Biologic Therapies for Isolated Recurrent, Persistent Complex Perianal Fistulas without Luminal Crohn's Disease

Hannah Fiske, MD[1], Chung Sang Tse, MD[2], Sean Fine, MD, MS[3]

[1]Department of Internal Medicine, The Warren Alpert Medical School of Brown University; [2]Division of Gastroenterology, Perelman School of Medicine at the University of Pennsylvania; [3]Division of Gastroenterology, The Warren Alpert Medical School of Brown University

Background

- Isolated complex perianal fistulas are abnormal connections between the epithelial surfaces of the anal canal and the perianal skin, but without endoscopic/histologic evidence of luminal inflammation in the remainder of the gastrointestinal (GI) tract that would be consistent with Crohn's disease (CD)
- While over half of patients with CD have perianal fistulas, isolated perianal CD is rare

Case Series

- Five adults (3 women, 2 men; mean age 38 years old) with no prior GI symptoms or diseases initially presented with perianal pain (3/5), perirectal mass (2/5), diarrhea (1/5), and abdominal pain (1/5)
- All patients underwent exam under anesthesia (EUA) with incision and drainage (I&D) of perirectal abscesses, and setons were placed in perianal/rectal fistulas in 4/5 cases
- Each patient had colonoscopy without evidence of inflammation on endoscopy or histology
- Radiographic imaging (MRI, MRE, CT) revealed fistulas and abscesses but no luminal inflammation
- 5/5 received antibiotics and 4/5 received biologic therapy (Adalimumab, Infliximab, or Ustekinumab)
- Despite initial surgical and medical management, complex perianal fistulas were persistent in all patients at follow-up after an average of 45 months

Discussion

- The differential diagnosis for recurrent complex fistula is broad and includes isolated perianal disease (IPD), isolated perianal CD, cryptoglandular abscess, hidradenitis suppurativa, tuberculosis, actinomycosis, lymphogranuloma venereum, HIV, diverticulitis, postoperative fistula, trauma associated with childbirth, and pelvic malignancy or subsequent irradiation therapy
- IPD is classically treated with antibiotics and local surgical intervention, whereas perianal CD often involves immunosuppressive therapy
- Multidisciplinary care is important for treating IPD in the absence of luminal findings of CD
- While classic medications for CD are unlikely to succeed when used alone for IPD, their incorporation into the treatment regimen may be critical in achieving eventual resolution of perianal disease
- Given the similarity in management, it is important to consider CD in the differential for IPD patients even in the absence of luminal findings

Contact: *Hannah Winthrop Fiske, Brown University / Rhode Island Hospital*
Email: hannahwfiske@gmail.com | Twitter: @HannahWFiske

Table 1: Case Series of Isolated Complex Perianal Fistulas

PT #	INITIAL PRESENTATION	DIAGNOSTIC EVALUATIONS	SUBSEQUENT DIAGNOSIS	MEDICAL THERAPIES ATTEMPTED	SURGICAL PROCEDURES	ULTIMATE DIAGNOSIS AND PLAN
(1) 39F	Painful perianal mass, presumed to be an abscess or hemorrhoids	Flexible sigmoidoscopy Colonoscopy with bx MRI EUA	Refractory perirectal and rectovaginal fistula with abscess	IBD medications: Adalimumab Methotrexate Non-IBD medical therapies: Ciprofloxacin Metronidazole Amoxicillin-Clavulanic acid Prednisone	I&D Seton placement Fistulectomy with sphincterotomy Diverting sigmoid colostomy Fistulotomy	Non-healing cryptoglandular anal fistula complicated by surgery Discontinue IBD therapy Surgical f/u with consideration for clinical trial of stem cell injection or transperitoneal repair
(2) 34M	Abdominal pain, diagnosed with sigmoid diverticulitis	Colonoscopy with bx MRI MRE CT scan EUA	Refractory perianal fistula with abscess	IBD medications: Infliximab Ustekinumab Tacrolimus Azathioprine Non-IBD medical therapies: Metronidazole Ciprofloxacin	I&D Seton placement	Isolated perianal disease in setting of presumed CD Chronic treatment with cyclical antibiotics (Ciprofloxacin or Amoxicillin-Clavulanic acid) IBD-directed therapy (Azathioprine + Infliximab; will consider Upadacitinib once approved by the FDA) Planning for surgical f/u
(3) 43M	Painful perianal mass, presumed to be a rectal abscess	Colonoscopy with bx MRI EUA	Refractory perianal abscess	Non-IBD medical therapies: Amoxicillin-Clavulanic acid	I&D	Isolated cryptoglandular abscess with potential hemorrhoids No need for chronic antibiotics Sitz baths and Preparation-H as needed If symptoms worsen will plan for EUA and surgical f/u
(4) 24F	Perianal pain, diagnosed as perianal abscess with fistula	Colonoscopy with bx MRI EUA	Refractory perianal abscess; inflammatory arthropathy	IBD medications: Adalimumab Infliximab Azathioprine Non-IBD medical therapies: Ciprofloxacin Metronidazole	I&D Seton placement	Presumed CD with perianal disease and inflammatory arthropathy IBD-directed therapy (Azathioprine + Infliximab) Planning for surgical f/u
(5) 50F	Diarrhea and rectal ulcers, presumed to have CD	Colonoscopy with bx MRI CT EUA	Refractory perianal fistula with abscess	IBD medications: Infliximab Non-IBD medical therapies: Colchicine Prednisone	I&D Seton placement Perineal debridement Lay open fistulotomy	Presumed CD with perianal disease IBD-directed therapy (Infliximab)

Abbreviations: Bx = biopsies. EUA = exam under anesthesia. F = female. F/U = follow up. I&D = incision and drainage. IBD = inflammatory bowel disease. M = male. MRE = magnetic resonance elastography. MRI = magnetic resonance imaging.