Joint Session Digestive Diseases Pathology / Infectious Diseases Pathology: Infectious lesions of the GI tract: new entities and pitfalls

CASE 5

Sudden acute illness and long history of chronic disease
Case #1: 36 year-old Togolese woman

- **Chief Complaint**: Digestive symptoms: abdominal pain, nausea, and vomiting
- **PMH**: Caesarean section for placenta previa 4 mos. prior to admission with steroid injection for fetal maturation.
- **Laboratory**: Worsening inflammatory syndrome
- **Upper gastrointestinal endoscopy**: Ulcerated gastro-ileitis. Slide (131B7241-HE)
- **Course**: Chronically ill, 10 kg weight loss, neurological disturbance, multiple organ failure.
Case #1: 36 year-old Togolese woman (cont.)

- **Upper GI Endoscopy:**
  - Aspirated with subsequent Aspiration pneumonia
  - Fluctuating sensorium

- Despite antibiotics & mechanical ventilation, developed cardiac dysfunction with major left ventricular dysfunction & septal hypokinesis, requiring circulatory assistance.

- **Pathology:**
  - *Strongyloides stercoralis*: fluid from bronchoalveolar lavage.

- **Rx:** Ivermectin 12mg intra-rectally, until patient’s stool cleared.

- Persistence of **disturbance of consciousness**. Contrast brain CT scan: normal.

- **Laboratory:**
  - Two pathogenic strains of *Escherichia coli* in blood culture, treated with Tazocillin
  - Serology HTLV1 was strongly positive 109 IU / L with major T CD3+ lymphocyte phenotype (53% of lymphocytes) and T clonality compatible with a diagnosis of lymphoma.
  - Serum protein electrophoresis including analysis of individual immunoglobulin subtypes: normal.
  - Cerebrospinal fluid: mild increased protein levels to 0.5g /l.

- Subsequently, the patient **was cured** of her septic myocarditis and disseminated strongyloidiasis infection, related to immunosuppression from T-HTLV1 lymphoma.
Case #2: 84 year-old woman
(from Martinique, 30 years in France)

- **HX:** long history of epigastric pain with vomiting.
  - First presentation at 51 years of age: Admitted to hospital for small bowel obstruction following umbilical hernia surgery.
    - Intra-visceral ultrasound showed ulcerative duodenal obstruction extending into the pancreatic duct.
  - Relapses at ages: 57, 73, and 76 years old.
    - *Slides Case2-07SG06950-HE*
Case #2: 84 year-old woman from Martinique (Cont.)

- At age 80 & 81 presented with
  - **Epigastric pain** with vomiting, followed by epistaxis & hemoptysis from right bronchi.
  - CT-scan evidenced major **dilatation of the biliary tract**.
  - cardiomegaly
  - vertebral lesions

- **Laboratory:** kappa light chain **myeloma** with 16% of plasma cells, hypercalcemia, anaemia & increase in beta 2-microglobulbin were discovered. HTLV1 positive PCR.
Case #2: 84 year-old woman from Martinique (Cont.)

- 2014-2015 Endoscopy: Duodenal, antral & fundic biopsies taken
  - Case2-14SG08452

  - Case2-15SG00998.
Case #2: 84 year-old woman from Martinique (Cont.)

- Represented at age 84:
  - Hospital admission for depressed sensorium & periumbilical infiltrative purpura **Case2-18SG10115-B-HE**, extending inferiorly to the superior thighs.
Case #2: 84 year-old woman from Martinique (Cont.)

- **Clinical Findings:**
  - Small bowel obstruction
  - **Encephalopathy** (Cerebrospinal fluid normal.)
  - Pneumonia
  - Cardiomegaly.
- **Abdominal ultrasound & CT scan:** Dilatation & thickening of the duodenum & biliary tract.
  - Upper GI endoscopy showed ulcerative, haemorrhagic & oedematous duodenitis. 
- **Stool for ova and parasites** showed numerous parasites
- **Laboratory:** Hypogammaglobulinemia with decreased IgA, IgM, IgG, hypercalcemia & hypoalbuminemia
- **Microbiology:** Escherichia coli sepsis from biliary tract

The patient unfortunately passed away
Chronic, disseminated strongyloidiasis

Strongylos= round
Eidos= similar
Strongyloidiasis

a neglected disease of global prevalence (2014)

370 million people are infected, more often asymptomatic

Tropical, subtropical and temperate regions (in some areas 60% of the population is infected)

Puthiyakunnnon, Santhosh et al, 2014
Strongyloidiasis
A soil transmitted helminthiasis

- **Strongyloidiasis**: First described in French colonial troops suffering from diarrhea in Vietnam in 1876.
- **Etiology**: nematode, *S. Stercoralis*.
- **Symptoms**:
  - Pruritus, urticaria when direct penetration of human skin
  - 2 weeks post infection: abdominal pain, watery diarrhea, constipation, anorexia, weight loss, nausea, & bilious vomiting.
  - Malabsorption syndrome, paralytic ileus, intestinal obstruction & GI bleeding.
- **Larvae**: Detectable in stool after 3-4 weeks.
Disseminated strongyloidiasis

- when the infective larvae migrate from the intestine
  - to lungs and to other organs usually not involved in the normal helminthic life cycle.
  - **Skin**: Larva currens is pathognomonic of cutaneous manifestation of *Strongyloides* infection.

