Skin and mucosal manifestations of systemic fungal infections

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Deep fungal infections

- Rare in healthy persons
- Major problem in
  - Immunocompromised patients
    - Haematological malignancy
    - Organ or stem cell transplantation
    - After complicated (abdominal) surgery
    - After prolonged ICU treatment
    - AIDS patients

Deep fungal infections

- Challenge to
  - Modern medical diagnostics
    - Imaging
    - Sampling for microbiological examinations
    - Microbiology
  - Therapy
    - Long term antifungal treatment
      - Adverse effects, interactions
      - costs
  - Prevention
    - Hospital or environmental acquired infections
    - HEPA and/or laminar air flow room ventilation
    - construction works of hospital
  - Patient outcome
    - High infection related mortality
    - Often poor prognosis of background disease
  - Economy of health care systems
    - Daily antifungal cost can reach 1 000 €
    - Treatment lasts usually months

Superficial vs deep fungal infections

- Superficial
  - Very common
  - Chronic
  - Easy to diagnose
  - Not disabling
  - Prognosis of patients good
- Deep
  - Uncommon
  - Acute or subacute
  - Difficult to diagnose
  - Disabling
  - Prognosis of patients poor

Deep fungal infections

- Deep Candida infections
  - Candidemia
    - Immunocompromised patients
    - After complicated abdominal surgery
    - After prolonged intensive care treatment
      - Severe burn patients
      - Pancreatitis etc
    - Broad specrtum antibiotic use and central venous catheter use etc.
  - Deep candida abscess
    - After abdominal or esophageal surgery
      - Usually with other microbes
  - Candida esophagitis or deep mouth infections
    - Cancer treatment, AIDS patients
  - Candida endophtalmitis
    - After Candidemia
    - Intravenous drug abuse
  - Candida endocarditis
    - Iv drug abuse, valvular surgery
  - Candida osteomyelitis
    - After candidemia, operation, iv drug abuse

Skin manifestations of systemic candida infections *(Bae GY et al Int J Dermatol 2004;44:550-555)*

- How common
  - 15 % in a study by Bae et al 2004 from Seoul, Korea (1989-2002)
    - Of blood culture positive cases 19/53 (35,8 %)
    - C.tropicalis 12/19
      - C.tropicalis candidemia 14, 12/14=86 %
    - C. Albicans 5/19
      - C.albicans candidemia 30, 5/30=17 %
    - C.glabrata 2/19
      - C.glabrata candidemia 3, 2/3= 67 %
- (1.1.2005-26.5.2007 One case of C.tropicalis candidemia at our Hospital district)

Skin manifestations of systemic candida infections *(Bae GY et al Int J Dermatol 2004;44:550-555)*

- Type of Candida skin lesions
  - Multiple, erythematous 4/19
  - Purpuric 15/19
  - Maculopapules, nodules, or plaques
  - From 2 mm to 10 cm
  - 9/19 central pale vesicular or pustular centers
    - Some necrotic centers
  - 16/19 generalized rash
- Conclusion: skin manifestations are typical signs in *C.tropicalis* Candidemia

Skin manifestations of Aspergillus

- In a review by Denning and Stevens(Rev Infect Dis 1990;12:1147-1201)
  - 29 reported cutaneous cases reported (in sufficient detail) out of 2121 published reports (1.4 % of all cases)
    - neutropenic 14
      - responders 79 %
    - non-neutropenic 15
      - responders 80 %
  - better respond than in other forms of aspergillosis

Skin manifestations of Aspergillus

Reviewed by van Burik et al J Clin Microbiol 1998;36:3115-21

- Primary cutaneous aspergillosis
  - skin injury
    - iv catheter sites
    - traumatic inoculation
    - occlusive dressing
    - burns
    - surgery
  - secondary
    - contiguous to the skin
    - haematogenous spread
- HIV-related cutaneous aspergillosis 10 patients
- Non HIV-infected immunocompromised patients, more common
  - burn victims
  - neonates
  - cancer patients
  - after stem cell transplantantation
  - after solid organ transplantation

