Disclosure

Declares the following financial relationships:

- My institution receives support on my behalf as a Site Investigator for a research grant from Gilead Sciences

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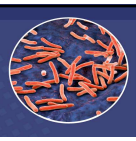
45-year-old female patient



Ethiopian female living in Aurora, CO with no known PMHx who presented to the emergency department with chronic weight loss and progressive weakness, admitted

HPI:

+Weight loss 40 lbs over last year.
+ Acute onset of RUE and RLE weakness a week prior.
Denied fevers, night sweats, cough, HA, n/v, GI sx.

History:

Moved to CO 14 years ago from Ethiopia. Last traveled to Ethiopia 4 years ago.
Not sexually active, no substance use. Last sexual contact with male ~6 years ago.
Has worked at airport and at a factory while in CO.
Lives with mother, no sick contacts or animals.

Exam:

Afebrile, 1 L NC. Flat Affect. RLE flaccid paralysis, RUE 4/5 weakness. Normal CN.

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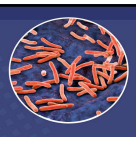
Labs & Imaging



Labs: WBC 5.5, Hgb 10.9, plts 223. Cr 0.48. LFTs wnl

Imaging:

CXR: Findings suspicious for mediastinal mass or adenopathy

Head CT: Suspect lesion in the left posterior frontal lobe with perilesional edema, this may be neoplastic.

CT Abd/Pelvis: diffuse retroperitoneal and mesenteric lymphadenopathy

CT Chest: no PE, bilateral perivascular bronchial wall thickening, mucous plugs, right apical subpleural nodular opacity, diffuse lymphadenopathy

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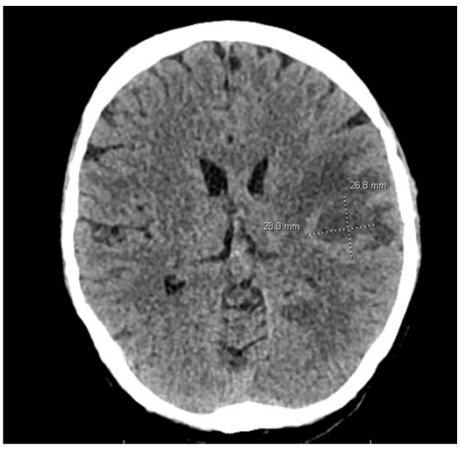
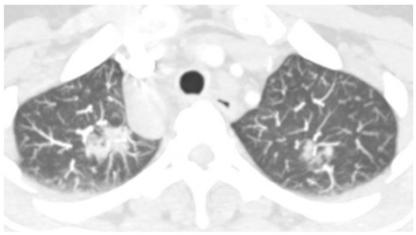
What is your differential? Next steps?





Patient Course

HIV ½ aby/ag screening & confirmatory antibody tests are positive
Advanced with CD4 18%, 280

Lumbar Puncture:
CSF: **38 nucleated cells (89% lymphs), protein 166, glucose 33**. Gram stain no orgs. MTB PCR neg. Meningoencephalitis panel negative.
Bacterial, fungal and AFB Cx in process.

MRI brain: multiple supratentorial and infratentorial enhancing lesions. Moderate vasogenic edema

MRI C/T/L spine: multiple enhancing intramedullary lesions in cervical and thoracic cord, diffuse lymphadenopathy

