Challenges in Early Recognition and Diagnosis of Invasive Fungal Infection

PROBLEM

- significant cause of morbidity, mortality, cost
- diverging trends in mortality rates[1,2]
  - reducing mortality rate with invasive candidiasis
  - increasing mortality rate with other organisms (aspergillosis)
- overall mortality in invasive aspergillosis: 58%[3]

Chamilos G, et al. Invasive fungal infections in patients with hematologic malignancies in a tertiary care cancer center: an autopsy study over a 15- year period (1989–2003). Haematologica 2006;91:986–9.
McNeil MM, et al. Trends in mortality due to invasive mycotic diseases in the United States, 1980– 1997. Clin Infect Dis 2001;33:641–7.
Lin SJ, et al. Aspergillosis case-fatality rate: systematic review of the literature. Clin Infect Dis 2001;32:358–66.

DIFFICULTY

- non-specific symptoms more dominant in early stages of IFI
- microbiological cultures may be negative

Bacterial and fungal bloodstream infections cannot be clinically differentiated in early stages

Stevens DA. Diagnosis of fungal infections: current status. J Antimicrob Chemother 2002;49(Suppl. 1):11–9

CURRENT KNOWN SOLUTION
Diagnostic algorithm during Neutropenia with persistent fever

persistent fever > 48-72 h – after std antibiotics based on unit policy

mandatory

- physical exam daily
- blood cultures from peripheral/central venous catheters
- CT scan of sinuses
- CXR and/or chest CT
- abdominal USG
- abdominal MRI or CT if indicated
- biopsy of organ lesions – skin, liver, lung

recommended

- bronchoscopy + BAL in patients with pulmonary infiltrates

optional

- aspergillus galactomannan antigen tests and/or PCR at least twice weekly

Method	Advantages	Disadvantages
Culture	Long history of use in diagnosis Accurate Specific Considered gold standard	May require invasive techniques to obtain a sterile site culture May be falsely negative
Histopathology	Direct visualization of fungal pathogens	Requires invasive techniques to acquire a tissue sample n because of ogens
High-resolution tomography sc		n other nycosis)
β-D-glucan test		*Aspergillus*, and other fungi Cannot be used for detection of Zygomycetes
Galactomannan test	Non-invasive High specificity	Prone to false-positives and false-negatives
Polymerase chain reaction	Non-invasive Can determine specific genus and/or species High specificity	Prone to false-positives Not standardized Not commercially available

Combinations of diagnostic assays may ultimately prove to be necessary to make a rapid, accurate, and definitive diagnosis

CHALLENGES

- Many available tests – sign of challenge
- Gold std test (culture) – takes long time
- Rapid test (Blood tests) – not accurate (except candida)
- Rapid and Fairly Specific (histopath) - Invasive

SOLUTION

- No one standard way
- Different institutional policies
- Important to have some type of policy/SOP within a unit/hospital

How We Work - Clinical

- Level of Suspicion:

Solid tumor<AML<ALL<Transplant<GVHD

Others – aplastic anemia, myeloma, CLL, High grade NHL on steroids

- Day of neutropenia – first week, first admission – less concern.

- Symptoms/Signs:

Fever, dry cough, chest pain esp if pleuritic; skin lesions

How We Work – Indirect tests

- CT Chest plain – High probability based on Halo sign (early) or air crescent sign (late) – generally no further test during period of severe neutropenia/thrombocytopenia – treat empirically
- Blood cultures – useful to detect candida
- CT sinuses, CT abdomen, Urine for candida, Sputum fungal stain and culture, ECHO for vegetation

How We Work - Biopsy

- Bronchoscopy – early (after few days of antibiotics) if CT shows non diagnostic lung infiltrates – even if it requires platelet transfusion e.g. in a case of long standing neutropenia with new persistent fever – especially after 2-3 weeks of neutropenia (important DD in India – TB)
- Lung biopsy – CT guided – not comfortable in most cases
- Skin biopsy – early, if any atypical lesion
- Liver biopsy – rare

Practical Issues

- Bronchoscopy – in a pt with low plat, hypoxia
- Bronchoscopy – yield in a peripheral lesion, yield in TBNA
- Bronchoscopy – bleeding from biopsy
- We continue to rely heavily on Biopsy – wide DD – TB, mucormycosis (not just aspergillus)
- Cost of invasive tests – Bronchoscopy cheaper than one day of antifungal therapy (except traditional ampho B)

Team work – imp to work with same group of people for such rare conditions

- Hospitalist team
- Pulmonary team
- Radiology
- Pathology
- Microbiology

COLLECTIVE DECISION or Lack of DECISION

THANK YOU