TNF-\(\alpha\) Inhibitors and TB


Key Points:
- Association between TNF-\(\alpha\) antagonists based on case reports of temporal association
- Based on limited data, patients being considered for TNF-\(\alpha\) antagonists should be screened and treated for LTBI first
- Consider active TB infection (including extrapulmonary) in your differential for these patients

Relationship between TNF-\(\alpha\) antagonists and reactivation of LTBI?
- Case reports of temporal association for infliximab (less for etanercept) – median of 12 weeks after infliximab
- Extrapulmonary and disseminated TB most commonly reported
- More frequently reported than other opportunistic infections
- Increased awareness vs. causal relationship – not proven, but generally accepted

Diagnostic challenges
- Rheumatoid lung disease and pulmonary TB
- Crohn’s disease and ileocecal TB
- What is the cut-off for the tuberculin skin test and prevalence of anergy in these patients?
- Masking of typical TB symptoms (weight loss, fever, sweats) by TNF-\(\alpha\) antagonists?

Therapeutic challenges
- Complete course of LTBI therapy or initiate therapy before starting TNF-\(\alpha\) antagonists
- No data for reduction in risk of TB activation after LTBI treatment course

Recommendations
- Screening before therapy
  - Exclude active TB: symptoms, exposures, CXR, AFB when appropriate
  - Determine adequacy of prior treatment
  - PPD with 2-step baseline in elderly and in those needing annual testing
- Treatment
  - LTBI treatment for 9 months for +PPD or CXR and history consistent with LTBI
  - Delay TNF-\(\alpha\) antagonists until after completed LTBI treatment
  - If necessary, consider possible TNF-\(\alpha\) antagonists 1 month after initiation of INH.

TB Meningitis


Key Points:
- There is no diagnostic gold standard because of limitations of culture
- Data applicable to our population are limited (often in endemic areas or for children)
- Treat immediately if high clinical suspicion based on risk of TB, CSF, or CT findings

- 300 to 400 cases in U.S. (1% of clinical TB); in endemic areas, associated with HIV
- Fatality ratio 15-40%
- Phases: I (2-3 weeks malaise, AMS, fever), II (CN palsies or hemiparesis), III (coma, seizures, focal findings)
- CSF: low glucose (<45 in 80%), elevated protein (100-500mg/dL), lymphocytic pleocytosis (cell count 100-500)
  - After rx, shift to PMN cellular with clinical deterioration (“therapeutic paradox”)
- Diagnosis:
  - Serial CSF AFB stain and culture (use last fluid removed and 10-15cc)
    - Positive for days after initiation of therapy
    - 37% \(\rightarrow\) 87% with four taps based on 1 case series
  - PCR: limited sensitivity and specificity
  - Radiology: basilar meningitis +/- hydrocephalus
- Rx: oral INH higher dose, rifampin, pyrazinamide, +/- ethambutol or streptomycin for resistance – no trials for length
- Adjunctive corticosteroids for stage II/III disease, acute encephalitis, therapeutic paradox, high risk CT findings