- Rare
  - in immunocompromised patients with a mortality rate up to 87%.
Strongyloides-related sepsis & other symptoms

- As infecting larvae migrate from the intestine, they carry pathogens from gut.
  - **Sepsis**: myocarditis, encephalopathy, meningitis
    - Strongyloidiasis should be considered as etiology of atypical suppurative meningitis.
  - **Hyponatremia**: SIADH (inappropriate antidiuretic secretion) due to anorexia, pulmonary infiltrate or CNS involvement.

Mukaigawara M, Nakayama I, 2018
Strongyloides: Life cycle

- The filariform larvae penetrate the intact skin by contact with infected soil and into the venous microcirculation via lymphatics.
- Larvae penetrate pulmonary alveoli, ascend the respiratory tree through which they enter pharynx and then are swallowed into stomach and small intestine.
- In the duodenum larvae mature into adult females.
- By parthenogenesis female worms produce up to 40 eggs/day. Eggs are 50-58 μ by 30-36 μ in size, delimited by a thin cuticle mostly transparent with either morula or tadpole stages of rhabditoid embryo inside.
- Once eggs hatch, rhabditiform larvae are released which can either be passed in stools, continuing their soil-based cycle or can cause autoinfection.

Tegegn G et al 2017
Strongyloidiasis: Immune response
Strongyloidiasis: Diagnosis

- **Routine stool examination**: very limited, output of the parasite in the stool is low.
  - Sensitivity: 50-70% from single general stool examination. (culture, concentration)

- **Absolute eosinophilic count**: Unreliable indicator of parasitic infection but ascending curve can be sign of reappearance of larvae in stools

- **ELISA- Enzyme-linked immunosorbent assay** for diagnosing Strongyloidiasis
  - **highly sensitive** but the test is not always available (luciferase immunoprecipitation system technique combined with a recombinant antigen (NIE) demonstrated a specificity of almost 100%),
  - cannot differentiate recent from old infection
  - shows cross reactions with other helminthic infections.

- **Molecular biology**
Strongyloidiasis: diagnosis

- **Upper GI endoscopy**
  - **Stomach:** Few cases
    - enlarged gastric folds
    - gastric ulcers
  - **Duodenum:** Most common
    - edema and hypertrophy of duodenal mucosa.
    - small bowel obstruction is secondary to intense infestation. ...... Biliary tract.

- **Histopathological examination of tissue sections**
  - definite diagnosis.
  - duodenitis: villous atrophy, ulceration, crypt distortion, infiltration of the lamina propria with plasma cells & eosinophils.
  - Strongyloides eggs, larvae & adult worms seen both within crypts & surface epithelium.
# Strongyloidiasis: Predisposing pathology

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
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<tbody>
<tr>
<td>Immunosuppressive drugs</td>
<td>Corticotherapy, chemotherapy, rituximab, solid organs transplantation, radiotherapy</td>
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<tr>
<td>Immunodepression</td>
<td>Hypogammaglobulinemia; autoimmune diseases</td>
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<tr>
<td>Infections</td>
<td>Leprosy, tuberculosis, AIDS</td>
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<td>Gastro-intestinal diseases</td>
<td>Gastrectomy with blind loop, anti-acid treatment, malabsorption, sluggish intestinal transit</td>
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<tr>
<td>Malignant disease</td>
<td>Leukemia, Lymphoma (HTLV1-T-lymphoma, myeloma), solid tumors</td>
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<tr>
<td>Others</td>
<td>Severe malnutrition, infant, pregnancy</td>
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Mobley CM, et al, 2017
Strongyloidiasis: Treatment

• Ivermectin: Single or several doses (Stromectol)
• Treatment in three phases:
  – With Flubendazole, Albendazole, then Ivermectin.
    • Oral solution of Flubendazole can be instillated directly into duodenum during endoscopy.
• Vaccine and passive immunization approaches are developed.
Strongyloidiasis
Conclusion & take-home messages

• **Duodenal biopsy:** provides definite diagnosis but is not always contributory (25%).
  • cutting levels ++++

• **Be aware of:**
  • contributing factors that can lead to disseminated form of Strongyloidiasis like hemopathy
    – hypogammaglobulinemia
    – or especially HTLV1-T-lymphoma
  • dangerous accompanying sepsis of migrating self-infesting larvae.
  • concomitant biliary disease is often associated with
  • the duodenal involvement, that leads to intestinal stenosis when severe and risk of self-infestation.

• **New diagnostic possibilities**
  • Serology
  • Molecular biology?
References


