Diagnosis and Management of Extraintestinal Manifestations of Inflammatory Bowel Disease

Nanda Venu MD; MS
Digestive Diseases Institute
Virginia Mason Medical Center
Disclosures

- None
Outline

• Extraintestinal manifestations of IBD
• Musculoskeletal manifestations
• Dermatological manifestations
• Ocular manifestations
• PSC
• Drug associated cutaneous disease
Extraintestinal Manifestations of IBD

- EIM common in both UC and CD
- Almost all organ systems can be involved
- Most EIM’s are primary manifestation of disease
- IBD disease activity can have secondary effects

Am J Gastroenterol 2001;96:1116-1122
Extraintestinal Manifestations of IBD

- 25-40% of IBD patients
- If secondary effects of IBD included nearly 100%
- Development of 1 EIM increases the risk of more lesions
- Colonic disease associated more with EIM
- EIM can present before onset of GI symptoms

Am J Gastroenterol 2001;96:1116-1122
Common Extraintestinal Manifestations

- Musculoskeletal
  - Peripheral arthritis
  - Axial arthritis
- Dermatologic and oral lesions
  - Erythema Nodosum
  - Pyoderma Gangrenosum
  - Oral aphthous ulcers
- Ocular lesions
  - Uveitis/Scleritis
  - Episcleritis
- Liver disease
  - PSC
  - Autoimmune disease

Am J Gastroenterol 2001;96:1116-1122
EIMs: Why do they occur?

• Directly related to disease activity
  ➢ Large joint arthritis, EN

• Triggered by gut inflammation/abnormalities
  ➢ AS, small joint arthritis, ?PG

• Shared genetic predisposition
  ➢ Ankylosing spondylosis

• Related to systemic inflammation
  ➢ Venous thrombosis

• Metabolic disease
  ➢ Osteoporosis

Am J Gastroenterol 2001; 96:1116-1122
J Rheumatol 1992;19:373-377
Treatment considerations

• Is the EIM associated with active bowel disease?
  ➢ Treatment of the bowel may heal the EIM
  ➢ Start of gut therapy may help the EIM

• Does the EIM need specific treatment and does that alter the natural history or treat the symptoms?
  ➢ Topical
  ➢ Systemic
Musculoskeletal Manifestations
Musculoskeletal Manifestations

- Arthritis
  - Axial: Ankylosing spondylitis
  - Type 1 (Pauciarticular)
  - Type 2 (Polyarticular)

- Osteoporosis

- Miscellaneous manifestations
  - Clubbing, periostitis
  - Polymyositis
  - Asceptic necrosis
Ankylosing Spondylitis

- Well defined clinical syndrome
  - Sacroiliitis
  - Progressive ankylosis of the vertebral facet joints
  - “Question mark posture” and respiratory embarrassment
  - 30-50% have associated peripheral arthritis
  - M:F ratio 3:1 in idiopathic, 1:1 in IBD
  - Present in 1-6% of IBD patients
  - Strong association with HLA-B27 (although weaker than in idiopathic AS (70% vs 94%)

Ankylosing Spondylitis Symptoms

• Back pain is common – How do AS/SI present?
  ➢ Pain and stiffness in the morning
  ➢ Improves with exercise
  ➢ Radiates into the buttocks
  ➢ Impairment of spinal flexion

• In contrast mechanical back pain
  ➢ Comes on later in the day
  ➢ Is worsened by physical activity

Current Medical Diagnosis and treatment Chapter 20:846
Ankylosing Spondylitis

Current Medical Diagnosis and treatment Chapter 20:846
Ankylosing Spondylitis Treatment

- Physical therapy
- Analgesia
  - NSAIDs if bowel disease quiescent
  - Sulfasalazine
  - Injection of SI joints
  - Methotrexate
  - Biologic therapy: TNF inhibitors
  - Oral Steroids have minimal impact
- All treatment in consultation with a rheumatologist

Current Medical Diagnosis and treatment Chapter 20:846
Isolated Sacroiliitis

- May be asymptomatic
- Radiology suggests a prevalence of 18% in IBD patients
- MRI suggests prevalence of 30-40% in UC & 40-50% in CD
- The rate of progression to AS is unclear

Current Medical Diagnosis and treatment Chapter 20:846
Peripheral arthritis

- **Type 1 (Pauciarticular)**
  - < 5 joints affected
  - Large joints involved
  - Self-limiting episodes parallels IBD disease activity
  - Knees, ankles, hips, elbows, shoulders common

