Los Angeles County TB Meningitis/CNS-TB Checklist (2023)

☐ **Step 1: consider and pursue diagnosis of TBM/CNS-TB**

Indications for CNS evaluation:

-signs/symptoms;

-miliary/disseminated[1] disease;

-immunosuppressed host[2];

-age ≤ 1-years-old;

-others per clinical judgment[3];

Components of adequate CNS TB evaluation:

-lumbar puncture to evaluate for **TB meningitis**: cell count/differential, glucose, protein; MTBc PCR and AFB stain/culture; opening pressure; ADA; +/- others per clinical judgment;

-optimize bacteriologic yield for DST's: repeating high-volume CSF specimens for AFB culture; sampling from multiple body sites (e.g. urine, blood, +/- stool); pursuing tissue/biopsy (i.e. dural/brain)

-imaging to evaluate for both **tuberculomas & TB meningitis** (as well as complications):

-head CT with IV contrast: may miss more subtle manifestations, but quick and widely available;

-brain MRI with IV contrast improves sensitivity, especially visualization of the posterior fossa;

-CTA/MRA may also be considered in the setting of suspected TB-associated CNS vasculitis/stroke syndromes;

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☐ **Step 2: optimize management of TBM/CNS-TB**

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[1] There is no consensus surveillance definition for "disseminated" TB in the United States. A local definition proposed in LA County since 2022 included patients with any of the following: 1) CNS involvement (CSF, meninges/dural sinus/choroid plexus, brain, spinal cord, pituitary gland); 2) miliary chest imaging; 2) involvement in any of these—pulmonary, laryngeal, epiglottis, trachea, bronchus, bronchiole, bronchial fluid, tracheal fluid, pleural, or lymph node: intrathoracic—PLUS at least one other site of disease not among those within the parentheses.

[2] Includes individuals who are HIV-positive or are receiving immunosuppressive medical treatment.

[3] Some experts consider hectic or recurrent patterns of fever despite adequate empiric anti-TB treatment to be an indication for CNS involvement.

Molecular and phenotypic DST's:

-expedite and expand panels according to specimen availability;

-use MTB/RIF (Xpert) PCR to predict susceptibility to rifampin, but also consider requesting PSQ/MDDR for isoniazid (+/- fluoroquinolones, etc.) as soon as appropriate specimens or isolates become available;

-consult TBCP to identify appropriate specimen(s) and acceptable indication(s) for PSQ/MDDR requests;

- if indicated to ensure adequacy of anti-TB treatment regimen, consider expanding phenotypic DST's to include fluoroquinolones +/- other second-line agents[4];

Anti-TB treatment regimen:

-**directly observed therapy (DOT)** administered by DPH is the standard of care for TBM/CNS-TB;

-**consider intensification and expansion of initial empiric anti-TB treatment regimen**, **according to indication/severity, availability, and site of care**:

-high-dose/IV rifampin;

-fluoroquinolones (levofloxacin, moxifloxacin);

- linezolid, ethionamide, injectable agents, etc.;

-**use therapeutic drug monitoring** to optimize dosing—especially for core agents;

-some experts continue an expanded anti-TB treatment until documentation of therapeutic drug levels for core agents in the definitive regimen;

-if possible or proven **drug-resistance** is discovered in patients with TBM/CNS-TB, promptly (re-)consult TBCP for guidance on anti-TB regimen composition;

Adjunctive immunomodulation:

-**glucocorticoids are strongly recommended for ALL patients with TBM/CNS-TB, regardless of disease severity;**

-steroids are available on Public Health Pharmacy formulary and should be included in DOT orders;

-minimum duration of steroids: 6 weeks (patients often require more gradual/longer tapers);

-individualized (not strictly scheduled) steroid tapers are the standard of care;

[4] Resistance to (or intolerance of) isoniazid is one scenario in which fluoroquinolone DST is indicated.

-conduct in-person clinical assessments every 1-2 weeks to inform a safe and well-tolerated steroid taper;

-consider other emerging strategies in consultation with TBCP: ASA; thalidomide, infliximab, anakinra;

Serial imaging:

-if baseline diagnostic imaging abnormal, must document radiographic improvement (or stability): repeat brain MRI with IV contrast after 2-3 months of initial therapy;

-for patients with HIV and baseline abs CD4 <200, may consider repeat brain MRI with IV contrast considered after immune re-constitution to evaluate for paradoxical TB-IRIS;

-**end-of-treatment imaging** can be informative for post-treatment monitoring (see Step 3 below), and for distinguishing between relapse (which is very rare in our setting) and other neurologic disorders that a patient may develop in the future;

-extending adequate rifamycin-based anti-TB treatment beyond 12 months for susceptible TBM/CNS-TB is unlikely to be beneficial for immunocompetent hosts even if there are stable residual radiographic abnormalities at end-of-treatment;

-consider repeat imaging at other timepoints on a case-by-case basis, as indicated according to a patient's clinical course;

Care coordination and clinical consultation:

-proactively coordinate with primary care and other provider(s) to facilitate timely accomplishment of several of the above recommendations;

-reinforce importance of managing comorbid conditions that may affect outcomes of treatment for TBM/CNS-TB (e.g. HIV, DM, chronic HCV, etc.);

-care coordination and case management must include medication reconciliation to address potential drug-drug interactions;

-identify and proactively manage sequelae, complications, and side effects (e.g. vascular events, sensorineural hearing loss, changes in visual acuity);

-request initial and longitudinal clinical consultation with TBCP physician consultant[5]

☐ **Step 3: treatment completion and post-treatment monitoring for TBM/CNS-TB**

Treatment completion and duration:

-a minimum of 9-month rifamycin-based treatment regimen is recommended for most patients with TBM/CNS-TB;

[5] Scheduling monthly—or even weekly—case review and clinical consultation with a TBCP physician consultant is a reasonable strategy to ensure optimized management of TBM/CNS-TB.

-treatment duration may be extended to a minimum of 12 months on a case-by-case basis for many patients with TBM/CNS-TB;

-repeat imaging at or near end-of-treatment can inform decisions regarding treatment duration;

-request clinical consultation with TBCP physician to assist with determination of treatment completion;

Post-treatment monitoring:

-some experts recommend clinical monitoring for a minimum of 2 years after completion of therapy for TBM/CNS-TB;

-post-treatment monitoring plans should be individualized, feasible, concrete, and consistent;

-may include surveillance AFB cultures from conveniently sampled sites of disease involvement such as sputa;

-bacteriologic relapse of TBM (i.e. CSF AFB culture+ for MTBc) is distinctly unusual, but has been described;

-there is not a single standard, evidence-based recommendation, and individualization is appropriate;

-monitoring can be conducted in coordination with a patient's primary care provider, but it is also reasonable to offer such monitoring to be conducted in Chest/TBE clinic;

-some experts also recommend repeat brain MRI with IV contrast at pre-determined intervals after treatment completion (e.g. ~6-12 months, 24 months);

-others recommend that any decisions regarding post-treatment imaging be guided by clinical assessments

-request clinical consultation with TBCP physician to assist with developing a post-treatment monitoring plan and for immediate guidance if there is suspicion of relapse