Thermal Dimorphs of Wisconsin

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Disclosures

- None
Goals of this Webinar

- Become knowledgeable of the epidemiology of endemic dimorph fungi Blasto and Histo
- Recognize the clinical features of illness caused by endemic dimorphs
- How to test for them
  - Culture
  - Other methods
- Recognize growth and staining characteristics of endemic thermal dimorphs in WI
  - Blastomyces
  - Histoplasma
- Share some cases!

What are thermal dimorphic fungi?

- Unlike other fungi, these change their morphologic form based on temperature to adapt to the environment (or host)
  - Filamentous (fuzzy) at ambient room temperature
  - Yeast phase at body temperature
- These all have a geographic niche
- Infection is acquired by breathing in spores while the fungi are in their filamentous form
  - Usually manifest in pulmonary infections

Who are the clinically significant thermal dimorphs?

- *Blastomyces dermatitidis* a.k.a. “Blasto”
- *Histoplasma capsulatum* a.k.a. “Histo”
- *Coccidioides immitis/posadasii* a.k.a. “Cocci”
- *Sporothrix schenckii*
- *Paracoccidioides brasiliensis/lutzii* (S. America)
- *Talaromyces marneffei* (formerly *Penicillium marneffei*) (South East Asia)

Geographic ranges
Blastomyces dermatitidis —a.k.a “Blasto”

Epidemiology

- A specific niche in nature is still unknown but:
  - Blasto loves flood prone areas near water
  - Blasto loves decaying/dead plant matter
- Geographic range reflects its love of waterways
Blasto Epidemiology and Clinical Presentation

- Risk factors:
  - Construction
  - Outdoor activities—hunting, fishing, camping, hiking
  - Travel history to endemic areas
- Affects males more than females
- Social aspects—
  - Less likely to seek medical attention
  - More likely to do outdoor activities such as hunting, fishing, construction, etc...
- All health backgrounds affected
  - Young and healthy
  - Old, medically complex
  - A detailed social history is KEY in diagnosing Blastomycosis
  - Travel to endemic area
  - Outdoor exposure
  - Pets? Blasto is deadly in dogs.

Blasto Clinical Presentation

- Incubation period: weeks to months
- Chronic disease can present similar to TB or even certain types of cancers
  - Unexplained weight loss
  - Night sweats/intermittent fever
  - Cough
  - X-rays are non-distinct
- Acute disease presents as a severe community acquired pneumonia
  - Flu-like symptoms: fever, chills, body aches, productive cough
  - Chest X-rays can be quite impressive and are distinct
    - Extensive infiltrates and confluent nodules

https://bestpractice.bmj.com/topics/en-us/1095/investigations
Blasto Clinical Presentation

- Primary disease is pulmonary in nature
  - Spore inhalation in environment
  - Can progress to chronic (old calcified granulomas) or acute respiratory illness (acute respiratory distress syndrome)
  - Host factors that decide this are still unknown
- From the lungs can disseminate to from abscesses/granulomas:
  - Bone and joints—has a propensity for this
  - Skin
  - CNS—6-10% of cases have involvement
  - Genitourinary systems
- Traumatic introduction of spores into skin/soft tissue can also occur
  - Present as non-healing sores on face or limbs
  - Very inflammatory looking (because of the body’s response to the fungi)
- Commonly misdiagnosed!

Blasto Growth and Morphology

- Grows as a white to beige fluffy mold on brain heart infusion based medias at room temperature
  - Dangerous to work with in lab when in this phase
  - Tape prep with lactophenol analine blue will inactivate it
- Microscopic exam yields delicate hyphae with “lollipop” fruiting structures
- “Spikey” textured yeast colonies at body temperature
  - Broad-based budding yeast
Blasto Growth and Morphology

- **Yeast phase** is most often encountered on direct staining
  - Best seen by GMS or calcofluor staining
  - KOH and Gram stain also but tricky to the inexperienced
    - **Refractile, crystalline appearance due to thick cell wall**
    - May or may not uptake crystal violet or safranin, the key giveaway is the shape and arrangement
    - **Provider suspicion helps tremendously with interpretation!**

