Inflammatory Bowel Disease: What We Should Know?

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Learning Objectives

• Describe the symptoms and signs of IBD
• Describe the basic investigations for suspected case of IBD
• Appreciate when and why to refer to Gastroenterologist
• Describe the complications of IBD
• Update knowledge on the treatment strategy of IBD
“Based on the definition of health by the WHO, inflammatory bowel disease (IBD) is a chronic disease that influences physical, psychological, familial, and social dimensions of life”
Spectrum of inflammatory bowel disease

- Ulcerative colitis (UC)
- Crohn’s disease (CD)

Indeterminate Colitis

Inflammatory Bowel Disease

The Spectrum of IBD

Inflammatory Bowel Diseases (IBD) >1 million persons in the United States

- Ulcerative Colitis (UC)
  - Proctitis
  - Pancolitis
  - Left-Sided Disease

- Indeterminate colitis

- Crohn’s disease (CD)
  - Gastro-duodenitis
  - Ileitis
  - Colitis
  - Ileocolitis

Perianal disease
Dysregulated intestinal immune system towards microbes or antigens perhaps augmented by random environmental factors with a background of genetic risk factors.
Global Epidemiology of IBD

Common aetiologic agents?

Environmental changes?

Cosnes et al. Gastro 2010
IBD cases diagnosed and follow up at HUKM

Graph showing the number of cases of ulcerative colitis and Crohn's disease from 1985 to 2009.
Anatomical location of ulcerative colitis

- Pancolitis: 15–25%
- Left-sided colitis: 75%
- Rectal involvement: 95%

(Shading indicates the frequency with which differing portions of the bowel are involved in ulcerative colitis)
Anatomical location of Crohn’s disease

Small intestine only 40%
Ileocolonic disease 30%
Colon only 30%

(Shading indicates the frequency with which differing portions of the bowel are involved in Crohn's disease)
Characteristics of IBD in Asia

- Median age at diagnosis for
  - IBD → 39 yrs, CD→ 34 yrs, UC→ 42 yrs
- More males with CD and UC vs Australia more females
- Complex disease behaviour more common in Asia
- Very low rate of familial clustering in Asia
- No differences in smoking rates
- Ethnic differences within the same country

Ng et al Gastroenterology 2013
Prideaux et al J Gastroenterol and Hepatol 2012
Why is IBD increasing in Asia?

• Dietary Influence – westernization of diet altering gut microbiota
• Changes in domestic hygiene (hygiene hypothesis)
• Use of antibiotics in early infancy, childhood and before IBD diagnosis
• Reduced rate of appendectomy
• Differing rates among different countries in Asia

Ng et al, GUT 2013
<table>
<thead>
<tr>
<th>Country</th>
<th>Crude annual incidence (per 100,000 persons)</th>
<th>95% confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia</td>
<td>23.67</td>
<td>18.46-29.85</td>
</tr>
<tr>
<td>Mainland China (Guangzhou)</td>
<td>3.44</td>
<td>2.47– 4.42</td>
</tr>
<tr>
<td>Hong Kong</td>
<td>3.06</td>
<td>2.49-3.73</td>
</tr>
<tr>
<td>Macau</td>
<td>2.20</td>
<td>0.12-2.75</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>1.59</td>
<td>1.11-2.21</td>
</tr>
<tr>
<td>Singapore</td>
<td>1.06</td>
<td>0.76-1.45</td>
</tr>
<tr>
<td>Malaysia</td>
<td>0.94</td>
<td>0.41-1.85</td>
</tr>
<tr>
<td>Indonesia</td>
<td>0.88</td>
<td>0.38-1.72</td>
</tr>
<tr>
<td>Thailand (Chiangmai)</td>
<td>0.67</td>
<td>0.33-1.19</td>
</tr>
<tr>
<td>Thailand (Bangkok)</td>
<td>0.63</td>
<td>0.41-0.92</td>
</tr>
<tr>
<td>Mainland China (Chengdu)</td>
<td>0.58</td>
<td>0.33-0.94</td>
</tr>
<tr>
<td>Mainland China (Xian)</td>
<td>0.54</td>
<td>0.40-0.71</td>
</tr>
</tbody>
</table>

Ng SC et al, Gastroenterology 2013
Differences in clinical presentation between ulcerative colitis and Crohn’s disease

