PARASITES IN IBD
AMEBIC COLITIS

Cem KALAYCI
Marmara University
Dept. Of Gastroenterology
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Entamoeba histolytica mature cyst
Entamoeba histolytica trophozoite
Epidemiology

- Found worldwide (10% of the world population), especially in tropical areas
- 40-50 million cases annually worldwide, resulting in 40,000-110,000 deaths.
- *E histolytica* probably is second only to malaria as a protozoal cause of death.
Mode of transmission

- Ingestion of cysts
- Anal-oral transmission due to sexual practice
- There is no animal reservoir.
- Prevention includes boiling water or filter sterilization. Chlorination is not effective.
Entamoeba histolytica life cycle

1. Mature Cysts
2. Ingested
3. Excystation
4. Multiplication

Diagnostic Parasite Forms

- A = Non-Invasive Colonization
- B = Intestinal Disease
- C = Extra-Intestinal Disease

-△ Inactive Stage
- △ Diagnostic Stage
NATURAL COURSE

- Asymptomatic intestinal infection occurs in 90-99% of infected individuals. Most infected individuals eliminate the parasite from the gut within 12 months *(Unknown in IBD)*;
- 10% of the carriers develop invasive disease
- Case fatality rates of amebic colitis range from 1.9-9.1%
Entamoeba histolytica: 2 FORMS

- **Commensal (non-invasive form)** *E. Dispar* Luminal form. The parasite causes no signs or symptoms. 10 times more common.

- **The pathogenic (invasive form): *E. histolytica***
  
  Invades the intestinal mucosa and produces dysentery, amoebomas or extra-intestinal lesions via the blood, mainly to the liver.
E. histolytica

- Invasive and non-invasive strains could be differentiated by isoenzyme electrophoresis.
- Accurate diagnosis is important to prevent unnecessary treatment of a non-pathogenic strain, and to ensure treating a pathogenic strain.
Intestinal abscess caused by *Entamoeba histolytica*
Amibic colitis may present simultaneously mimic IBD and exacerbate underlying IBD.
Several weeks of abdominal pain, diarrhea, and bloody stools.

Fever (10-30%)

Weight loss (40%)

Diffuse abdominal tendernessness (12-85%)

Heme-positive stools (70-100%)
Making the correct diagnosis is a greater problem in climates where both amebic and ulcerative colitis may occur than in the tropics, where ulcerative colitis is rare and toxic megacolon has a much higher probability of being amebic in origin.
DIAGNOSIS

- Stool examination: The cysts of *E. histolytica* cannot be distinguished from the non-pathogenic species *E. Dispar*.
- Trophozoites containing erythrocytes in the stool is regarded as conclusive evidence. Some *E. dispar* trophozoites might contain ingested RBC.
- Trichrome staining should be used. (Low sensitivity and specificity with Wet mount/Lugol’s Iodine staining)

Doganci L et al. Accurate diagnosis is essential for amebiasis. World J Gastroenterol 2004;10:1231
Trichrome stain of *Entamoeba histolytica* trophozoites. Two diagnostic characteristics are observed. Two trophozoites have ingested erythrocytes, and all 3 have nuclei with small, centrally located karyosomes.
Trichrome stain of an *Entamoeba histolytica* cyst. Each cyst has 4 nuclei with characteristically centrally located karyosomes. Cysts measure 12-15 mm.
E. Histolytica determined in IBD patients

<table>
<thead>
<tr>
<th></th>
<th>Wet mount + Lugol’s iodine staining</th>
<th>Formol ethyl acetate staining</th>
<th>Trichrome staining</th>
<th>Parasite/total</th>
</tr>
</thead>
<tbody>
<tr>
<td>UC</td>
<td>5 (3.8 %)</td>
<td>8 (6.1 %)</td>
<td>13 (10 %)</td>
<td>13/130</td>
</tr>
<tr>
<td>CD</td>
<td>-</td>
<td>1 (3.3 %)</td>
<td>1 (3 %)</td>
<td>1/30</td>
</tr>
<tr>
<td>Control</td>
<td>1 (0.9 %)</td>
<td>2 (1.9 %)</td>
<td>2 (1.9 %)</td>
<td>2/105</td>
</tr>
</tbody>
</table>