- **Mold phase** growth can be mistaken for Chryseosporum
  - Definitive ID by 35°C conversion to yeast phase, MALDI-TOF, or PCR
  - Urine and CSF antigen testing is also helpful but not necessarily definitive due to cross reactivity with Histoplasma

Treatment

- Mild to moderate Blastomycosis can be treated with Itraconazole
- Severe disease is typically treated with Amphotericin B
- This takes several months to successfully treat
Histoplasma capsulatum (a.k.a Histo)

Epidemiology

- In general, more is known about Histoplasma than Blastomyces
  - Identified as an illness in the 50s and 60s
- Known niche in nature:
  - Association with bird/bat feces but details of this unknown
- Lots of serologic studies
Histoplasma capsulatum Epidemiology:

- Evidence of exposure via serology is widespread according to studies done in the 1960s/70s.
- Stands to reason that it’s widespread in the environment.

Histo Epidemiology and Clinical Presentation

- Similar symptoms and disease progression to tuberculosis!
  - A detailed history social and travel history is KEY.
- Risk factors are very similar to Blasto:
  - Outdoor activities—construction, hiking, cave diving, rock climbing.
- Like Blasto affects males more than females for the same social factors.
- Unlike Blasto, the young and healthy will typically clear infection.
  - Age and immunosuppression are risk factors.
Histo Clinical Presentation

- Primary disease is pulmonary in nature
  - Spore inhalation in environment
- Acute illness presents with flu like symptoms
  - Incubation of weeks to months
- Can progress to chronic lung disease
  - Cavitary lung lesions
  - Granulomas (can become calcified)
  - Fibrosis
- From the lungs can disseminate to from abscesses/granulomas:
  - CNS
  - Spleen
  - Lymph nodes
  - Blood stream — more apt to see with histo than blasto
    - Development of adrenal insufficiency is common
- Commonly misdiagnosed!

Histo Growth and Morphology

- Grows as a white to beige filamentous mold on various media at room temperature
  - Dangerous to work with in lab when in this phase
  - Tape prep with lactophenol analine blue will inactivate it
- Microscopic exam yields delicate hyphae with “starburst” shaped macroconidia and tear shaped microconidia
- “Spikey” textured yeast colonies at body temperature
  - Narrow based, almost “lancet” shaped, budding yeasts
  - Abortive delicate hyphae may be present
  - May take several passages to convert to yeast phase
Histo Growth and Morphology

- Yeast phase is most often encountered on direct staining
  - Best seen by GMS or calcofluor staining
  - Gram staining: May or may not uptake crystal violet or safranin, the key giveaway is the shape and arrangement
    - Provider suspicion helps tremendously with interpretation!
- Mold phase growth can be mistaken for Sepedonium
  - Big hint: Histo makes micro conidia
  - Definitive ID by 35°C conversion to yeast phase, MALDI-TOF, or PCR
  - Urine and CSF antigen testing is also helpful but not definitive due to cross reactivity with Blastomyces

Treatment

- Same as Blasto!
- Mild to moderate disease can be treated with Itraconazole
- Severe disease is typically treated with Amphotericin B
- Also takes several months to successfully treat
Case #1: the cabin by the lake

- 57 yr old male presents to out of system ER with influenza like-illness Jan 19th
  - Felt poorly for 2-3 weeks
  - General malaise, productive cough, body aches, fevers
- Past medical hx
  - Well controlled type 2 diabetic
- Chest X-ray remarkable for what was interpreted as community acquired pneumonia
  - Given abx and sent home with instructions to return if symptoms worsened
- Returned 2 days later with blood tinged sputum and worsening symptoms (1-21)
  - Chest CT showed impressive lower lobe infiltration
  - Admitted to outside hospital where pt went into acute respiratory failure
  - Sent to LaX for more advanced support

Image courtesy of Dr. A. Sabin GHS Infectious Disease
Case #1: the cabin by the lake

- Upon admission to GHS (1-23), cultures ordered
  - Sputum culture
  - Blood cultures
  - Legionella and S. pneumo urinary antigen screens
- A gram stain was done on the sputum and yielded something unusual...
  - Non-staining, refractile, broad based budding yeast
  - Morph confirmed by calcofluor fluorescent staining
- ID notified...

