Blastomycosis

A chronic granulomatous and often supperative disease having a primary pulmonary stage that is frequently* followed by dissemination to other body sites, particularly skin and bones.

Causative Agent:

teleomorph - *Ajellomyces dermatitidis*
anamorph - *Blastomyces dermatitidis*

Synonomy:

North American Blastomycosis
Gilchrist's Disease
Chicago Disease

***much more so than in histoplasmosis (as far as is known). More like chronic histoplasmosis with some dissemination to other body sites. Traditionally not considered opportunistic. Sporadic AIDS association.**

Blastomycosis vs Histoplasmosis

Similarities:

1. **both have approximately the same endemic U.S location**
2. **both caused by a single species of genus *Ajellomyces*, which are closely related and heterothallic**
3. **both are initiated most often as primary pulmonary infections brought about by inhalation of conidia**
4. **both caused by fungi whose dimorphism is regulated similarly by temperature**
5. **both thought to be generally fatal before pulmonary forms discovered and before use of Amphotericin B**

Differences:

1. **caused by different species**
2. **although former is not opportunistic, it does not appear that many infections are self-limiting**
3. **induction of specific immunity after exposure and resolution may be uncommon (maybe even non-existant)**
4. **the propensity of the disease is to progress to production of active skin lesions and bone lesions (like hybrid disease among histoplasmosis, sporotrichosis and cryptococcosis)?**
5. **does not involve intracellular pathogen**
6. **resolution, when it occurs, does not leave residual lesions (e.g. calcified lesions)**

History

Gilchrist* - 1894 - new skin disease by unknown yeast in tissue**

Gilchrist & Stokes* - 1896 - 2nd case
- long-term study of disease

- isolated & studied fungus
- recognition of dimorphism
-1898 named fungus *Blastomyces dermatitidis*

Ricketts* ~ 1900's - studied Chicago Disease (15 cases)

1. **used X-ray for treatment**
2. **began to define endemic area**
3. **experimented with KI therapy**
4. **began to distinguish from cryptococcosis**

Pre-1950's - mainly thought that only 2 clinical forms of blastomycosis existed

1. **Cutaneous form initiated by traumatic implantation of fungus into skin and subcutaneous tissue (e.g. like sporotrichosis and chromoblastomycosis)**
2. **Systemic form initiated in lungs and then disseminated to internal organs**

Schwarz and Baum, etc. 1950s → 1970s virtually all cases of blastomycosis (except very rare primary cutaneous) originate in lungs

1 above therefore was an erroneous concept.

***All Americans; Ricketts better known for studies of Rocky Mountain Spotted Fever and Typhoid Fever (*Rickettsia rickettsii* named in his honor as is therefore *Rickettsia typhi*.).**
****a formalin-killed autopsy specimen**

Taxonomy

Ajellomyces dermatitidis*^
A. capsulatus*

Ascomycota
Euascomycotina
Plectomycetes
Onygenales (blastoconidia/gymnothecia)
Gymnoascaceae (Sessile spiral-forming cleistothecia)

*** heterothallic, dimictic teleomorphs****
*** holoblastic, hyphomycete anamorphs**
^ varietal differences uncertain; African form may be a variety or species

Teleomorphs discovered

Dermatophytes 1960 -->1970's
Blastomyces* 1968**
***Histoplasma* 1972**
***Cryptococcus* 1975**

**** 1 contrasting "set" of mating-type genes (idiomorphs) at the same locus of homologous chromosomes of self-sterile mating strains.**
***** McDonald & Lewis - 1968.. 1st of the "endemic" pathogens induced to sex**

Blastomycosis - Clinical Forms

1. **Primary pulmonary**
2. **Chronic cutaneous***
3. **Generalized systemic***
4. **Single organ systemic***
5. **Inoculation blastomycosis**

***pre-1950s recognized main forms.**

Primary Pulmonary (resolve spontaneously or disseminate)

1. **Inhalation of spores**
2. **Alveolitis with M invasion**
3. **Inflammatory reaction involving PMNs & granuloma formation**
4. **a. often lung disease resolves, but lesions appear at other sites**
   b. less often resolution in lungs and no progression
   c. severe progressive pulmonary form

Distribution

1. **originally thought to be more common in whites, however today thought to be equal distribution among races**
2. **most cases traditionally among older individuals (30->60 age group); exception with AIDS cases**
3. **male/female ratio of 6-9/1. Among 309 cases diagnosed from 1994-2003, 57% of which occurred between 2001-2003, only 13% were in children and young adults (< 19 years).**
   -since same in dogs may not be occupational only
   -some thoughts about hormonal relationship (no direct evidence)

Signs of cutaneous involvement in blastomycosis

1. **formation of subcutaneous nodules or ulcerating lesions**

2. **usually occur singly or in groups on exposed areas (face, hands, wrists, arms, lower leg and infrequently mucocutaneous regions; e.g. larynx, tongue, mouth surfaces)**

3. **25 - 50% of these cases with cutaneous lesions may show bone involvement (sometimes only presenting symptom; occult osteolytic lesion, pain in joints, mostly lesions in nonjoint bone; ribs, skull, long and short bone)***

1. **Amphotericin B drug of choice**
2. **hydroxystilbamidine (in children) (not used today except rarely)**
3. **Itraconazole (current or near future drug of choice); compliance problems w/ oral drugs apply here too.**

Mortality rate ~78% in untreated; Ampho treatment in life-threatening; 90% effective
keto 90 . 95% effective, but w/ side effects
itra only -> 8% relapse, 90% > effective

Serodiagnosis

1. **Compliment fixation test**
2. **Immunodiffusion test**

C.F - uses broken yeast cells as antigen
- many false negatives & some false positives ~50% undetected
- newer tests with antigen A* better. -- Titer of 1:8 positive

ID - uses antigen A*
- positive band of identity basis for immediate treatment, ~80% reliable

*** culture filtrate antigen from yeast form**

-selective labs & CDC have very good records of detection by serodiagnosis today.

-positive sputum culture also often leads to diagnosis; characteristic yeast cells in pus or biopsy tissue; ID also by gene-probe technology (AccuProbe™)
