

ENTEROPATHIC ARTHRITIS

BOTTOM LINE

Inflammatory arthritis can occur in a significant minority of inflammatory bowel disease (IBD) patients, particularly those with large bowel and other extra-enteric IBD manifestations. Peripherally, patients can have Type 1 (acute/remitting/oligoarticular) or Type 2 (chronic, can include MCP) arthritis. Axial arthritis occurs more frequently in men. HLA-B27 is associated with axial arthritis. DMARDs that treat both IBD and arthritis can be helpful.

EPIDEMIOLOGY

- Prevalence of inflammatory arthritis in IBD (Crohn's and Ulcerative colitis)
 - Peripheral arthritis: 13%
 - Sacroiliitis: 10%
 - Ankylosing spondylitis: 3%
- Incidence of inflammatory arthritis in IBD (5-year cumulative)
 - Crohn's Disease: 0.020 ankylosing spondylitis, 0.009 peripheral arthritis
 - Ulcerative colitis: 0.030 ankylosing spondylitis, 0.050 peripheral arthritis
- Risk: Inflammatory arthritis more common if large-bowel involvement or other extra-enteric features
- Timing:
 - Type 1 arthritis more common in first few years of bowel disease;
 - Arthritis precedes IBD in 30% of cases
 - Arthritis flares with colitis 60-80% of the time.

CLINICAL FEATURES

Peripheral arthritis	Type 1	• ~5% of IBD, more often associated with flares of IBD • Acute, oligo-articular large joint, self-limited, nonerosive. Knee most common
	Type 2	• ~3-4% of IBD, not associated with IBD flares • Chronic, polyarticular symmetrical, sometimes migratory, nonerosive • MCP common; can also involve knees, ankles, shoulders, elbows, wrists, PIPs, MTPs
Enthesitis/dactylitis	• Like all seronegative spondyloarthropathies, can present with: Enthesitis—inflammation at tendon insertion (ex: Achilles tendonitis, plantar fasciitis), Dactylitis—inflammation of the digit (2-4% of IBD patients)	
Axial arthritis	• M > F (3:1); 5-30% of IBD patients present with characteristic inflammatory back pain • Onset often precedes IBD, does not flare with IBD, and does not follow same disease course as IBD • Symptomatic/asymptomatic uni-/bilateral radiographic sacroiliitis in 2-35%; increases with IBD duration	
Other extra-enteric	MSK	• Osteoporosis and avascular necrosis (from steroid exposure)
	Cutaneous	• Pyoderma gangrenosum • Aphthous stomatitis • Erythema nodosum — more associated with “Type 1” inflammatory arthritis • Neutrophilic dermatoses, metastatic Crohn's, cutaneous vasculitis
	Ocular	Uveitis; episcleritis, scleromalacia, corneal ulcers. More common in Crohn's
	Hepato-biliary	PSC, autoimmune hepatitis, fatty liver disease, cholelithiasis
	Most common extra-enteric manifestations mnemonic: PAIN • Pyoderma gangrenosum • Aphthous stomatitis • Inflammatory eye disease • Nodosum, erythema	

INVESTIGATIONS

Bloodwork	CBC	May see Leukocytosis, thrombocytosis
	ALT	May be elevated (fatty liver, autoimmune hepatitis)
	CRP, ESR	Elevated, could be from either/both of inflammatory arthritis or colitis

