Ileo-Caecal Crohn’s Disease
Great imitators and how to get the right diagnosis

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Which one has Crohn’s disease?

Case 1: 18 year old M

Case 2: 45 year old M

Case 3: 48 year old F

Case 4: 18 year old F
Impact of wrong diagnosis
Intestinal TB (ITB) is the main imitator.

Misdiagnosis rates between ITB and CD range between 50% to 70%.
Intestinal TB (ITB) or ileo-caecal Crohn’s?

- Similar clinical symptoms
- Imaging insufficiently sensitive peritoneal, mesentery or lymph node disease favour ITB
- Endoscopic features
  - direction of ulceration
  - surrounding mucosa
  - appearance of ileo-caecal valve
Tissue diagnosis of TB is gold standard but...

• Smear for AFB
  only positive in 20% of cases of ITB

• Histology
  caseating granulomas <30% of cases

• Culture
  delay and positive <20%

• PCR assays
  Performance depends on assay type, site of TB and quantity
How to improve the diagnostic yield

• Enhance the yield of tissue diagnosis
  – Number of biopsies
  – Biopsies from edge and base of ulcers
  – Segmental biopsies

• Other tools
  – interferon-gamma release assay (IGRA)
IGRA for the diagnosis of intestinal TB
(systematic review and meta-analysis, Ng 2014)

• interferon-gamma release assay (IGRA) for the diagnosis of ITB
  – pooled sensitivity 81% (95% CI: 75% to 86%) low probability false negative
  – pooled specificity 85% (95% CI: 81.2% to 88.6%) low probability FP positive

• Studies all from Asia high TB incidence rates
Not all cases of TB are confirmed by test

Notified TB cases in England in 2014 was 6520

Culture confirmed 3914/6520 (60%)
   pulmonary (72.3%) vs extra- pulmonary (46.7%)

Non-culture confirmed cases 2606/6520 (40%)
   positive test in 478/2606 (18.3%) (microscopy, histology, PCR)
   histology (302/478)
   2148/2606 (82.4%) no known positive test

Overall 2148/6520 cases (33%) not confirmed by laboratory test
Diagnosing TB with negative tests

- Incidence of conditions in local population
  - Crohn’s disease estimated 5300 cases (incidence 10/100,000)
  - TB notified case 6520 (ITB 368 cases 5.7%)

World Health Organization (WHO) considers high incidence rate of > 40 per 100,000 as high rate
Diagnosing TB with negative tests

Of the 6520 TB notified cases in England (2014) majority (73%) born in high incidence countries

<table>
<thead>
<tr>
<th>Country of birth</th>
<th>Number of cases</th>
<th>Percentage of cases (%)*</th>
<th>Median time in years since entry to UK (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>1,774</td>
<td>28.2</td>
<td>-</td>
</tr>
<tr>
<td>India</td>
<td>1,288</td>
<td>20.5</td>
<td>7 (3 - 14)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>791</td>
<td>12.6</td>
<td>10 (3 - 25)</td>
</tr>
<tr>
<td>Somalia</td>
<td>230</td>
<td>3.7</td>
<td>10 (3 - 14)</td>
</tr>
<tr>
<td>Bangladesh</td>
<td>207</td>
<td>3.3</td>
<td>8 (4 - 19)</td>
</tr>
<tr>
<td>Nepal</td>
<td>168</td>
<td>2.7</td>
<td>4 (3 - 9)</td>
</tr>
<tr>
<td>Nigeria</td>
<td>118</td>
<td>1.9</td>
<td>7 (2 - 17)</td>
</tr>
<tr>
<td>Philippines</td>
<td>111</td>
<td>1.8</td>
<td>9 (4 - 13)</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td>107</td>
<td>1.7</td>
<td>11 (9 - 12)</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>96</td>
<td>1.5</td>
<td>8 (4 - 13)</td>
</tr>
<tr>
<td>Romania</td>
<td>88</td>
<td>1.4</td>
<td>1 (0 - 6)</td>
</tr>
<tr>
<td>Eritrea</td>
<td>83</td>
<td>1.3</td>
<td>3 (0 - 8)</td>
</tr>
<tr>
<td>Kenya</td>
<td>81</td>
<td>1.3</td>
<td>19 (8 - 41)</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>78</td>
<td>1.2</td>
<td>11 (4 - 15)</td>
</tr>
<tr>
<td>Poland</td>
<td>70</td>
<td>1.1</td>
<td>6 (2 - 8)</td>
</tr>
<tr>
<td>Others (each &lt;1%)</td>
<td>1,007</td>
<td>15.8</td>
<td>8 (3 - 16)</td>
</tr>
<tr>
<td>Total*</td>
<td>6,297</td>
<td>100.0</td>
<td>9 (3 - 20)</td>
</tr>
</tbody>
</table>
Approach to ITB vs CD