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>*</td>
<td>** *</td>
</tr>
<tr>
<td>General malaise</td>
<td>** *</td>
<td>* *</td>
</tr>
<tr>
<td>Fever</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>** *</td>
<td>*</td>
</tr>
</tbody>
</table>

**Stools**

<table>
<thead>
<tr>
<th>Stools</th>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>** *</td>
<td>*</td>
</tr>
<tr>
<td>Mucus</td>
<td>*</td>
<td>** *</td>
</tr>
<tr>
<td>Pus</td>
<td>*</td>
<td>** *</td>
</tr>
</tbody>
</table>

The number of * symbols indicates the frequency with which each symptom is present.
Pathological and anatomical features distinguishing ulcerative colitis from Crohn’s disease

<table>
<thead>
<tr>
<th>Feature</th>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localisation</td>
<td>Distal</td>
<td>Segmental, proximal</td>
</tr>
<tr>
<td>Rectum affected</td>
<td>Always</td>
<td>50% of cases</td>
</tr>
<tr>
<td>Intestinal wall</td>
<td>Normal thickness</td>
<td>Thickened</td>
</tr>
<tr>
<td>Adhesions</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Inflammation</td>
<td>Superficial layers</td>
<td>All layers</td>
</tr>
<tr>
<td>Ulcerations</td>
<td>Superficial</td>
<td>Deep</td>
</tr>
<tr>
<td>Mucous membrane</td>
<td>Denuded</td>
<td>Cobblestones</td>
</tr>
<tr>
<td>Granulomas</td>
<td>0–4%</td>
<td>50–70%</td>
</tr>
<tr>
<td>Lymphocytic infiltration</td>
<td>Rare</td>
<td>Always</td>
</tr>
<tr>
<td>Fistulae</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>
## UC vs CD

<table>
<thead>
<tr>
<th></th>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location</td>
<td>Colon</td>
<td>Entire GI tract</td>
</tr>
<tr>
<td>Lesion type</td>
<td>Mucosal</td>
<td>Transmural</td>
</tr>
<tr>
<td>Lesion pattern</td>
<td>Continuous, proceeding upward from the rectum</td>
<td>Skips areas, with rectal sparing</td>
</tr>
<tr>
<td>Symptoms/signs</td>
<td>Bloody diarrhea; frequent small volume diarrhea with urgency</td>
<td>Crampy abdominal pain, diarrhoea, malnutrition, abdominal mass, perianal disease</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>UC</th>
<th>CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgery recognised by many as curative</td>
<td>Surgery <strong>not</strong> curative</td>
</tr>
<tr>
<td>Patients very resistant to surgery; not comfortable with the life-altering implications of surgery</td>
<td>Patients <strong>not</strong> as resistant to surgery because generally maintains previous bowel function/habits</td>
</tr>
<tr>
<td>Bowel wall disease</td>
<td>Disease of entire bowel wall thickness</td>
</tr>
<tr>
<td>More often life-threatening when severe: pancolitis causes septicemia risk</td>
<td><strong>Not</strong> as often life-threatening</td>
</tr>
<tr>
<td>Less progressive than CD</td>
<td>Progressive disease</td>
</tr>
<tr>
<td>True stricture <strong>uncommon</strong></td>
<td>Stricture common</td>
</tr>
</tbody>
</table>
CD is a progressive disease...

Natural History of Ulcerative Colitis with Standard Therapy

*Percent of patients with disease activity, in remission, or having colectomy performed each year after diagnosis

Extra-intestinal manifestations of IBD
Background – endoscopic findings

Normal

Mild

Moderate

Severe
The Impact of IBD

- Chronic incurable disease
- Increasing IBD in Asia
- Major implications in local health care planning and resource allocation
- Afflicts young people when they are most productive in their private and professional life
Investigations / what to do for suspected IBD patient:

Through history and clinical examination

Routine bloods: FBC, ESR, CRP, LFTs, Renal profiles, albumin

Repeated stool tests

Other faecal test: Faecal calprotectin (Very easy / suitable to do at GP’s service)

Referral for early endoscopy assessment

Follow up care and liaise with physician / surgeon interest in IBD
Treatment Goals in IBD

- Cure
- Maintained tissue healing
- Maintenance of remission
- Steroids weaning
- Remission
- Improvement
Treatment Option for IBD

