Too Competent for Cryptococcus

Starr Steinhilber, MD
Victoria Johnson, MD
48 yo healthy AAM

Sx
Fevers
Chills
Headache
Back pain
Vomiting

Tx
ED visit
Doxycycline

- 4 weeks

- 1 week
ED visit
Unknown antibiotic

- 3 days
Blurry vision

Increased headache

Current

Admission in August

23 lb weight loss
Histories

- PMH: Rocky Mountain Spotted Fever with rash post tick bite in ~1992
- Family History: +sarcoidosis, DM, gout
Social History

- Lives in north Alabama - hunter, outdoorsman
- Veteran - served internationally in the 1980s
  - No travel x 30 years
- Prior heavy ETOH/cocaine/marijuana in military
- Multiple female sexual partners, uses condoms
Physical Exam

T 99.4     P 99     BP 122/64     R 21     98% on RA     BMI 19.6

- Gen: good muscle tone
  - mild distress, diaphoretic, warm to touch
  - neck stiffness with meningismus

- Neuro: Alert and oriented x 4, CN 2-12 intact
  - persistent bilateral horizontal nystagmus
  - with left lateral gaze

- Skin: no inoculation escar, target lesions, or other rashes
Laboratory Data

135 99 17
3.3 30 1.0

Ca 8.6
Mag 1.9
Phos 2.4

Hepatic Function normal

UDS neg
CT head normal
CXR normal

Normal differential
Laboratory Data

Fever + Headache + meningismus = meningitis

Next Step: Lumbar Puncture

Ca 8.6
Mag 1.9
Phos 2.4
Hepatic Function normal
Cerebrospinal Fluid

Opening pressure 46 mmHg
Nucleated Cells 538 mg/dl
  N 19%
  L 71%
Protein 141 mg/dl
Glucose 23 mg/dl
Gram stain – few neutrophils, moderate mononuclear cells

VDRL negative
India Ink positive
Cryptococcal Antigen 1: 512
Further evaluation of immune status

- HIV nonreactive
  - CD4, CD8 % and absolute wnl
- IgA, IgG, IgM, IgD, IgE wnl
- C3, C4, CH50 wnl
- Negative malignancy w/u

Serum cryptococcus Ag 1:2048
Cryptococcus

- Affects 1 million annually
- 600,000 deaths/year worldwide
- Incidence 2-7/1000 HIV patients
- Of cryptococcus cases, up to 20% will be normal hosts
Healthy Male
+ Intact Immune System
+ Cryptococcus
+ Not improving with treatment
Cryptococcus gattii !!
## C. neoformans vs C. gattii

<table>
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<tr>
<th>neoformans</th>
<th>gattii</th>
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<tbody>
<tr>
<td>Immunocompromised</td>
<td>Immunocompetent</td>
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<td>Acute</td>
<td>Subacute</td>
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<td>Mortality</td>
<td>Morbidity</td>
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<td>Proven treatment regimen</td>
<td>Longer and more complex treatment</td>
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Capsule

gattii

neoformans
Treatment?

A. Amphotericin lipid complex
B. Flucytosine
C. Fluconazole
D. Interferon gamma
E. Steroids
Treatment

Amphotericin
Flycytocine
VP Shunt
Interferon
gamma
Discharged on
Fluconazole +
Steroid taper
Stable
On Fluc/Steroids

Day 1 14 20 75 Now

Headaches
High opening
pressure
CSF Crypto Ag
1:2048
CSF negative
CSF Cryptococcal Ag
still positive
Cryptococcus can be found in normal hosts

C. gattii is harder to treat

Speciating cryptococcus early in a normal host could lead to faster escalations of treatment

Scan for cryptococcomas in C. gattii patients
Questions?


Things to read about:
- Australia history
- Why immunocompetent
- CSF profile
Latent vs Primary Infection?

1980s
Marines
Hawaii, Philippines, Thailand, Australia, Okinawa, Hong Kong

1990s
National Guard
Missouri, Mississippi

2000s
Worked in a scrapping yard with pigeons, in a North AL chicken house, and construction

2010s
Hunts/east/skins rabbits, squirrels, deer, groundhogs, turtles, wild hogs

Current
The Capsule

- Negatively charged protects from phagocytosis
- Causes adherence and inhibition of neutrophil migration
- Capsule increases by:
  - Decreased iron
  - Increased CO₂ concentration
  - Increased age of organisms
  - Increase in duration of infection
- Increased capsule = resistance to drugs and phagocytosis
Cryptococcus

- **Serotype A**: C. neoformans var grubii
- **Serotype B & C**: C. neoformans var gattii
- **Serotype D**: C. neoformans var neoformans

**C. gattii**
Risk Factors

- Steroid use
- Underlying pulmonary disease.
- > 50 yo
- Current smokers
- Immunosuppression due to HIV or invasive malignancy.
- Exposure
- Negative workup:
  - Urine Histoplasma
  - Chlamydia
  - Gonorrhoea
  - Aspergillus
  - CMV Ag
  - RMSF Ag
  - Hepatitis A, B, C
Why immunocompetent?

- Was it just lack of disease awareness and reporting? No.
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