasculitis** – affect superficial blood vessels; may be palpable purpura on lower extremities; associated with active IBD
Erythema Nodosum
Pyoderma Grangrenosum - Ankle
UC - IBD Systemic Complications
Sweet’s Syndrome

Aphthous Stomatitis (oral ulcers)

Vasculitis
Skin Cancer

- Both non-melanoma skin cancer (NMSC) and melanoma can be seen in IBD patients
- Kappelmen et al. Danish Study, 2014:
  - NMSC risk: CD 2.1, UC 1.8 vs non-IBD pt
  - Melanoma risk: CD 1.4, not in UC
- Singh et al. Mayo Clinic Study, 2014: Melanoma only
  - Melanoma risk: 37% higher than non-IBD pt.
  - Before 1998 (pre-biologic era): 52% higher risk
  - After 1998 (post-biologic era): No significant risk (limited study)
  - CD 1.80 vs UC 1.23
Skin Cancers

• NMSC risk higher in thiopurine treatment (6-mercaptopurine, azathiopurine) by increasing photosensitivity to ultraviolet A (UVA)
  - higher risk in longer treatment duration

• Prevention:
  1. Sunscreen lotion, sun protection clothing
  2. Avoid tanning salon
  3. No smoking
  4. Get regular dermatology exam, careful self-exam for skin lesion
Liver, Bile Ducts

Primary Sclerosing Cholangitis (PSC)

- The most common bile duct injury seen in IBD – 2.5-7.5%
- Causes inflammation, fibrosis leading to stricture of the bile ducts
- Strong association with Ulcerative Colitis – 5-10%
- Fever, chills, abnormal LFT, RUQ abdominal pain, jaundice, dark urine, itching (pruritus)
- Slowly progressive, leading to cirrhosis, portal hypertension, liver transplantation
- May lead to cholangiocarcinoma (5-15% of PSC) & higher risk of colon cancer
Ulcerative Colitis

PSC-Associated Colitis

- Mild or subclinical colitis
- Microscopic ileitis
- High risk of colonic neoplasia
- High risk of pouchitis
- Usually pANCA positive
UC - IBD Systemic Complications
Pancreas

Pancreatitis – Multifactorial:

1. **Drug Induced** – 6-Mercaptopurine, azathioprine, steroid, mesalamine, metronidazole
   - most common cause of acute pancreatitis
2. **Duodenal Crohn’s disease** – fistula from duodenum to pancreatic duct, ulcer into duct
3. **Biliary tract disease** – Gallstone, primary sclerosing cholangitis
4. **Autoimmune** – when no other cause is found, pancreatic auto-antibodies CD>UC
5. **TPN** - ↑ Triglyceride during TPN use
Kidney stones seen up to 1-5% of IBD patients - CD>UC

- Oxalate stones – most common in small bowel CD
- Uric acid stones – most common in an ileostomy without colon; due to dehydration and acidic urine which precipitates uric acid crystals in kidney

- Risks of kidney stones – dehydration, UTI, acidic urine, steroid use (more Ca\(^{2+}\) absorption), sodium loss due to diarrhea
- Symptoms: dysuria, abdominal/flank pain, hematuria
- Rx: Good hydration, dietary oxalate restriction, treat IBD, sodium bicarbonate, anti-diarrheal medicine
Oxalate Kidney Stone Formation

Foods to Avoid
- Vitamin C
- Sorrel
- Rhubarb
- Buckwheat
- Spinach/chard
- Nuts
- Chocolate
- Berries
- Beets
- Tea
- Cola
- Celery
- Carrot

CD with surgery
<table>
<thead>
<tr>
<th>Extraintestinal Manifestations and Response to Treatment</th>
<th>Response to Treatment?</th>
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</thead>
<tbody>
<tr>
<td>Ankylosing spondylitis, sacroilitis, axial arthritis</td>
<td>No</td>
</tr>
<tr>
<td>Peripheral arthritis</td>
<td>Yes</td>
</tr>
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<td>Uveitis</td>
<td>No</td>
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<tr>
<td>Sclerosing cholangitis</td>
<td>No</td>
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<tr>
<td>Vitamin and Mineral Deficiencies</td>
<td>Manifestations</td>
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<tr>
<td>----------------------------------</td>
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<tr>
<td><strong>Vitamin B₁₂ / Folate Iron</strong></td>
<td>anemia, glossitis, cheilitis, angular stomatitis, diarrhea*, paresthesias*, ataxia*</td>
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<tr>
<td><em>Vitamin B₁₂ only</em></td>
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<tr>
<td><strong>Vitamin D</strong></td>
<td>osteoporesis, osteomalacia, paresthesias, tetany</td>
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<tr>
<td><strong>Calcium / magnesium</strong></td>
<td></td>
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<tr>
<td><strong>Zinc</strong></td>
<td>anorexia, diarrhea, rash, alopecia</td>
</tr>
<tr>
<td><strong>Vitamin A</strong></td>
<td>night blindness, dry eyes, hyperkeratosis, diarrhea</td>
</tr>
<tr>
<td><strong>Vitamin K</strong></td>
<td>ecchymoses, bleeding</td>
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<tr>
<td><strong>Vitamin E</strong></td>
<td>paresthesias, ataxia, retinopathy</td>
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