1979 – Sulphasalazine, steroids
1980 – Azathioprine / 6MP
1983 - 5 ASA
1994 – Budesonide
1995 – Methotrexate
1998 – Anti-TNF, IFX
2005 – Other Biologic
> 2006 ‘Next Generation of Biologics’
Treatment Paradigm of IBD

Current step-up approach

Moderate

- Antibiotics
- Aminosalicylates

Severe

- Surgery
- TNF antagonists

Possible step-down approach

Early

- TNF antagonists
- Selective adhesion molecules

Late

- Corticosteroids
- AZA/6-MP, MTX

Late

- Surgery

Innate immunity activation

TNF = Tumour necrosis factor; AZA = azathioprine; 6-MP = 6-mercaptopurine; MTX = methotrexate

Source: Panaccione, R. Data presented at the Digestive Disease Week 2008. San Diego, CA, USA.
The ‘treat-to-target’ concept in chronic diseases: Lesson Learnt

**Treatment targets in chronic diseases**

- **Hypertension**
  - BP: 140/90 mmHg
  - (135/80 mmHg for diabetic patients)
  - LDL-cholesterol: 70 mg/dL (to lower incidence of cardiac events)

- **Diabetes**
  - <7% HbA1c

- **Rheumatoid arthritis**
  - Remission
  - Low disease activity

References:
- Diabetes: ADA. *Diabetes Care* 2011;34(Suppl. 1):51–98;
Early Intervention to Reach the Target

Adapted from Pariente B, et al. Inflamm Bowel Dis 2011;17:1415–
Tight control through monitoring is necessary to reach the target.
Treating earlier gives better remission and healing
Risk of colorectal cancer in IBD

In the general population the risk of colorectal cancer is 1 in 33

 Increased lifetime risk vs general population in:

All UC patients  x8
Total colitis       x19
Left-sided disease x4
Distal disease     x1.5
Optimal Management of IBD

Proactive Gastroenterologists

Enthusiastic Endoscopists

GENERAL PRACTIONERS

Experienced Colo-rectal Surgeon

Expert Radiologists

Experienced GI pathologist
Self discharged?

Disease stratifications and prognostication

Therapy:
Step-up or Top-Down

Pre-biologic check list, vaccinations, exclude TB!

AZA metabolites, MTX, nutrition, TMPT level

Disease assessment at 3/12: HBI, CDAI, UCDAI
Clinical, surrogate markers /?endoscopy

Mucosal healing? Reduced CRP, Hgb, Plt, FCP

Flares? Treat accordingly

Close disease monitoring.. 6/12

In remission...treat to target...

Continue to get better...

Watch for latent TB

IBD nurse
Clinical Psychologist
Patient Support group
Education

Discharge? Or annual f/u or GP

Continue f/u in IBD clinic

In remission...treat to target...

Physical exam, lymph node, CXR

‘Life cycle of IBD patients’

Referral case by GPs

Clinical(thorough history), bloods and endoscopy/imagings assessments

?Develop complications, MDT with Colorectal surgeon, Pathologist, Surveillance for CRC (methylene blue..)
Clinical case A

A 39 year old man presented with 6 weeks history of a bit of bloody diarrhoea and crampy lower abdominal pain.

Initial blood results;
WCC= 12.9, Platelets = 480, Albumin=29, CRP=5, stool C/S=awaiting results

What would you do?

a) Give antibiotics (metronidazole or ciproxin) & follow up
b) Write a referral letter for colonoscopy
c) Reassurance and supportive care
d) Do other blood tests such as ESR and repeat stool C&S
e) Do nothing and discharge the patients
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Clinical case B

A 33 year old lady (Lawyer) presented with 3 months history of tummy discomfort with bloated feeling (sometimes constipated) and relieved by defaecation. Her body weight is stable.

WCC= 8, CRP/ESR= Normal, Liver/renal profiles and thyroid functions - Normal

What would you do?

a) OK, You have IBS, reassure & discharge and no follow up
b) Write a referral letter for upper and lower endoscopies
c) OK you probably have IBS, prescribe a trial of anti-spasmodic medication and perform faecal calprotectin and follow up care
d) Do other blood tests, stool C&S, abdominal ultrasound
e) Give antibiotics, metronidazole and follow up care
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e) Give antibiotics, metronidazole and follow up care
Thank you!

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