Ustun S et al, World J Gastroenterol
Previous studies

- E. histolytica in 69 % of the 19 UC patients (Istanbul)
  Turk J Gastroenterol 1997;8:94-6
- E. histolytica in 54 % (22/43) of the UC patients (Antalya)
- Incidence of E. Histolytica/E. dispar is diminishing in Turkey.
Western World

- 1997-2001 237 relapses in 213 patients with IBD in London
- E. Histolytica in 3 cases

Mylonaki M et al. Eur J Gastroenterol 2004; 16: 775-8
DIAGNOSIS

Microscopy

- Microscopic examination of a single stool specimen is only 33-50% sensitive.
- The World Health Organization (WHO) recommends that intestinal infection be diagnosed with an *E. histolytica*-specific test, thus rendering the classic stool ova and parasite examination obsolete in this setting.
Antigen detection

- Stool antigen test specific for *E histolytica*
- Sensitive ELISA: specifically recognise antigens associated with pathogenic entamoebas
- This test uses monoclonal antibodies specific for the galactose (Gal)/\(\text{N}\)-acetyl-\(\text{D}\)-galactosamine (GalNAc) lectin of *E histolytica*
- Sensitivity: 87% Specificity > 90%
Serology

- Tests for antibodies to amebae are 90% sensitive for amebic liver abscess and 70% sensitive for amebic colitis.
- Problem: the antibody persists for years after the initial infection; differentiating between current and previous infection may be difficult, especially in endemic areas.
Polymerase chain reaction

- Strain-specific detection of *E histolytica* in stool and liver abscess aspirates appear encouraging.
- Sensitivity on stool samples is estimated at 87%.
COLONOSCOPY

- Friable and diffusely ulcerated mucosa (similar to IBD)
- Ameboma may be present in the form of an annular lesion, which usually occurs in the cecum and ascending colon and often is visually indistinguishable from colonic carcinoma.
Ameboma
Histologic Findings

- Biopsy specimens should be taken from the edge of ulcers and evaluated for motile trophozoites.
- Mucosal thickening, flask-shaped ulcerations to necrosis.
- Periodic acid-Schiff stains *E. histolytica* magenta and may increase detection of the parasite.
PAS-positive amebic trophozoites in the ulcer base (Surgical specimen)
Complications

- Fulminant or necrotizing colitis: occurs in 0.5% of patients, mortality > 40%
- Toxic megacolon
- Ameboma
- Rectovaginal fistulas
Diffuse antimesenteric ameboma narrowing the lumen of the proximal transverse colon.
Marked thumbprinting involving the transverse colon
AMI BIC COLITIS-I BD: PROBLEMS

- Steroids can provoke amebic activity and even cause fulminant colitis
- False negative stool studies are increased by diarrhea, prep for colonoscopy
- False positivity due to WBC
- Stool studies and serologies are compromised by steroids.
Predisposing factors for fulminant colitis

- Poor nutrition
- Pregnancy
- Corticosteroid use
- Very young age
Toxic megacolon
TREATMENT

- **Metronidazole**
  - Binds DNA and inhibits protein synthesis, causing cell death. Indicated for invasive *E histolytic* infections. 500-750 mg PO tid for 10 d

- **Tinidazole (Fasigyn)**
  - Indicated to treat intestinal amebiasis and amebic liver abscess 600 mg PO bid for 5 d; alternatively, 2 g PO qd for 3 d with food
TREATMENT

- Iodoquinol
  - Amebicidal, effective against trophozoite and cyst forms 650 mg PO tid for 20 d

- Paromomycin (Humatin)
  - 25-35 mg/kg/d PO divided tid for 7 d

- Diloxanide (Furamide)
  - Amebicidal against trophozoite and cyst forms 500 mg PO tid for 10 d
Thank you..............
Trichrome stain of *Entamoeba histolytica* trophozoites in amebiasis. Two diagnostic characteristics are observed. Two trophozoites have ingested erythrocytes, and all 3 have nuclei with small, centrally located karyosomes.
Sensitive ELISA: specifically recognise antigens associated with pathogenic entamoebas in the stools using monoclonal antibodies.

In addition Corpro antibodies (mainly of IgA class but also IgG and IgM) can be detected in stools.

Early data on antigen detection tests for serum and liver abscess aspirates are promising.
MORTALITY

- *E histolytica* probably is second only to malaria as a protozoal cause of death.

- The prevalence of amebic colitis and liver abscess is estimated at 40-50 million cases annually worldwide, resulting in 40,000-110,000 deaths.