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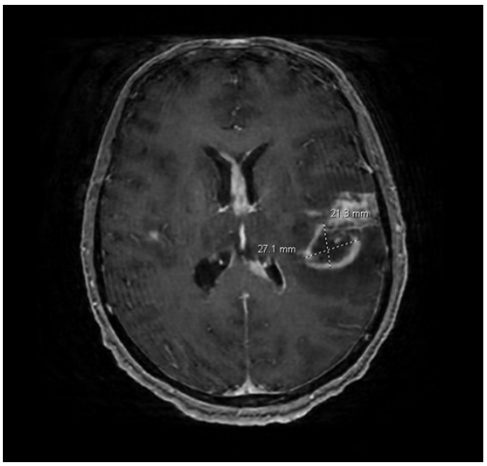
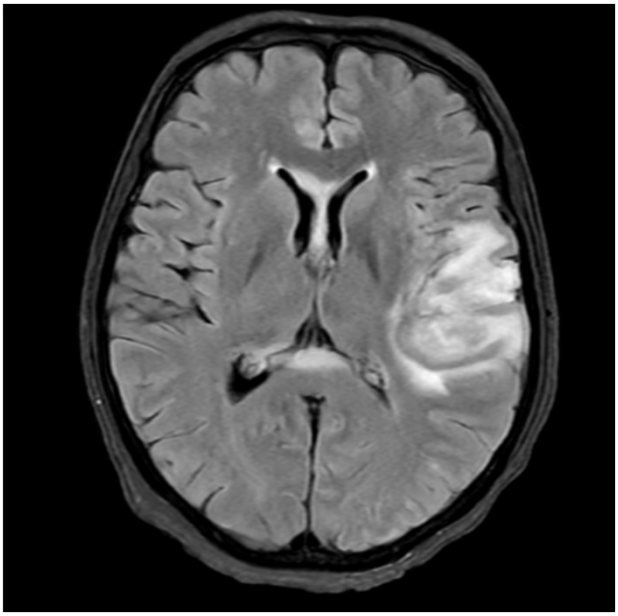
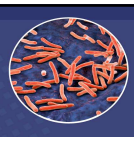
MRI Brain





Hospital Course



S/p EBUS and bronchoscopy

Aerobic cx/ AFB/ fungal cultures sent, negative MTB PCR on BAL fluid
Pathology: 1 of 3 lymph nodes with focal areas of possible granuloma formation, no AFB or fungal forms seen on special stains

CNS Toxoplasmosis & EBV PCRs +, started on Bactrim Rx

No improvement clinically or radiographically 2 weeks post-treatment
LN & BAL cultures for AFB/fungal NGTD x 14 days
CSF CRAG/JCV/CMV/path negative for malignancy, AFB/fungal cx 15 days

She starts having fevers & hypotensive episodes with AMS

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What would you do now?

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Follow Up

- **RIPE started Day 15 due to fevers, lack of improvement on Bactrim**
  - Continued to hold ART due to IRIS risk
  - Within a few days of RIPE fevers resolved, AMS improved
- **Day 16 the LN biopsy AFB culture comes back positive**
  - One week later mycobacterium tuberculosis confirmed, pan-S
  - After 2 weeks of Bactrim + RIPE her lower and upper extremity weakness improved
  - Started on ART (dolutegravir BID plus tenofovir disoproxil fumarate/emtricitabine) for HIV treatment plus steroids for possible CNS TB
  - All AFB cultures in CNS, BAL remain NGTD

***Seen in clinic 3 weeks after starting RIPE able to walk w/support!**

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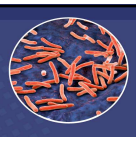
Tuberculous Meningitis (TBM)



- **Pathology:** rupture of subependymal or parameningeal tubercle->subarachnoid space ->meningeal infection->**basilar inflammation**
  - Can cause: CN injury, vasculitis w/stroke, communicating hydrocephalus
  - **CN III, VI and IV** most commonly impacted
  - Basal cerebral artery->**pons, basal ganglia and thalamus**

- **Diagnostics:**
  - CSF: Aseptic meningitis: lymphocytic, high protein, **low glucose**
  - *CSF AFB cultures only 56% sensitive,* 87% if multiple samples obtained
  - High index of clinical suspicion is needed for suspected cases!

