IBD: Outside the Gut

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Extraintestinal Manifestations of IBD

- IBD is primarily manifested in the gastrointestinal tract
- IBD can also have disease outside the intestines
- “Extra-Intestinal Manifestations” (EIM)
Extraintestinal Manifestations of IBD

Many causes of EIMs

- Related to underlying IBD
  - e.g., arthritis, skin, eye

- Related to loss of function (malabsorption)
  - e.g., vitamin deficiency, osteoporosis, low blood levels

- Related to treatment complications
  - e.g., damage to liver and kidneys, infections, psoriasis

Extraintestinal Manifestations of IBD

Common EIMs related to IBD

- Joints
- Eyes
- Skin
- Liver
Joints

- Most common EIM
- 30-40% of IBD patients

Subtypes
- Axial
- Peripheral

Joints: Inflammatory Back Pain

- 5-30% of IBD patients

Unlike mechanical back pain
1. Gradual onset
2. Pain at night (improved when getting up)
3. Age at onset <40 years old
4. Improves with exercise
5. Does not improve with rest
Joints: Sacroiliitis

[Images of a skeleton highlighting the sacroiliac joints]
Joints: Sacroiliitis
- 2-46% of IBD patients
- Can be asymptomatic or painful
- Can be on one or both sides
- More common among those with longer disease (>10 years) than those with shorter disease (<5 years)

Joints: Ankylosing Spondylitis
- 1-16% of IBD patients
- Fusion of vertebrae
- Limitation of spine motion
Joints: Peripheral
Joints: Peripheral

**TYPE 1**
- Fewer joints
- Larger joints (legs)
- Acute and self-limiting (typically < 10 weeks)
- Parallels IBD activity
- No permanent joint damage

**TYPE 2**
- Multiple joints
- Smaller joints
- Chronic (months to years)
- Less likely to parallel IBD activity
Joints: Peripheral

**TYPE 1**
- Fewer joints
- Larger joints (legs)
- Acute and self-limiting (typically < 10 weeks)
- Parallels IBD activity
- No permanent joint damage

**TYPE 2**
- Multiple joints
- Smaller joints
- Chronic (months to years)
- Less likely to parallel IBD activity
Joints: Treatment

Type 1 peripheral arthritis → treat underlying IBD

Type 2 peripheral and axial arthritis

- Physical therapy and exercise (stretching, aerobics)
- Ibuprofen (?) – not good for IBD
- COX-2 inhibitors (Celebrex)
- Steroids
- Sulfasalazine
- Methotrexate
- Azathioprine (Imuran), hydroxychloroquine (Plaquenil) not as effective
- Biologics may help

Joints: CARE Study

Crohn’s Treatment with Adalimumab: Patient Response to a Safety and Efficacy Study

- 945 enrolled patients with moderate-severe CD
- 187 sites in 17 European countries
- Infliximab naïve or non-responder
- Open-label trial

- Evaluated clinical effectiveness, EIM resolution, fistula healing, and safety
**Eyes**

- 6% of IBD patients

**Most common types**
- Episcleritis
- Uveitis

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**TABLE 2. Incidence of EIMs at Baseline and Week 20 in the Overall CARE Population**

<table>
<thead>
<tr>
<th>EIM</th>
<th>Baseline (N=945) n (%)</th>
<th>Week 20 (N=942) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthralgia</td>
<td>445 (47.1)</td>
<td>252 (26.8)</td>
</tr>
<tr>
<td>Arthritis</td>
<td>82 (8.7)</td>
<td>20 (2.1)</td>
</tr>
<tr>
<td>Oral aphthous ulcers</td>
<td>49 (5.2)</td>
<td>20 (2.1)</td>
</tr>
<tr>
<td>Sacroiliitis</td>
<td>34 (3.6)</td>
<td>18 (1.9)</td>
</tr>
<tr>
<td>Erythema nodosum</td>
<td>23 (2.4)</td>
<td>4 (0.4)</td>
</tr>
<tr>
<td>Ankylosing spondylitis</td>
<td>16 (1.7)</td>
<td>15 (1.6)</td>
</tr>
<tr>
<td>Nephrolithias</td>
<td>8 (0.8)</td>
<td>8 (0.8)</td>
</tr>
<tr>
<td>Iritis</td>
<td>7 (0.7)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Pyoderma gangrenosum</td>
<td>4 (0.4)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>Uveitis</td>
<td>3 (0.3)</td>
<td>3 (0.3)</td>
</tr>
<tr>
<td>CD-related hepatic disease</td>
<td>1 (0.1)</td>
<td>1 (0.1)</td>
</tr>
</tbody>
</table>

*Percentages calculated on non-missing values; 3 patients had no EIM assessments after baseline so these patients' data were not carried forward; no patients had thrombosis at baseline or week 20.

*As determined by investigator.

*P < 0.001 vs. baseline.

*P = 0.016 vs. baseline.

*Incidence too small for comparison.
Eyes: Episcleritis

- Painless redness of white part of eye
- No visual changes
- Parallels IBD activity
- Treat with topical agents: NSAIDs, steroids, lubricants

Eyes: Uveitis

- Inflammation of middle chamber of eye
- Symptoms
  - Pain, sensitivity to light, blurry vision, or floaters
  - Independent of IBD activity
- If untreated, can lead to permanent visual defects
- Treat with steroids, anti-inflammatory medications
- Biologics for refractory cases
Skin: Many Manifestations

- Aphthous ulcers
- Erythema nodosum
- Pyoderma gangrenosum
- Cutaneous Crohn’s disease
- Erythema multiforme
- Epidermolysis bullosa
- Psoriasis

Skin: Erythema Nodosum

- 4% of IBD patients
- More common in CD than UC
- Painful raised red / violaceous nodules
- Usually on lower extremities (occasional face/trunk)
Skin: Erythema Nodosum

- Clinical diagnosis
- Biopsy rarely required
- Tend to occur with disease activity
- Self-limited and resolves with IBD treatment
- Lesions tend to heal without scarring

Skin: Pyoderma Gangrenosum

- 1% of IBD patients
- May start as a nodule or pustule
- Then progresses to an ulcer
- Scarring after it heals
- Not infectious
- Diagnosis based on clinical findings and, occasionally, biopsy
Skin: Pyoderma Gangrenosum

- Local care
- Avoid unnecessary trauma
- Barrier cream / ointment
- Rapid response to steroids
- May need steroid-sparing agent afterwards
- Independent of IBD activity
- Complete remission 44% (median 26.5 months follow-up)

Liver

- Primary sclerosing cholangitis (PSC)
- 70-80% of PSC patients have IBD (UC)
- 2-7% of UC patients have PSC
- High risk of colon cancer
- High risk of pouchitis
Thank You

Acknowledgements

Dr. Christina Ha (UCLA Medical Center)
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Skin: Cutaneous Crohn’s or PG?
Liver

- Hepatobiliary issues may include autoimmune hepatitis, autoimmune pancreatitis, gallstones, PSC
- PSC is most common (8% UC, 3% CD)
- Chronic cholestasis with inflammation and fibrosis of biliary tree
- Imaging features include multifocal bile duct strictures with segmental dilation
- Characterized by recurrent episodes of acute cholangitis (treated with sphincterotomy and antibiotics)
- Can progress to cirrhosis and decompensated liver disease → possible need for OLT
- Increased risk of CCA (7-9% cumulative risk over 10 years)
- Up to 5 x greater risk of CRC/dysplasia → annual colonoscopy once diagnosed
- Urso recommended
- No benefit shown with steroids, immunomodulators, CsA, FK506, anti-TNF