

Crohn's disease

Definition of Crohn's disease

- A chronic inflammatory disease characterised by transmural granulomatous inflammation that can occur throughout the entire gastrointestinal tract

Epidemiology of Crohn's disease

- Incidence about 7 per 100,00 per year
- Prevalence is about 140 per 100,000
- Any age, but bimodal peaks in age of onset:
 - Large peak at 15-30 years
 - Small peak at 60-80 years
- More prevalent in Caucasian westerners
- Slightly higher prevalence in females

Causes and risk factors for Crohn's disease

- Genetic element
 - 10x risk in first degree relatives, 70% concordance in identical twins
- Risks
 - Smoking (unlike UC, where it seems to be protective)
- Immune regulatory dysfunction
 - Upregulation of macrophages and Th1 helper cells?
- Hygiene hypothesis: being too 'clean' and thus not properly training immune system to offer moderate response to minor infections and bacterial flora

Presentations of Crohn's disease

- Diarrhoea
 - Can be bloody and/or chronic
- Abdominal symptoms
 - Abdominal pain/tenderness
 - Palpable masses
 - Anal/perianal skin tags, fissures and fistulas (may be asymptomatic)
- Mouth ulcers
- Systemic features
 - Weight loss
 - Malaise, anorexia, fever

Extra-intestinal manifestations of Crohn's disease

- Arthritis
- Conjunctivitis/Uveitis/Episcleritis
- Erythema nodosum
- Pyoderma granulorum (purulent ulcers with blue-black edge)
- Clubbing

Common differential diagnosis of Crohn's disease

- Other colitis

- Ulcerative colitis
- Ischaemic colitis
 - Microscopic colitis (watery diarrhoea, normal colonoscopy but inflammatory infiltrate in lamina propria)
- Coeliac disease
- Colorectal cancer
- Infectious diarrhoea e.g.
 - Giardia
 - Shigella, salmonella, campylobacter, EHEC
- Irritable bowel syndrome

Pathology of Crohn's disease

- **Macroscopic**
 - Distribution: 20% colonic; 30% ileocaecal; 40% small bowel
 - Bowel thickened and narrowed
 - Deep fissures and ulcers in mucosa, giving a 'cobblestone' appearance
 - Fistulae, abscesses and strictures
 - Fat wrapping
 - 'Skip lesions'
 - Areas of unaffected bowel between inflamed areas
 - Mouth ulcers and anal/peri-anal disease (ulcers, fissures, fistulae)
- **Microscopic**
 - Full-thickness (transmural) inflammation
 - Increase in macrophages
 - Granulomata (not caseating)

Initial assessment and management of Crohn's disease

- **Assessment**
 - Assessing disease severity is more difficult than in UC.
 - The site (ileal, ileal-colonic and colonic), pattern (inflammatory, fistulating, stricturing) and disease activity all need to be taken into account
- **Emergency management**
 - ABCDE including good IV access
- **Immediate investigations**
 - Bloods
 - FBC, U&E, LFT, CRP, ESR, coagulation, G&S
 - B12, folate, iron studies
 - Amylase and beta-HCG
 - Consider TPMT levels (see below)
 - Cultures
 - Blood culture
 - Stool culture
 - Small bowel follow through (barium or gastrografen) classically looking for:
 - Skip lesions
 - 1-2mm small aphthous craters with surrounding halos which can coalesce to form 'cobblestoning'
 - Deep fistulas

- CT/MRI, can be used to look for extent of disease in small bowel
 - MRI is optimal
- Colonoscopy
 - Colonoscopy with biopsies from affected and seemingly normal areas can confirm diagnosis – try to get to terminal ileum
- Supportive management
 - IV fluids (replace deficit followed by maintenance fluids)
 - Thromboprophylaxis (e.g. prophylactic LMWH)
 - Stool chart
 - Weigh daily
 - Assess nutritional status: if deplete then enteral feeding is preferable
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Initial medical treatment of Crohn's disease

- Click here for full details:
http://www.bsg.org.uk/images/stories/docs/clinical/guidelines/ibd/ibd_2011.pdf
- Supportive management
 - IV fluids (replace deficit followed by maintenance fluids)
 - Thromboprophylaxis (e.g. prophylactic LMWH)
 - Stool chart
 - Weigh daily
 - Assess nutritional status: if deplete then enteral feeding is preferable
 - No role for being NBM and can increase lactose intolerance
- Steroids
 - Patients with moderately active Crohn's flare should be started on 20-40mg Prednisolone daily, tapered to stop over 8 weeks
 - Budesonide 9mg daily can be used in patients with isolated ileo-caecal disease as this has a better side-effect profile
 - Failure to wean steroids should be regarded as treatment failure
- Anti-TNFs
 - Anti-TNF therapy can be used in patients with severe active Crohn's or steroid-refractory Crohn's
 - Azathioprine, Mercaptopurine and Methotrexate can also all be used to induce remission
 - All patients should have thiopurine methyltransferase levels (TPMT) measured before starting thiopurines (mercaptopurine and azathioprine) to avoid fatal administration to those with no or low TPMT levels.

Maintenance therapy for Crohn's disease

- Smoking cessation
- Azathioprine or Mercaptopurine should be first-line agents for the following patients:
 - Any patient who has a severe relapse
 - Patients who need 2 or more courses of steroids in 12 months
 - Relapse within 6 weeks of stopping steroids
 - Patients who relapse when steroid dose is <15mg
- Anti-TNFs
 - Active infection needs to be treated prior to giving these
 - Iv Infliximab
 - Anti TNF-alpha (20% murine, 80% human)
 - Can also be used as maintenance
 - Give steroids at the same time
 - Adalimumab

- Anti-TNF alpha (humanised)
 - Trade name humira
- Natalizumab
 - Monoclonal Ab against alpha-4 integrin (necessary for white cell adhesion)
 - Very small risk of PML (reactivation of JC virus)

Treatment for specific types of Crohn's disease

- Peri-anal Crohn's disease
 - The cumulative risk of developing a peri-anal fistula is 10% at 1 year, 15% at 5 years and 20% at 10 years.
 - Investigations
 - Ultrasound and/or MRI pelvis
 - Medical management:
 - Metronidazole 400mg three times daily and/or Ciprofloxacin 500mg twice daily
 - Azathioprine or Mercaptopurine
 - Anti-TNF treatment
 - Surgical treatment (close liaison with surgical team recommended):
 - Seton drainage
 - Surgical drainage of abscesses
- Non peri-anal fistulating Crohn's disease
 - Surgery is usually needed if patients are symptomatic

Surgery in Crohn's disease

- Surgery is likely to be needed in up to 75% of patients after 10 years of disease
- Though complication and recurrence rates remain high, in selected patient groups there is good evidence that surgery provides good long-term disease control.
- The need for surgical intervention will be determined by disease extent, response to medical therapy and the presence/absence of complications.
- MDT discussions for these patients are essential

Complications of Crohn's disease

- Toxic megacolon and perforation
- Strictureing and bowel obstruction
- Fistulae
- Small bowel cancer (if ileal involvement)
 - NB. No *overall* increased risk of bowel cancer in IBD – only certain subgroups have increased risk (NEJM 2013)
- Iron, folate and B12 deficiencies (terminal ileum disease)
- Osteoporosis from steroid therapy
- Short bowel syndrome and malabsorption
- Malnutrition

Prognosis of Crohn's disease

- Mortality slightly higher than general population
- 80% lifetime risk of needing surgery
- 75% remain in work 10 years after diagnosis