- **Outcomes:**
  - Even with Rx**, death or severe neurologic impairment** is outcome in **most patients (50% with disability following dx)**
  - **Late sequelae:** CN palsy, hemiplegia, blindness, dementia

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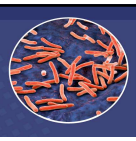
Schlossberg. Tuberculosis and NTM infections. 6th edition 2011. Hosoglu S, Geyik MF, Balik I, et al. Predictors of outcome in patients with tuberculous meningitis. Int J Tuberc Lung Dis 2002;6:64-70

TBM in PLWH



- People living with HIV (PLWH) are **14 times more likely to develop TB with 2x mortality rate** vs. general population
- PLWH are at higher risk for TBM, particularly with lower **CD4 counts (<200, especially <50) & with a poorer prognosis**
  - The prevalence and incidence of TB meningitis in people living with HIV (PLWH) was approximately 13.6% and 1.5 per 1000 per year
  - **Case fatality rate was 38.1%, in some cohorts up to 50%**
    - High morbidity and mortality rates were observed among PLWH and TB in resource-limited countries (sub-Saharan Africa) compared to other locations
    - Poorer outcomes in studies with higher proportions of women

Chen et al. Prevalence, incidence, and case fatality of tuberculous meningitis in adults living with HIV: a systematic review and meta-analysis. BMC Public Health 2024

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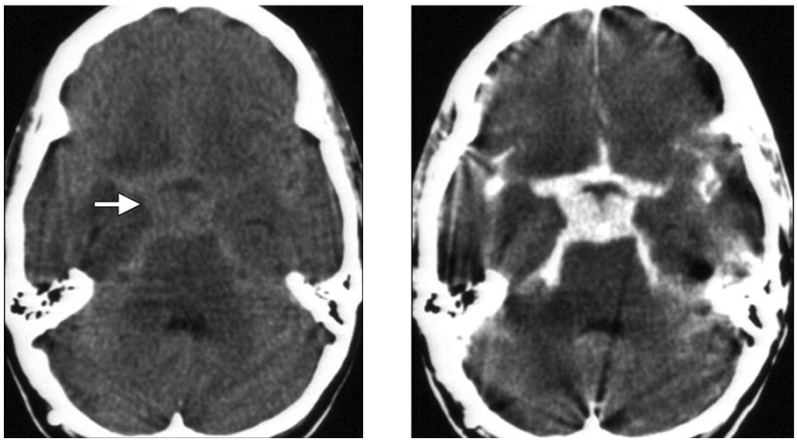
TB meningitis: Imaging



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TB Meningitis: Treatment

1. **Intensive Phase**
   - Isoniazid (INH), Rifampin (RIF), Pyrazinamide (PZA) and Ethambutol (**RIPE**) + B6 x 2 months
     - *For meningitis only: add high dose **dexamethasone taper** for 12 weeks*
     - First 2 to 3 weeks are spent in home isolation
       - Can't work, go to school or be out in public places

2. **Continuation Phase**
   - INH & RIF x 7-10 months (**9-12 total months**)

https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-opportunistic-infections/mycobacterium-0?view=full

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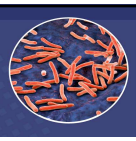
HIV in African-born US residents



- HIV diagnosis rates among African-born US residents are **six times higher** than the general population
  - **HIV diagnosis rates among African-born women** are **12 times** higher than estimated incidence among women in US population
    - 3 times higher than Black US-born women
    - 2 times higher than Black foreign-born women
- Diagnosed with lower CD4 counts and higher rates of advanced HIV (AIDS) than US-born persons and other foreign-born
  - Black Africans more likely to present with AIDS (45%), compared to both US-born non-blacks (25%) and US-born blacks (35%)

1.Blanas et al. HIV/AIDS Among African-Born Residents in the United States. J Immigr Minor Health. 2013 Aug; 15(4): 718–724.
2.Page LC et al. **Access to regular HIV care and disease progression among black African immigrants.** J Natl Med Assoc. 2009 Dec;101(12):1230-6.