- **Type 2 (Polyarticular)**
  - > 5 joints
  - Small joints involved most common MCP
  - Symptoms running a course independent of the IBD

- **Arthritis is **NOT** erosive or deforming**

_Gastroenterology._ 2000 Feb;118(2):274-8
Peripheral arthritis-Treatment Strategies

• Physical therapy
  ➢ May be useful in large joint arthritis to maintain muscle strength
• Assistive devices
  ➢ Walking stick for large joint arthritis
  ➢ Splints
• Local treatments
  ➢ Intra-articular steroid injection

Current Medical Diagnosis and treatment Chapter 20:846
Peripheral arthritis-Treatment Strategies

• Analgesia
  ➢ Simple analgesia (acetaminophen, tramadol)
  ➢ NSAID’s – consider if the bowel disease is quiet
  ➢ COX 2 specific inhibitors can be considered, but probably not

• 5-ASA Medication
  ➢ Sulfasalazine may help some patients

Mahadevan et al Am J Gastroenterol 2002;97:910-14
Ferraz et al J Rheumatol 1990;17:1482-1486
NSAID’s for IBD arthritis

• Mahadevan et al
  ➢ Retrospective review of 27 IBD patients receiving COX-2 inhibitors
  ➢ 22 patients showed no change in IBD activity
  ➢ 14 patients showed improvement in arthritic symptoms

• Reinsch et al
  ➢ Open label trial of Rofecoxib in 32 IBD patients
  ➢ No worsening of IBD symptoms in 20 day trial
  ➢ 60% improvement in arthritis/arthralgia

Mahadevan et al Am J Gastroenterol 2002;97:910-14
IBD Arthritis Treatment

• Immune suppression
  ➢ If already used for the IBD Methotrexate may be the best choice
  ➢ Occasionally the arthritis alone may require immune suppression and low dose MTX can be 1st choice
  ➢ Low dose oral steroids may be required in some patients

• Biological agents
  ➢ Anti-TNF agents are effective in IBD arthritis
  ➢ Doses used similar to IBD therapy

Osteoporosis in IBD

- Osteoporosis is characterized by loss of bone osteoid reducing bone integrity resulting in increased fracture risk
- In IBD risk of fracture is 40% higher compared to general population
- WHO criteria for diagnosis
  - T score $\geq -1.0$: Normal
  - T score $-1.0$ to 2.5: Osteopenia (low bone density)
  - T score $<-2.5$: Osteoporosis
  - T score $<-2.5$ with fracture: Severe osteoporosis
- Low Bone Mass Z-score $\leq 2$

Gastroenterology 2003;124:791–94
Osteoporosis in IBD - Risk Factors

- Corticosteroid therapy
- Reduced physical activity
- Inflammation
- Decreased absorption and poor intake: Vit-D, Ca, Mg
Osteoporosis in IBD - Recommendations

**IBD Patient**
- Steroid use
- Low trauma or fragility fracture
- Postmenopausal females
- Men > 50 years of age
- Hypogonadism

**DEXA**
- T-score > -1.0
  - Ca/vit D supplementation
  - Exercise
  - Alcohol/smoking cessation
  - Minimize CS use
  - Treat Hypogonadism

- T-score -2.5 - 1.0
  - Basic prevention
  - Repeat Dexascan in 2 years
  - Consideration of bisphosphonate therapy and repeat Dexascan in 1 year if prolonged CS usage

- T-score < -2.5
  - Basic Prevention
  - Referral to Bone clinic/specialist for bisphosphonate therapy

American Gastroenterological Association medical position statement: guidelines on osteoporosis in gastrointestinal diseases.
Gastroenterology & Hepatology 2011;7:235-41
Dermatological Manifestations
Dermatologic Manifestations of IBD

• EIM involving skin 2-34% of IBD patients

• Most common lesions
  ➢ Erythema nodosum
  ➢ Pyoderma gangrenosum
  ➢ Oral Aphthous ulceration

• Less common lesions
  ➢ Psoriasis
  ➢ Sweet’s syndrome

Aliment Pharmac Ther.2004;(4):50-53
Erythema nodosum

- Characteristic skin rash - raised nodules on shins and other extensor surfaces
- Panniculitis (inflammation) in subcutaneous tissue
- May occur in up to 20% of IBD patients, depending on study population
- CD>>UC
- F>>M

Aliment Pharmac Ther.2004;(4):50-53
Can J Gastroenterol 2005:19;603-606
Erythema nodosum

