EXTRAINTESTINAL MANIFESTATION OF INFLAMMATORY BOWEL DISEASE

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I have no disclosures
Objectives

- Identify the various extraintestinal manifestation of IBD

- Understand the pathophysiology of extraintestinal manifestations of IBD

- The clinical importance and how to manage various extraintestinal manifestations

WHY SHOULD PRIMARY CARE CLINICIANS BE CONCERNED ABOUT IBD?
Scope of IBD in USA

Estimated prevalence:
- UC: 37-346:100,000
- CD: 26-199:100,000

Physician visits: >700,000/year

Hospitalizations: 100,000/year

Annual direct costs: ~$4 billion


Clinical Consequences of Delayed IBD Diagnosis

Early referral to GI is important for effective treatment

Delayed diagnosis
- Delayed treatment
- Worse outcomes

Poor quality of life
Relapse rates
Increased cancer risk
Infection risk
Anemia
CD: Progressive disease w/ strictures
CD: penetrating disease

GI, gastrointestinal.
The Role of Primary Care Clinicians in IBD

Initial recognition of signs + symptoms that warrant specialist investigation and diagnostic evaluation

Ongoing health maintenance for the IBD patient

Extraintestinal Manifestations

- Common- affect 21- 36% of IBD patients
- Includes:
  - Disorders of the skin, eyes, and joints –parallel disease activity (some exceptions)
  - Complications or direct extensions of the bowel disease (kidney stones, obstructive uropathy, malabsorption, and gallstones)
  - Nonspecific extraintestinal manifestations: osteoporosis, hepatic diseases, and amyloidosis
Prevalence

- 25-40% of IBD patients will exhibit extraintestinal manifestations of the disease
- Virtually 100% of patients will have disease outside the GI tract if “secondary effects” of the disease are considered
- In large series, EIMs more common in CD than UC

Pathophysiology

- Multiple theories
  - Immune complex type hypersensitivity to a colonic antigen – would explain why patients with colonic disease are more likely to have pathology
  - Cytotoxic antibodies
  - Delayed type hypersensitivity reaction
  - Cross-reacting colon protein that affects eyes, joints and skin
**IBD: Systemic Complications**

- Eye inflammation
- Liver and bile duct inflammation
- Skin lesions
- Lower bone density
- Kidney stones
- Gallstones
- Arthritis and joint pains
- Growth failure in children
- Subfertility
- Ovaries
- Uterus
- IBD: Systemic Complications

*Higher incidence in women.*

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**Take Home Point #1**

**Parallel disease activity:**
- Peripheral arthritis (Large joint>small joint)
- Erythema nodosum
- Pyoderma gangrenosum (in UC)
- Episcleritis

**Independent of disease activity:**
- PSC
- Uveitis
- Axial arthropathy
The presence of EIMs increases the risk of developing subsequent EIMs

- CD patient without any EIM has 2% risk of developing EN – risk increases to 24% if they have Type I arthropathy
- Risk of developing ocular manifestations increases from 2 (no EIMs) to 17% (one EIM)
- Similar increases seen with UC

Walker D, Orchard, T. Do extraintestinal manifestations predict disease course, severity, and/or activity in IBD? Inflammatory Bowel Disease;14(S2):S200Inflammatory S200-201.

EIMs more common with colonic disease

- In general – colonic involvement means more likely to have extraintestinal manifestations
- In a study of 700 patients, Colonic disease(42%) had a higher association with extraintestinal manifestations than small bowel (23%) disease alone

Pyoderma Gangrenosum

- Approximately 5% UC patients – Less common with Crohn’s
- Most often on the leg or around a stoma – can occur on face, trunk or upper extremities
- Exhibits pathergy (worsens with trauma and debridement)
- Begins as a papule, pustule or nodule and progresses to ulceration
- Often occurs without flare in bowel symptoms in Crohn’s but parallels disease activity in UC
Erythema Nodosum

- Female > Male
- Tender, red subcutaneous nodules
- Usually pretibial
- Strongly associated
- w/ arthropathy
- Occurs with flares of bowel symptoms

Mucocutaneous Manifestations
Less Common

- Apthous ulcerations in mouth
- Metastatic Crohn’s (granulomatous inflammation of the skin)
- Leukocytoclastic vasculitis
- Sweet’s syndrome (neutrophilic dermatosis)
- Increased rates of psoriasis
Ocular Manifestations

- < 10% with IBD will have ocular manifestations
- Can lead to permanent vision loss
- Important to know when to refer to ophtho

Which of the following patients needs urgent referral to an ophthalmologist?