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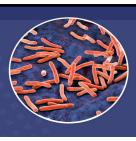
HIV testing: East-African immigrant women



- "Getting tested is almost like going to the **Salem witch trials.** The witches are doers of all evil, it is a **metaphor of everything they have done wrong**. Especially if you are not supposed to be having sex because you are not married, they assume that is the only way you can get it."
  - Kenyan woman
- "I think people don't want to be judged by the community. Getting an **HIV test brings shame** to the family."
  - Ugandan woman

De Jesus et al. "Getting tested is almost like going to the Salem witch trials": discordant discourses between Western public health messages and sociocultural expectations surrounding HIV testing among East African immigrant women". **AIDS Care: Psychological and Socio-medical Aspects of AIDS/HIV. Volume 27, Issue 5, 2015**

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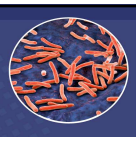
Advanced HIV: CNS opportunistic infections



- **Ddx CNS lesions:**

  1. Non-Advanced HIV conditions:
  HSV/VZV encephalitis, neurosyphilis, neurocysticercosis, brain abscess, malignancy, etc

  2. Opportunistic Infections:
  - **Space occupying lesions:** Toxoplasmosis, primary CNS lymphoma
    - Rarely cryptococcoma/tuberculoma
  - **Non-space occupying lesions**:
    - *Life threatening: TB meningitis, Cryptococcal meningitis*
    - Others: PML (progressive multifocal leukoencephalopathy), HIV or CMV encephalitis

- **DDx: CNS & lung infections**
  - Atypical bacteria (nocardia), mycobacteria (TB), fungal (cocci, histo, blasto, crypto), non-infectious (malignancy, vasculitis/autoimmune)

  ***Always consider multiple OIs can be present in the same patient at same time!**

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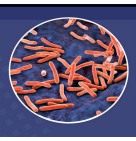
HIV treatment: When to start



- **Antiretroviral therapy (ART) is recommended for all persons with HIV** to reduce morbidity and mortality **(AI)** and to prevent the transmission of HIV to others **(AI)**

- **Start ART immediately (or as soon as possible) after HIV diagnosis** in order to increase the uptake of ART and linkage to care, decrease the time to viral suppression for individual patients **(AII)**

- When initiating ART, it is important to educate patients regarding the benefits of ART and to deploy strategies to optimize care engagement and treatment adherence **(AIII)**

- **Delay ART if concern for TB meningitis or cryptococcal meningitis (risk of life threatening IRIS)**

Initiation of Antiretroviral Therapy. *Guidelines for the Use of Antiretroviral Agents in Adults and Adolescents with HIV*
https://clinicalinfo.hiv.gov/en/guidelines/hiv-clinical-guidelines-adult-and-adolescent-arv/initiation-antiretroviral-therapy?view=full

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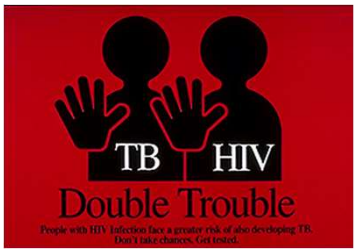
Treatment for TB-HIV co-infection

- Recommendation: treat co-infected patients with TB-HIV with ARV within 2 weeks of TB treatment if CD4<50
  - May delay by 4-8 weeks if CD4>50, especially if >200
  - **Exception: TBM: delay therapy for 8 weeks after starting RIPE**

- Complicating factors:
  - Drug-drug interactions
  - IRIS
  - Pill burden



Torok et al. Timing of initiation of antiretroviral therapy in human immunodeficiency virus (HIV)--associated tuberculous meningitis. Clin Infect Dis. 2011 Jun;52(11):1374-83. doi: 10.1093/cid/cir230.

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Thank you to our patient!

- Questions on complex HIV management: Katherine.frasca@cuanschutz.edu

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