A detailed medical and social hx was taken
- Patient had been remodeling their cabin and boat house in the Hayward area every weekend since early August 2019
  - Lots of exposure to dust and debris
  - Lots of dead and decaying plant matter surrounding the boat house
Case #1: the cabin by the lake

- A Blastomyces urinary antigen was done:
  - Very positive
- Several respiratory specimens were submitted for fungal culturing:
  - BAL: positive for broad based budding yeast by calcofluor
  - Expectorated sputum: positive for broad based budding yeast by calcofluor
- Other specimens were also submitted:
  - Blood cultures (Wampole Isolators): negative
  - CSF: negative by culture but antigen positive by referral testing

The patient was initially treated with IV itraconazole but then transitioned to IV Amphotericin B.
- They made a full recovery!
Case #2: the mechanic

- 1-16: 58 yr old male presents to CAH ER with community acquired pneumonia
  - Productive cough, fever, shortness of breath
- Past medical hx:
  - Malignant neoplasm of chest wall (melanoma stage 2), no chemo or radiation
  - ANA positive, autoimmune disorder?
  - Hx of asthma
- 1-29: Patient still not feeling well. Visits PCP. A chest CT is ordered and is read as abnormal.
  - Numerous pulmonary nodules
- Patient is referred to GHS Pulmonology for further studies to rule out metastatic cancer

The differential on this CT:
- Metastatic cancer
- Histo
- Blasto
- TB

Image courtesy of Dr. A. Sabin GHS Infectious Disease
Case #2: the mechanic

- 2-3: A BAL and biopsies of hilar lymph nodes are done.
  - Routine, fungal, and AFB cultures performed.
  - Smears were all negative
  - Other referrals are done including Fungitell assay, Histo/Blasto antigens, and PCP PCR
- 2-7: Urine Blasto antigen comes back positive, Histo detectable but below threshold
- 2-10: Patient is seen by Infectious Disease.

A detailed social history is taken by ID at initial consult.
- Patient had recently been doing some excavating in an open field
- Patient owns chickens
- Patient lives near a river
- Doesn’t hunt or fish
- Hasn’t had any recent travel out of the Northern IA area

Some factors for Blastomyces
- But also so some for Histoplasma too
Case #2: the mechanic

- 2-19: one colony of beige fluffy mold growing on IMA and BHI
- Tape prep shows...

- Numerous tuberculate macroconidia and tear shaped microconidia are noted
- Presumptively ID’d as Histoplasma!
- Mold subbed to BHI for conversion to yeast phase 2-19-20
- Conversion 3-2-20
In Sum...

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<thead>
<tr>
<th></th>
<th>Blasto</th>
<th>Histo</th>
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<tbody>
<tr>
<td><strong>Range</strong></td>
<td>Upper Midwest/Great Lakes, Canada</td>
<td>Mississippi, Missouri, and Ohio river valleys</td>
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<td><strong>Niches</strong></td>
<td>unknown, associated with fluctuant bodies of water</td>
<td>Bird and bat feces</td>
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<td><strong>Clinical presentation</strong></td>
<td>Acute and chronic pulmonary disease, likes bone, CNS</td>
<td>Acute and chronic pulmonary disease, likes blood, lymph nodes, adrenals</td>
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<td><strong>Patient populations</strong></td>
<td>Young, healthy to old, immunosuppressed</td>
<td>Old, immunosuppressed</td>
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<td><strong>Morph at 35C</strong></td>
<td>Broad based budding yeast</td>
<td>Narrow, more Candida like yeast</td>
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<tr>
<td><strong>Morph at 25C</strong></td>
<td>Lollipop fruiting structures</td>
<td>Tuberculate macroconidia</td>
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<td><strong>Rapid Testing</strong></td>
<td>Antigen tests exist for both but there are cross-reactivity issues!</td>
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Questions? Thank you!
References: