Giardia lamblia

Introduction

- Primitive eukaryote lacking mitochondria
- Pear-shaped flagellated protozoan: 15um
- Zoonotic hosts
Giardia lamblia

Clinical Spectrum in Children

- Asymptomatic giardiasis
  - 60% possibly higher in children
- Acute giardiasis
  - 1 to 4 week incubation
  - Loose, foul-smelling stools
  - Steatorrhea: fat malabsorption
  - Cramping, bloating, nausea
  - Anorexia, malaise, weight loss
  - No blood
  - Fever early on
- Chronic giardiasis
  - Steatorrhea
  - Growth Retardation

Giardia lamblia

Chronic Giardiasis Malabsorption

- Second to cystic fibrosis as cause of steatorrhea
- Toddlers
- Growth retardation
- Increased fat excretion in stool
- Decreased serum carotene
- Abnormal xylose absorption

Giardia lamblia

Fecal Exam

- Entero-test
  - Patient swallows a capsule on end of string
  - String moves to jejunum, where trophozoites attach
  - After 4 to 24 hours, string withdrawn
- Duodenal aspiration biopsy
- Fecal ELISA
- Serum antibody
- PCR (fecal Inhibitors)
Giardia lamblia

Treatment

• 10% to 20% Rate of Persistent Symptoms Even After Treatment
  • Metronidazole
    • 15 mg/kg/d PO in 3 doses X 5-7 days
  • Tinidazole
    • 50 mg/kg PO once (max 2 g)
  • Niazoxanide
    • 1-3 years: 100 mg PO q 12h X 3d
    • 4-11 years: 200 mg PO q12 h X 3d
    • >12 years: 500 mg PO q12 h X 3d

New Drugs for the Treatment of Giardiasis

• Albendazole (Broad Spectrum + Anthelminthic)
• Paromomycin (Non-absorbable aminoglycoside)
• OLD DRUGS
  – Furazolidone (availability problems)
  – Quinacrine

Cryptosporidium parvum

Introduction

• Coccidian protozoan infecting gastric and respiratory epithelium of vertebrates
• Obligate intracellular, small (2-6um) parasite
• Initially recognized as infection of birds, cattle
• First reported case in 1976 recognized as zoonotic disease
• Since recognition as important pathogen in children and HIV-infected patients
• Even asymptomatic infection may cause failure to thrive in children
Cryptosporidium parvum

Epidemiology and Transmission

- Prevalence of active infection in North America: 1%-3%
- Seroprevalence: 25%-35%
- Seasonal peaks in late summer and early fall
- Person-to-person
  - Outbreak in day care centers
  - Secondary spread from day care centers
- Zoonotic transmission
  - Farmers and animal handlers
- Waterborne infection
  - Swimming pools
  - Public drinking water

Diagnosis of Cryptosporidiosis

- Acid Fast
- Several fecal exams
- MAB staining
- ELISA

Nitazoxanide (Alinia®)

- Oral Suspension (100 mg/5 ml)
- Interferes with Pyruvate: Ferredoxin Reductase (PFOR) enzyme-dependent electron transport
- Effective in pediatric patients for Giardia and Cryptosporidium
- Safety and efficacy in HIV+ patients not yet established
- Age 1-3 yrs: 100 mg PO BID X 3d
- Age 4-11 yrs: 200 mg PO BID X 3d
- Age >12 yrs: 500 mg PO q 12 hr X 3d
Cyclosporiasis

- “Big Cryptosporidium”
- Watery diarrhea and fatigue
- Periods of remission and relapse
- Treatment with TMP-SMX effective

Isospora Infection

- Self limited diarrhea
- Prolonged and more severe in AIDS patients
- 5.8 months in Haiti
- Oocysts stain bright red with acid fast
- DS TMP-SFX
- Oral Pyrimethamine

