Surveillance of Invasive Mold Infections

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Disclosures

• None
Objectives

• Importance of Molds

• Mold Surveillance systems

• EIP Pilot project
Importance of Invasive Molds

- Molds (v yeasts) = hyphal structures, grow by branching/extension
- Spectrum of Disease
  - superficial (e.g. allergic bronchopulmonary aspergillosis)
  - invasive (e.g. cavitary lung mucormycoses)
- Major cause of morbidity and mortality, especially in immunocompromised hosts
PATH Alliance Registry, 2009

A. 12-wk survival
*Overall mortality - 46.7%
Zygomycetes – 64.3%
Invasive Aspergillus – 35%

B. 12 wk post transplant, response to therapy for invasive fungal infections

No. of days after diagnosis

P < .0001
Epidemiology

• 12.4 infections per million persons/yr for *Aspergillus* spp
• Sporadic outbreaks
  – natural disasters (Mucorales)
  – combat injuries (Fusarium, Aspergillus, Mucorales)
  – nosocomial (Exserohilum)
• Increasing use of anti-fungal prophylaxis in high risk patients = increase in mold infections over recent decades
  – HSCT patients, invasive mold infections may be more common than candida (43% v 28%)

Rees, CID 1998
Kontoyiannis CID 2010
Neofytos CID 2009
Pfaller CID 2006
Antifungal Resistance – an Emerging problem

- Low-prevalence (3.2%), but global problem
- Associated with poorer clinical outcomes
- Associated with antifungal (-azole) use?
- Environmental mechanisms?
  - chronic colonization in cystic fibrosis or allergic bronchopulmonary aspergillosis
  - Widespread use of azoles for agricultural purposes
Surveillance Systems in Place

- Current State - Limited
  - Single center studies
  - Large Database/Hospital discharge diagnoses
  - Population based – Berkeley/CDC – 3 N. California Co
  - Host-specific
    - solid-organ (TRANSNET)
    - stem cell transplant networks (PATH Alliance, TRANSNET)
  - Limited Diagnostic ability
    - >50% speciation lacking

Rees, CID 1998
Kontoyiannis CID 2010
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Goals for Invasive Mold Surveillance

– Determine population-based mold incidence rates
– Estimate mortality
– Monitor trends of mold species causing infections (emerging threats, outbreaks)
– Evaluate potential resistance patterns
– Examine the types of hosts (risk factors for disease) impacted by invasive mold
Catchment Area

- GA EIP - 8 counties
  - 28 hospitals
  - 4 million residents (2015)

- Pilot Project
  - Emory Hospital System
  - Grady Hospital
  - Atlanta Veterans Affairs
Partners

- Hospital microbiology, pathology personnel
- Georgia EIP
  - Hospital Acquired Infections
    - Candidemia Surveillance → Invasive Mold Surveillance 😊
- CDC Mycotic Diseases Branch
  - Epidemiology and Laboratory teams
- CDC Infectious Diseases Pathology Branch
Case Definition

“A diagnostic specimen (culture isolate, or fresh or fixed tissue) identified as a mold, including but not limited to: *Aspergillus*, Mucormycete molds, Phaeohyphomycete molds (pigmented molds), *Scedosporium*, and *Fusarium*, causing infection in a patient living in the catchment area.”

A new case will be triggered by a positive culture or tissue histopathology for an invasive mold species - excluding endemic fungi (dimorphic) - excluding nails, allergic aspergillosis - incident case if specimen collected is >60 days from first sample
CDC Diagnostics

**Mycotic Disease Branch Laboratory**
- Tissues
  - First forwarded to IDPB for evaluation
  - PCR: rDNA ITS 4/5, β-tubulin, IGS
  - Amplicon sequencing
- Cultures
  - Subculture for reference archive
  - PCR: rDNA ITS 4/5, β-tubulin, IGS
  - Amplicon sequencing
  - Antifungal susceptibility testing
    - Azoles
    - Echinocandins
    - Amphotericin B

**Infectious Diseases Path Branch Lab**
- Tissues
  - Stains (H & E, GMS)
  - Immunohistochemistry
  - Confirm presence of mold
  - Identify genus when possible
  - Return to MDB for sequencing

Chambers 2017
Case Report Form (CRF)

- Demographic information
- Co-morbidities, immunosuppressant medications
- Clinical Syndrome
- Co-infections – bacterial, viral (e.g. CMV)
- Radiographic information
- Laboratory information
  - Indirect tests for mold – galactomannan, B-D glucan
- Use of antifungals before/after diagnosis
MOLD INFECTION 2016 CASE REPORT FORM

Patient name: ________________________________  Medical Record No.: ____________________

Address: ____________________________________  Hospital: ________________________________

(Number, Street, Apt. No.)  Acc No. (Positive specimen): ________________________________

(City, State)  (Zip Code)

Check if not a case:  [ ] Out of catchment area  [ ] Duplicate case


4. Date of birth: [ ]/[ ]/[ ]/[ ] (mm/dd/yy)  5. Sex at birth:  [ ] Male  [ ] Female  [ ] Other (specify) ____________________________

6. Ethnic Origin:  [ ] Hispanic or Latino  [ ] Not Hispanic or Latino

7. Race (check all that apply):  [ ] White  [ ] Black or African American  [ ] Asian  [ ] Native Hawaiian

8. Incident Specimen

Specimen ID: ____________________________

DC DASH #: ____________________________

Specimen Type:  [ ] Culture  [ ] Histopathology

13. Mold Identification (check all that apply to this specimen)

[ ] Aspergillus

[ ] A. fumigatus

[ ] A. niger

[ ] A. flavus

[ ] A. terreus

[ ] Other (specify) ____________________________

14. Antifungal susceptibilities

[ ] None performed or no results available

MIC (e.g. 0.5, 2)

Amphotericin B (Ambisome, Abelcet)  [ ] Unk

Anidulafungin (Eraxis)  [ ] Unk

Caspofungin (Cancidas)  [ ] Unk

Flucytosine (Diflucan)  [ ] Unk
Work Flow

Microbiology culture

Pathology specimen

Microbiology Culture list

Pathology specimen list

GA EIP

Case Report Form

REDCap database

Linked PII file

Feedback summary reports to labs

PCR, sequencing & AS typing

Final specimen identification

CDC Mycotics Lab

CDC ID Pathology Lab

Analysis & Publications

Clinical Education

Microbiology Culture list

Pathology specimen list

CDC Mycotics Lab

Pathology Lab

PCR, sequencing & AS typing

Final specimen identification
Challenges

• Engaging and enlisting pathologists to submit tissue samples

• Diagnostic
  – Reliance on indirect methods is common (73%)
  – Probable (88%) > Proven

• Clinical data collection from medical records
Strengths

• Population based surveillance
• Collection of both microbiological and pathological specimens
  – Maximize the number of “proven” diagnoses
• Robust clinical data collection
• Use of electronic case reporting platform (REDCap)
• Molecular diagnostics for identification
• Antifungal resistance testing
• Provide feedback to local pathologists, microbiology lab
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