28 yo CD patient with active bowel disease and a burning, red left eye

36 yo with CD and severe right eye pain with ocular exam notable for a diffusely red eye

40 yo with UC and new onset visual blurring and photophobia in his right eye which is also somewhat painful

42 yo CD patient with history of steroid dependent disease requiring multiple courses of steroid in the past few years
Episcleritis

- Acute redness of one or both eyes
- Symptoms of irritation and burning
- Characteristically flares with disease flares
- Pain is common
- Not associated with loss of vision, photophobia, or loss of normal pupillary response to light
- Symptoms usually improve with treatment of underlying IBD

Scleritis

- More severe than episcleritis
- Severe eye pain
- Eye is more diffusely red than in episcleritis with pink areas between dilated blood vessels (as opposed to white with episcleritis)
- Can lead to vision impairment
- Can lead to retinal detachment or optic nerve swelling
- Must be treated with systemic steroids, NSAIDs, or immunosuppressants to prevent vision loss
- Requires urgent referral to ophtho
Uveitis

• Present with painful eye with visual blurring and photophobia
• Serious cases feature miotic pupils and abnormal pupillary response to light
• “Ciliary flush” – intense redness at the limbus and radiates outward for a short distance

Long-term complications include intraocular adhesions that can lead to cataracts and secondary glaucoma

Treatment – cycloplegics and topical steroids

Which of the following patients symptoms are more likely to be associated with active bowel disease?

- 28 yo with CD who complains of morning stiffness and low back pain
- 32 yo with CD and tender, hyperpigmented nodules on his shins and joint pain
- 40 yo with CD and pain and swelling of his MIP and wrist joints
### Peripheral Arthropathy

**Classification**

- **Type I Pauciarticular** (4 or fewer joints)
  - typically large joints
  - 20-40% will have recurrent episodes
  - associated with increased incidence of EN and uveitis
  - Parallels disease activity

- **Type II Polyarticular** (5+)
  - typically small joints
  - persistent symptoms
  - increased risk uveitis but not EN
  - Independent of disease activity

### Axial Arthropathy

- Less common than peripheral (3-5%)

- Spondylitis and Sacroilitis

- Presents as low back pain and morning stiffness

- Disease does not parallel bowel activity
Axial Arthropathy

**Spondylitis**
- 5-10%
- Most HLA -B27 positive
- Positive Schober’s test (limited spinal flexion)
- Progressive course - permanent skeletal damage
- Advanced cases characteristic squaring of vertebral bodies and anklyosis (bamboo spine)

**Sacroilitis**
- May be asymptomatic
- Majority HLA -B27 negative
- Most do not progress to spondylitis unless bilateral

Metabolic Bone Disease

**Osteopenia / Osteoporosis**
- 30-60% patients with Crohn’s
- Low bone density is associated with Crohn’s (malabsorption of calcium and vitamin D +/- effects of pro-inflammatory cytokines and osteoblasts)
- Exacerbated by chronic steroid use
- Low BMD is a risk factor for these disorders, but IBD patients are still at higher risk even with normal BMD
Hepatobiliary Complications

PSC

- PSC Most common hepatobiliary complication of IBD
- 70-80% PSC patients have concomitant IBD
- 1.4-7.5% IBD patients will develop PSC

- Distinct pattern of clinical findings in IBD patients with PSC:
  - higher prevalence of rectal sparing
  - more backwash ileitis
  - more likely to have pancolitis
  - higher incidence of colorectal neoplasia (risk persists after OLTx)
  - poorer survival overall
Thromboembolism

- Both UC and Crohn’s disease are prothrombotic
- Venous thromboembolism > arterial
- In > 50% with thrombosis, no precipitating factor found
- Associated factors include - thrombocytosis; increased levels of fibrinogen, fibrinopeptide A, factor V, and factor VIII; antithrombin III deficiency; and free protein S deficiency

All are related to active bowel inflammation.

THANK YOU