Dientamoeba fragilis

- Ameboflagellate
- Ameboid morphology by light microscopy
- Electron microscopy and 16s rRNA = trichomonad
- Association with Enterobius infection
- Linked to chronic abdominal pain/gastroenteritis
- Treatment: Tetracycline, Flagyl
Blastocystis hominis

- Protozoan parasite of poorly defined taxonomy and life cycle
- Large glycogen-like vacuoles
- Pathogenicity is controversial

Microsporidiosis

- Phylum Microspora (1000 species in 144 genera)
- Related to fungi – Eukaryotes
- Spore forming (water borne)
- Sexual transmission
- Enterocytozoan (Septata)
- Self-limited in immunocompetent hosts
- Immunocompromised hosts – diarrhea, malabsorption, weight loss, wasting
- Gastroenteritis, keratitis, sinusitis, urethritis, hepatitis, peritonitis, ocular infection
- Stools for special stains, EM
- Rx – Restoration of immunity, albendazole, fumigillin

Amebiasis
DISTRIBUTION

• This condition can occur anywhere in the world, but it is most common in tropical areas where crowded living conditions and poor sanitation exist. Africa, Latin America, Southeast Asia, and India have significant health problems associated with this disease.

FREQUENCY

• In US-overall prevalence is 4%
• In 1993 there were 2970 cases reported to CDC
• 33% occurred in Hispanic immigrants and 17% in immigrants from Asia or other Pacific islands

INTERNATIONAL Freq

• Aprox 10% of world population infected
• Prevalence as high as 50% in areas of Central and South America, Africa and Asia
• E. histolytica probably is second only to malaria as a protozal cause of death
Human Amebiasis

- Etiologic agent: *Entamoeba histolytica*
- *E. dispar* = non-pathogenic deme
- 1 million cases in Mexico
- Major cause of morbidity in Central & South America, Indian subcontinent
- Peak seropositivity 5-9 y.o. age group
- All socioeconomic groups
- In U.S.: Hispanic males 20-40 y.o.

Amebiasis Clinical Syndromes

- Asymptomatic colonization
- Amebic Dysentery
- Amebic Colitis
- Liver Abscess

Amebic Colitis
(Signs & Symptoms)

- Gradual onset
- H/O symptoms > 1 wk
- Diarrhea
- Dysentery
- Abdominal pain
  - Peritonitis
  - Abdominal Tenderness
- Weight Loss
- Fever
- Heme + Stools
- Immigrant/Traveler from endemic area
Amebic Liver Abscess

**Signs and Symptoms**
- History of symptoms > 4 wks
- Fever
- Abdominal Tenderness
- Hepatomegaly
- Jaundice
- Diarrhea
- Weight Loss
- Male: Female Ratio 9:1
- Cough
- Immigrant/Traveler from endemic area

**Morbidity and Mortality**
- Amebic colitis and liver abscess is estimated at 40-50 million cases annually worldwide, resulting in 40,000-110,000 deaths
- Amebic liver abscess is 7-12x more common in men than in women

**Diagnosis of Amebiasis**
- Differential with Shigella dysentery, IBD
- Microscopy:
  - Single stool exam – 30-50% sensitive
  - E. dispar vs. E. histolytica
  - Erythrophagocytic amebae
  - Liver aspirate – 20% sensitive
- Stool antigen detection
  - Gal/GalNAc lectin in stool (TechLab, Inc.)
  - 67% Sensitive
- Stool PCR
- Serology
  - IHA
  - 99% Sensitive for Liver Abscess
  - 88% Sensitive for Amebic Colitis
  - Remains Positive for years
- Colonoscopy + Wet Prep
- Radiographic Imaging
Treatment of Amebiasis

• Asymptomatic colonization treatment with luminal agent alone
  – Diloxanide furoate (not available in U.S.)
  – Paromomycin
  – Iodoquinol
• Invasive Amebiasis (Colitis, Liver Abscess)
  – Metronidazole + Luminal Agent
  – Percutaneous drainage not usually required

TREATMENT

Metronidazole

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Free-living Amebae

• Acanthamoeba, Balamuthia, Nagleria
• Healthy individuals 15-18 years, swimming diving in warm fresh water
• Clustering of cases from environmental source
• A&B cause granulomatous amebic encephalitis
  (cutaneous or pulmonary source with hematogenous spread, insidious; progressing to coma, lymphocytic pleocytosis). Multidrug therapy with pentamidine, 5’FC, fluconazole, itraconazole, TMP/SMX, azithromycin
  – Acanthamoeba keratitis – chronic ulceration of the cornea
  – Treatment with Pentamidine, sulfadiazine, 5’FC, fluconazole or itraconazole
• N causes primary amebic meningoencephalitis (PAM) in hosts with recent contact with fresh water, entering through olfactory neuroepithelium, with neutrophilic pleocytosis. Usually fatal – one case Rx with intrathecal amphotericin B, miconazole, and rifampin
  – Fresh CSF – amebae destroyed by refrigeration (hanging drop)
  – Adding distilled water results in flagellate forms
Free-living Amebae

<table>
<thead>
<tr>
<th>Disease</th>
<th>Agent</th>
<th>Trophozoite</th>
<th>Course</th>
<th>Entry</th>
<th>CSF</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAM</td>
<td>N. fowleri</td>
<td>Trophozoite</td>
<td>Acute, Fulminant</td>
<td>Olfactory</td>
<td>Active trophs, Neutrophils</td>
</tr>
<tr>
<td></td>
<td>&gt;20 species</td>
<td>Transient flagella</td>
<td>Chronic</td>
<td>Lung, Skin, Eyes</td>
<td>Not isolated from CSF</td>
</tr>
</tbody>
</table>

Granulomatous Encephalitis/Keratitis

Double walled cyst

Course

Acute, Fulminant

Chronic

Entry

Olfactory

Lung, Skin, Eyes

Neutrophils

Lymphocytes

Human African Trypanosomiasis (HAT)

- “Sleeping Sickness”
  - Blocked European exploration of Africa
  - Helped to establish European tropical medicine institutes
- Two morphologically identical subspecies of trypanosomes
  - Gambian HAT: Trypanosoma b. gambiense
  - Rhodesian HAT: Trypansosoma b.rhodesiensis
- Transmitted to human by tsetse flies
- Two stage Illness
  - Early Stage: Asymptomatic: Tryps found in blood and LNs
  - Late Stage: CNS involvement and tryps in CSF

Daily threat

- 60 million persons in 36 countries at risk
- 37,000 cases reported in 1999
- Estimated new cases, 50,000-70,000 a year
- 5% of population at risk is screened

R & D needs

- Enhance existing epidemiological surveillance systems in endemic countries

Human African trypanosomiasis

Disease Burden
Clinical Manifestations of HAT

- Gambian HAT
  - Winterbottom’s cervical adenopathy
  - Asymptomatic months or years
  - Intermittent fever: Antigenic variation
  - Weight Loss
  - CNS involvement
    - Diurnal Somnolence, Nocturnal insomnia
    - Constant Headaches
    - Behavior Changes
- Rhodesian HAT: Weeks not months or years

Neurologic manifestations of HAT

- Meningoencephalitis
  - Diffuse perivascular infiltration with lymphocytes, macrophages, astrocytes, and Mott cells – modified plasma filled cells with eosinophilic inclusions of IgM
- PTRE – Post-treatment Reactive Encephalopathy
  - Antigens released during melarsoprol therapy
  - Direct arsenical drug toxicity
### Treatment of HAT

**Eflornithine + Nifurtimox for Gambian HAT**

- **Suramin**: 1925
  - Early stage Rhodesian HAT

- **Pentamidine**: 1940s
  - Early stage Gambian HAT
  - Painful injections
  - 1% patients die

- **Melarsoprol**: 1940s
  - Arsenical
  - Late stage CNS disease
  - Highly toxic