Fistulising and Perianal Crohn’s Disease

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Head of GI division
Conflict of interest

No conflict of interest for this presentation
Epidemiology of CD fistulas

- Frequent manifestation of CD: 23-38%
- The risk increases with CD duration
- Significantly affects quality of life
- Significant morbidity
- Faecal incontinence
- Proctectomy in 10–18% of patients
- The risk of developing perianal fistulas increases when CD affects the distal bowel: 92% if rectal involvement vs. 12% in exclusive ileal disease
Epidemiology of CD fistulas

- Entero-cutaneous: 54%
- Perianal: 24%
- Entero-enteric: 7%
- Recto-vaginal: 9%
- Other: 6%

Characteristics relevant for management

• **Abscess**
  – Perianal
  – Intersphincteric
  – Ischiorectal
  – Supralevator

• **Luminal inflammation**
  – Proctitis
  – Stricture

• **Fistula tracts**
Parks Classification

- Simple
- Multiple
- Complex
- Horseshoe

Primary tracts

A. Superficial fistula
B. Intersphincteric fistula
C. Transsphincteric fistula
D. Suprasphincteric fistula
E. Extrasphincteric fistula
AGA Classification: Prognostic value
AGA Technical Review

• Simple Fistulas
  – Low tract
  – Single external opening
  – Not associated with abscess, stricture or rectovaginal fistula
  – With/without proctitis

• Complex Fistulas
  – High tract
  – Single or multiple openings
  – May be associated with abscess, rectovaginal fistula or stricture
  – With/without proctitis

A low fistula tract runs through the lower one third (1/3) of the externa anal sphincter

Durable remission rate: 67% simple vs. 37% complex fistulas (p<0.001)

Additional prognostic factors: Proctitis, Smoking, Disease duration
Principles of Surgical management of sepsis

- Adequate drainage of sepsis
- Avoid tissue destruction
- Avoid secondary tracts
- Simplify situation
- Identify anatomy
- Preserve continence
- Setons

- Repeat Under Anesthesia Examination (UAE)
- Early perianal MRI
Surgical management of sepsis
WGO, International Organization for Inflammatory Bowel Disease, European Society of Coloproctology

• **Statement 17 - abscess drainage**
Surgical drainage of perianal abscesses is generally recommended before initiating medical therapy.
*Grade of recommendation : 1C*

• **Statement 18 – Setons**
Non-cutting seton placement is useful in order to prevent recurrent abscess formation.
*Grade of recommendation : 1C*
Diagnostic tests

The optimal way to define perianal CD is the combination of 2 of the following tests:

- Magnetic resonance imaging (MRI) of the pelvis
- Endoscopic ultrasound (EUS)
- Examination under anesthesia (EUA)
Diagnostic Algorithm

Physical examination

- Fluctuation present
  - 1st EUA: I+D (± Seton)
    - MRI/EUS + endoscopy
      - Optional 2nd EUA: Seton placement

- Stricture present
  - Endoscopy + dilation + MRI

- No fluctuation No stricture
  - MRI/EUS + endoscopy
    - EUA ± Seton

Medical management

**Antibiotics** may improve symptoms and contribute to healing

<table>
<thead>
<tr>
<th>Drug</th>
<th>Study</th>
<th>No pts</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present et al. 1980</td>
<td>6-MP</td>
<td>RCT</td>
<td>46</td>
</tr>
<tr>
<td>Present et al. 1995</td>
<td>6-MP, AZA</td>
<td>Meta-analysis</td>
<td>70</td>
</tr>
<tr>
<td>Prefontaine et al. 2010</td>
<td>6-MP, AZA</td>
<td>Meta-analysis</td>
<td>18</td>
</tr>
</tbody>
</table>

**Immunomodulators**

- **Thiopurines** No RCTs assessing fistulas as primary endpoint
- **MTX and Cyclosporin A** No relevant trial data
- **Tacrolimus** Shows therapeutic benefits
## Medical management

**Anti TNF:** Infliximab

<table>
<thead>
<tr>
<th>Patients</th>
<th>Drug(vs)</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present et al. 1999</td>
<td>94</td>
<td>IFX vs. placebo</td>
<td>18 w</td>
</tr>
<tr>
<td>Sands et al. 2004</td>
<td>195</td>
<td>IFX vs. placebo</td>
<td>54 w</td>
</tr>
</tbody>
</table>
## Medical management

