Cryptococcal Meningitis In Africa

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Case presentation

- 23 years f, admitted 02/02/04
- Fever, headache x 2/52,
- Altered mental status, seizures x 3/7
- HIV positive, no previous HIV associated or AIDS defining conditions
- LP done 9/02/04, turbid, high pressure
- Lab: WBC 0, protein 238 mg/dl, glucose 36mg/dl, indian ink negative
Case presentation cont:

RX: 02/02/04- 9/02/04 - xpen & ccol & gentamicin
- 05/02/04- iv fluconazole 800mg & sp 2 tab od
- 12/02/04- TB meningitis RX (2SRHZ/7RH)

Course and outcome:
- No clinical improvement seen
- Death on 17/02/05

NB: retrospective cryptococcal antigen test CSF was positive.
MENINGITIS PROFILE – ADULTS MALAWI 2003

Cryptococcus neoformans
Streptococcus pneumoniae
Non-typhi Salmonella
Neisseria meningitidis
Other Gram negative rods
Other

wellcome Trust Laboratories
Blantyre, Malawi, 2003
INCIDENCE IN OTHER AFRICAN COUNTRIES

- **SOUTH AFRICA**: 1998- 26%
  (Silber et al. J. Neurol Sci. 1999 Jan 1;162 (1) 20-6)
- **RWANDA**: 1983-1992- 19%
- **ETHIOPIA**: 1998-2000- 7%
- **GHANA**: 1998 0%
Epidemiology

- Incidence of C. neoformans has increased from 1981.
- It is the most common form of adult meningitis in Africa.
- Third most common neurologic presentation of AIDS sub Saharan.
- First AIDS defining condition in 40-91% of patients.
Clinical presentation

- Insidious onset with non specific symptoms mean duration of 2wks
- Clinical features:
  - Headache 97%
  - Fever 61%
  - Altered consciousness 58%
  - Neck stiffness 74%
  - Seizures 13%,
Other associated OI

- Oral candida
- Tuberculosis
- Herpes Zoster
- Wasting syndrome
APPROACH TO MANAGEMENT
1. Lab investigations

- CSF:
  - Elevated opening pressure
  - Abnormal WBC, glucose, protein *(but may be normal)*
  - Indian Ink Stain
  - Cryptoccocal antigen test
  - CSF culture
Lab investigations

- Serum cryptococcal antigen test
- Serum fungal culture

Others:
- Neuroimaging: MRI/CT scan
2. Treatment

- AMPHOTERICIN B 0.7-1.0mg/kg/d × 2wks +/− 5-Flucytosine 100mg/kg/day followed by
- Fluconazole 400mg po qd 8wks or itraconazole 400mg/day

- Maintenance
  - Fluconazole 200mg od po or
  - Itraconazole 200mg bd po or
  - Amphotericin B 1mg/kg iv X 1-2 times/ wk
Treatment in Malawi

- Fluconazole 800mg od x one week
- Then 400mg od x4 weeks
- Then 200mg od lifelong
- Or amphotericin B initiation phase
Treatment

- If evidence of raised intracranial pressure:
  
  Repeated lumbar punctures
  acetazolamide  250mg qid
  Intraventricular shunting
What is the optimal treatment for Resource limited areas?

- Success stories with fluconazole and flucytosine
  
  (Kiza et al. CID 1998;26 June)

- Failures and success on high dose fluconazole

- Need for therapeutic trial in subsaharan Africa
3. Prevention

- Primary and secondary prophylaxis
- Screening
- Monitoring
- Early diagnosis
- HAART
Course and prognosis

- Poor indicators:
  - altered mental status
  - cranial nerve involvement
  - high intracranial pressure
  - high number of organisms
Course & prognosis

- Untreated cryptococcal meningitis is almost 100% fatal
- Median survival without treatment in Blantyre is 4 days, Harare 14 days, Zambia 10 days
- 35% hospital deaths in patients treated with fluconazole only at Lilongwe Central Hospital.
Course and prognosis for a cohort on HAART-LCH 2003-2005

- 35 patients with CSF Indian ink positive
- Mean age 35.8 (range- 25- 52)
- Mean CD4 98.6 cells/mm³ (range-1-420 cells/mm³)
- Associated OIs: 61 % (n=16) TB, weight loss, shingles, oral thrush, diarrhea
Course and prognosis for a cohort on HAART-LCH 2003-2005

- Treatment:
  1. Fluconazole 800mg od
     400mg od x1 week
     200mg prophylaxis
  2. ART: Stavudine, lamuvidine, nevirapine
Course and prognosis for a cohort on HAART-LCH 2003-2005

- Duration of follow up 1 month-1 yr 4 months
- Loss to follow up 8/26, 1 transfer out
- Relapse or post CM IRIS? in 5/18 (27.8%)
- Follow up CD4 on only 4 clients,
Conclusion

- Cryptoccocal meningitis is a common opportunistic infection in sub-Saharan Africa.
- Cryptoccocal meningitis still carries a high morbidity and mortality rate even with antifungals.
- More research is needed to see the impact of fluconazole monotherapy on the treatment of cryptoccocal meningitis in resource-limited settings.
Conclusion

- Pharmacokinetic studies of possible drug interactions between drugs for other Ois and fluconazole
- Good laboratory facilities are needed for prompt and accurate diagnosis of cryptococcal disease
- A call for widespread use of HAART to reduce mortality and morbidity associated with cryptococcal disease.
WHAT IS THE OPTIMAL MANAGEMENT FOR CRYPTOCCOCAL MENINGITIS PATIENTS IN RESOURCE LIMITED SETTING?
Thank you for your attention~~