Ileocolic inflammation
No caseating granuloma or AFB

Clinical risk assessment, tuberculin test (IGRA) and CXR

Suspicion of ITB
CT Abdomen/pelvis, await PCR and culture results

ITB confirmed
Treat with Anti-TB

No evidence of ITB
Discuss with ID team

ITB unlikely
Treat as Crohn’s

Adapted from Am J Gastroenterol 2009
non-specific ileitis – is it Crohn’s disease?

- Other infections
  - Yersinia
  - CMV
  - HIV-related infections
- Drug induced
  - NSAID
- Malignancies
  - Lymphoma
  - Adenocarcinoma
- Miscellaneous
  - Lymphoid hyperplasia
  - Isolated terminal ileal ulcers
Positive diagnosis of Crohn’s disease


Infection, ischaemia, physical damage, or specific immunologic sensitivity should be excluded as far as possible before a diagnosis of non-specific inflammatory bowel disease is made. Non-specific inflammations can be subdivided on the basis of macroscopic and microscopic anatomical criteria. Macroscopic structural abnormalities can be recognized by clinical examination, endoscopy, radiology, and inspection of an operation specimen. These complementary methods of data collection combine with microscopic examinations of tissue to separate disorders that differ in prognosis and possible response to treatment. Anatomic classifications do not necessarily imply differences in aetiology and may change with advances in knowledge.

The characteristic granuloma, when present, is regarded as diagnostic and may thus be given greater weight than other features.
-Omics revolution for diagnosis of Crohn’s disease – hype and hope

• Hype
  – Genomics, Metagenomics, Metabonomics

• Hope
  – Transcriptomics, Proteonomics

ORIGINAL ARTICLE

Bacterial protein signals are associated with Crohn’s disease

Catherine Juste,¹ David P Kreil,²,³ Christian Beauvallet,⁴ Alain Guillo,⁵ Sebastian Vaca,⁶ Christine Carapito,⁶ Stanislas Mondot,¹ Peter Sykacek,² Harry Sokol,¹,⁷ Florence Bion,¹ Pascale Lepercq,¹ Florence Levenez,¹ Benoît Valot,⁵ Wilfrid Carré,⁶ Valentin Loux,⁸ Nicolas Pons,¹ Olivier David,⁹ Brigitte Schaeffer,⁹ Patricia Lepage,¹ Patrice Martin,⁴ Véronique Monnet,¹ Philippe Seksik,⁷ Laurent Beaugerie,⁷ S Dusko Ehrlich,¹ Jean-François Gibrat,⁸ Alain Van Dorsselaer,⁶ Joël Dore¹

Surpassing single-layer health care with precision medicine

Sam Hawgood et al., Sci Transl Med 2015;7:300ps17
Key messages for diagnosis of ileo-caecal CD

• Always be suspicious about diagnosis of isolated IC Crohn’s disease

• Missing intestinal TB major consequences

• Only 70% of cases of ITB test positive
  – Collate clues to lead to likeliest diagnosis
  – Consider it in those born in high incidence countries

• Other conditions mimic erosions of CD – NSAID, infections, lymphoid hyperplasia, malignancies

• Need diagnostic tool for Crohn’s disease
Spectrum of cases

Case 1: 18 year old M

Case 2: 45 year old M

Case 3: 48 year old F

Case 4: 18 year old F

CD

Laparscopic resection

ITB

IBS

ITIU