### Anti TNF: Adalimumab

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Patients with Fistulas</th>
<th>Outcome</th>
<th>FU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hanauer et al. 2006 CLASSIC-1</td>
<td>RCT</td>
<td>32</td>
<td>Fistula response/closure: ADA vs. Placebo (ns)</td>
<td>4 W</td>
</tr>
<tr>
<td>Colombel et al. 2007 CHARM</td>
<td>RCT</td>
<td>117</td>
<td>Complete closure: 33% ADA vs. 13% placebo (p &lt;0.05)</td>
<td>56 W</td>
</tr>
<tr>
<td>Colombel et al. 2009</td>
<td>OL</td>
<td>117</td>
<td>Sustained healing: 90% ADA</td>
<td>2 Y</td>
</tr>
</tbody>
</table>
Medical management

Infliximab + azathioprine combination

Perianal CD
Combo IFX + AZA/6-MP

• Decreased rate of adverse reactions related to antibody formation to infliximab
• Preservation of drug efficacy
• Increased and more prolonged response rates.

## Definitive Surgical Management

### Fibrin glue and fistula plug RCTs

<table>
<thead>
<tr>
<th>Study</th>
<th>Pts</th>
<th>Intervention</th>
<th>Comparison</th>
<th>Duration</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lindsey et al. 2002</td>
<td>42</td>
<td>Fibrin glue</td>
<td>Conventional treatment (Fistulotomy in simple, Seton +/- advancement flap in complex fistulas)</td>
<td>8 w</td>
<td>Remission: Simple: 50% glue vs. 100% fistulotomy, p=0.06 Complex: 69% glue vs. 13% conventional, p=0.003</td>
</tr>
<tr>
<td>Grimaud et al. 2010</td>
<td>77</td>
<td>Fibrin glue</td>
<td>Placebo</td>
<td>8 w</td>
<td>Remission: 38% glue vs. 16% Placebo P=0.04</td>
</tr>
<tr>
<td>Senejoux et al. 2015</td>
<td>106</td>
<td>Seton removal +Fistula plug</td>
<td>Seton removal</td>
<td>12 w</td>
<td>Remission: 31% fistula plug vs. 23% Seton removal P=0.19</td>
</tr>
</tbody>
</table>
Definitive Surgical Management

Anal Fistula Plug in CD

- Systematic review of 16 studies
- Each series 1-20 patients with perianal CD fistula
- 84 patients with perianal CD fistula
- Closure fistula tract in 49/84 (58%)
Combined medical and Surgical Management

Combined surgical and anti TNF treatment

Large retrospective cohort:
• 117 patients: surgery alone
  (Seton, fistulotomy, advancement flap)
• 101 patients: surgery + anti TNF

Clinical response: 36% vs. 71% ($p=0.001$)
Novel technologies

Cx601 mesenchymal stem cells

- Panes et al. 2016
- 212 patients (ITT): treatment refractory complex fistulas
- Local injection of mesenchymal stem cells vs. placebo

- Outcome: clinical remission & no abscess > 2 cm on MRI at w 24

- Stem cells injection 49% vs. 34% Placebo \( (p=0.024) \)
Fecal Diversion

- Diverting stoma may improve QOL in patients with perianal CD (1B)
- Fecal diversion is indicated in uncontrollable sepsis (1C)
- Fecal diversion may be considered for symptom control (1C)

- Fecal diversion may be considered if proctitis cannot be medically managed

- The Association of Coloproctology of Great Britain and Ireland, Colorectal Dis, 2017;19:418-29
Treatment Algorithm

No abscess, No stricture, No Proctitis

• Medical therapy + surgical repair
  – **Superficial:**
    • Fistulotomy
  – **Intersphincteric:**
    • Sphincter preserving techniques
  – **Transsphincteric:**
    • Sphincter preserving techniques
  – **High or multiple:**
    • Sequential surgical interventions
Treatment Algorithm

Abscess: incision + drainage + antibiotics ± seton

Stricture: dilation

Proctitis: medical therapy ± seton

Biologicals ± IS ± AB

Tacrolimus

Diverting stoma

Proctectomy
Thank You