Skin manifestations of Aspergillus

Reviewed by van Burik et al J Clin Microbiol 1998;36:3115-21

- Othrerwise healthy
  - surgical wounds
  - traumatic inoculation
  - by exposure high spore counts such as farming
- **Initial lesions**
  - macules, papules, nodules or plaques
  - hemorrhagic bullae
  - ulcerative nodules
  - purulent lesions in neonates
- **Mirobiology**
  - A.fumigatus most common in HIV patients
  - in non-HIV, non-burn patients A.flavus 44 %, A.fumigatus 26 %
- **A.ustus** 3/ 7 published cases primarily cutaneous (Verweij et al J Clin microbiol 1999; 37:1607-1609)

Epidemiology and outcome of zygomycosis: a review of 929 reported cases by *Roden et al CID 2005:41:634-53*

- Review of all zygomycosis reports in the English-language literature since 1885
- 929 Cases analyzed
  - 65 % male
  - median age 40
  - overall mortality 44 %

Epidemiology and outcome of zygomycosis: a review of 929 reported cases by *Roden et al CID 2005:41:634-53*

- 179/929 (19 %) had cutaneous involvement, mortality 31 %
  - localized 98/176 (56 %)
    - mortality 10 %
  - deep extension 43/176 (24%)
    - mortality 26 %
  - disseminated 35/176 (20 %)
    - mortality 94 %
- Rhizopus species 47 % of all patients
- Mucor species 18 %
- Cunninghamella bertholletiae 7 % etc.

Patient case:oral mucormycosis

- 68 years old male
- Pancytopenia
  - AML, M2
  - Idarubicine+Cytarabine induction
  - Mitoxantrone+etoposide+cytarabine consolidation
  - B-neut < 0.1x10E9/l: 54 days
- Cariotic teeth problems

Patient case:oral mucormycosis

- Mucormycosis of the mouth
  - operated, bone involvement evacuated
  - liposomal Amphotericin B
  - healed
- Mucormycosis quite rare in hematological patients
  - therapy: radical operation+ posaconazole ±Amphotericin B

Skin Fusariosis

Dignani and Anaissie Clin microbiol Infect 2004;10(suppl 1):67-75, Nucci and Anaissie CID 2002;35:909-20

- Second most common mold infection in immunocompomized patients
- Most common Fusarium sp
  - F.solani
  - F.oxysporum
  - F.moniliforme
- Skin involvement common
  - Precede fungemia by about 5 days
- Blood culture positive >50 % in disseminated form
- Review of 259 patients
  - 232 (90 %) immunocopomised
    - Cancer 205, aplastic anemia 15, solid organ transplantation 7
  - 27 (10 %) immunocompetent
    - Tissue breakdown >70 %

Skin Fusariosis

Dignani and Anaissie Clin microbiol Infect 2004;10(suppl 1):67-75, Nucci and Anaissie CID 2002;35:909-20

- Immunocompromised
  - Skin lesions 72 %
    - localized 12 %, disseminated 88 %
  - Immunocompetent
  - skin lesions 52 %
    - localized 93 %, disseminated 7 %
- Type of skin infection
  - Disseminated papules and nodules 145
    - Necrotic 87
      - Echtyma gangrenosum 16
      - Surouding erythema(target) 16
    - Without necrosis 58
    - Cellulitis 2
  - Rapid progression in disseminated forms
- Mortality
  - In patients with disseminated lesions 76 %
  - Local skin lesions 39 %

Cutaneous Scedosporium apiospermum

Source:Uenotsuchi et al Acta Der Veneraol 2005;85:156-159

- Case report 65 year-old man with Still disease and a lesion in right hand
- Literature review 1998-2003: 19 cases
  - 18/20 immunocompromised patients
  - 15/20 male, age 18-81 years
  - 5 disseminated , 4/5 died
  - 15 local, 10 cured

Skin and mucosal manifestations of systemic fungal infections

- Rare occurrence
- When occurs, may help the clinician in the diagnosis
  - typical outlook
  - easy to biopsy
  - rapid to diagnose (slide preparate: yeast, mold, aspergillus type, mucor type etc)
- Most cases in immunocompromised patients
- Usually not the only site of infection
- Start antifungal therapy immediately
- If local, consider radical surgery
- Means often poor prognosis to patients
  - typically patients have concomitantly other problems