INVESTIGATIONS—Continued		
Bloodwork	RF, ANA	Negative
	HLA-B27	Positive in 50-75% of IBD patients, increases risk of axial disease
	ANCA	pANCA 55-70% of UC patients, <20% of Crohn's (colon-predominant)
	ASCA	Anto-Saccharomyces antibodies 40-70% Crohn's, <15% ulcerative colitis
Fluids	Synovial fluid: >5000-12,000 WBC/mL. Consider sending for culture if presenting with very acute red/warm monoarthritis for septic arthritis	
Imaging	X-rays, CT-abdo/pelvis: may show sacroiliitis which can be asymptomatic/incidental	
DIAGNOSIS		
In patients with known IBD, Enteropathic Arthritis should be suspected if presenting with inflammatory back pain or joint swelling. Review should detect other extra-enteric features like erythema nodosum and uveitis. Elevated CRP may support diagnosis of an enteropathic arthritis, though can be high due to active IBD too. Conversely, patients with a undifferentiated SpA presenting with unexplained weight loss, abdominal pain, and diarrhea should be investigated for underlying inflammatory bowel disease		
DIFFERENTIAL DIAGNOSIS: diarrhea and inflammatory arthritis		
Enteropathic	- IBD (Crohn's Disease, Ulcerative Colitis): Type 1, Type 2, Axial arthritis - Microscopic colitis (lymphocytic colitis, collagenous colitis): non-erosive oligo-articular - Celiac disease: non-erosive oligo/polyarticular - Intestinal bypass: polyarthritis, higher in jejunocolic bypass (not done now) and in females	
SpA	- Ankylosing spondylitis: up to 50% may have asymptomatic IBD on histology, ~5% overt IBD - Psoriatic arthritis	
CTD	Scleroderma (bacterial overgrowth and inflammatory polyarthritis)	
Vasculitis	- ANCA associated vasculitis (GPA, EGPA, MPA) - IgA vasculitis: nonerosive oligoarticular lower extremity large joints; can do upper extremity arthritis as well	
Infectious	- Post-infectious/post-viral self-limited inflammatory arthritis - Reactive arthritis: mono/oligoarticular lower-extremity SpA 1-4 weeks after mucosal infection - Whipple's disease: seronegative migratory oligo/polyarthritis, abdominal pain, weight loss - Pseudomembranous colitis: after <i>C. difficile</i> infection - Parasitic: including <i>Strongyloides</i>, <i>Giardia lamblia</i>, and <i>Taenia saginata</i>	
TREATMENT		
- Effective treatment of underlying IBD is often helpful for controlling peripheral arthritis of IBD - Coordination needed between rheumatology/gastroenterology; challenging when discordant disease activity between gut/joint		
Peripheral arthritis		
Initial treatment	- NSAIDs (if okay with gastroenterologist, concern for exacerbating GI mucosal inflammation) - Local or short-course of systemic steroids	
Subsequent	- csDMARDs - Sulfasalazine, methotrexate, azathioprine - If no improvement in 3-6 months then use bDMARD/tsDMARD - bDMARDs or tsDMARDs (listed in no particular order) - TNF inhibitors (infliximab, adalimumab, golimumab, certolizumab) - JAK inhibitors (tofacitinib, upadacitinib)	
Axial arthritis		
Initial treatment	- NSAIDs (if okay with gastroenterologist, concern for exacerbating GI mucosal inflammation) - Local corticosteroid to SI joint for refractory isolated sacroiliitis	
Subsequent	- bDMARDs or tsDMARDs (listed in no particular order) - TNF inhibitors (infliximab, adalimumab, golimumab, certolizumab) - JAK inhibitors (tofacitinib, upadacitinib)	

Treatment	IBD	Peripheral SpA	Axial SpA
NSAIDs	May exacerbate IBD ¹	✓	✓
Corticosteroids	✓	✓	Intra-articular to SI Joint
Sulfasalazine	✓	✓	✓
Mesalamine	✓		
Methotrexate	Crohn's, not UC	✓	
Azathioprine/6MP	✓	✓ (rarely used)	
Apremilast		✓	
JAK inhibitors ²	✓	✓	✓
TNF inhibitors	✓	✓	✓
Vedolizumab	✓		
IL-17 inhibitors	May exacerbate IBD ¹	✓	✓
Ustekinumab	✓	✓	
IL-23 inhibitors	✓	✓	

✓ indicates use for particular disease

1. Exacerbation is controversial. Has been used if IBD is stable; liaise with gastroenterologist if considering use.

2. TNF inhibitors approved for IBD in Canada: Adalimumab, Certolizumab (Crohn's, considered weaker acting), infliximab

FURTHER READING

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