- Parallels intestinal disease activity
- Skin lesions usually resolve with control of underlying intestinal disease
- Rarely skin lesions can precede development of IBD

Aliment Pharmac Ther.2004;(4):50-53
Can J Gastroenterol 2005:19;603-606
Pyoderma Gangrenosum

- Lesions begin as pustules or papules
- Initial lesions break down to form ulcers
- Characteristic feature is pathergy
- CD >> UC
- Can Parallel disease activity

Aliment Pharmac Ther.2004;(4):50-53
Pyoderma Gangrenosum Treatment

- Control Bowel Inflammation
- Treatment options
  - High dose steroids
  - Cyclosporine
  - Azathioprine
  - Tacrolimus
  - Infliximab
Infliximab for Pyoderma Gangrenosum

- 30 patients in randomised double blind placebo controlled trial
- 13 Infliximab and 17 placebo
- Response at week 2: 6/13 (46%) vs 1/17 (6%) (p=0.025)
- Non-responders were offered open label infliximab
- Open label phase 29 patients received infliximab
  - Response at week 6 in 20/29 (69%)
  - Remission at week 6 in 6/29 (21%)

Brooklyn T N et al Gut 2006;55:505-9
### IFX Response at week 6

<table>
<thead>
<tr>
<th></th>
<th>Improved N (%)</th>
<th>No response N (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Site</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>limbs</td>
<td>12 (80)</td>
<td>3 (20)</td>
<td>0.284</td>
</tr>
<tr>
<td>peristomal</td>
<td>6 (67)</td>
<td>3 (33)</td>
<td></td>
</tr>
<tr>
<td>Perineum</td>
<td>2 (40)</td>
<td>3 (60)</td>
<td></td>
</tr>
<tr>
<td><strong>Male</strong></td>
<td>9 (69)</td>
<td>4 (31)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>11 (69)</td>
<td>5 (31)</td>
<td></td>
</tr>
<tr>
<td><strong>NO IBD</strong></td>
<td>8 (73)</td>
<td>3 (27)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>IBD</strong></td>
<td>12 (67)</td>
<td>6 (33)</td>
<td></td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 12 wks</td>
<td>13 (93)</td>
<td>1 (7)</td>
<td>0.014</td>
</tr>
<tr>
<td>&gt; 12 wks</td>
<td>7 (47)</td>
<td>8 (53)</td>
<td></td>
</tr>
</tbody>
</table>

Psoriasis and IBD

- 12-13% IBD patients develop psoriasis
- Psoriasis can increase risk of CD (RR=4)
- Scalp and Palmo-plantar lesions most common
- Anti-TNF agents can be used for treatment
- Psoriasis can develop during anti-TNF therapy
- Anti-TNF withdrawal ~ 23% cases

Aliment Pharmacol Ther. 2011 Dec;34 (11-12):1318-27
Ocular and Other Extraintestinal Manifestations of IBD
Ocular Manifestations

- < 5% of IBD patients
- Episcleritis most common
- Parallels intestinal disease

- Other ocular EIM’s
  - Uveitis
  - Scleritis
- May occur with arthritis
- Needs urgent ophthalmological care

Inflamm Bowel Dis 2004;10:135-139
PSC

- U.S.: 2-7 cases/100,000 general population
  - 2.4 to 7.5% of patients with IBD (UC > CD) develop PSC
  - 60%-80% of patients with PSC have underlying IBD
- Two-thirds are male
- Median age at diagnosis 36-39

Hepatology 2010; 51(2):660-678
PSC

- Increased risk
  - Cholangiocarcinoma: 10% develop CCA within 10 years of diagnosis
  - Colorectal cancer (OR = 4.79)
  - HCC risk in patients with cirrhosis ~ 2%
  - Gall bladder neoplasia

Hepatology 2010; 51(2):660-678
Gastrointest Endosc. 2002 Jul;56(1):48-54
Dermatologic Complications of Immunosuppressive Therapy in IBD
Drug related Cutaneous lesions

- Psoriasis
- Drug induced lupus
- Non-Melanoma Skin Cancers
- Opportunistic infections: Herpes zoster
- Sweet’s syndrome

EIM of IBD can involve any organ system
Can be difficult to manage
Targeted treatment may be needed in addition to IBD control
Consult with appropriate medical specialty
Assess Osteoporosis risk in all IBD patients
Ocular manifestation need emergent care
PSC has cancer implication appropriate surveillance needed