Sp13: In patients with inconclusive biopsy, can empirical therapeutic trial with anti-tuberculosis drugs be initiated or repeat biopsy is necessary?

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Recommendation: Based on available data, in patients with inconclusive biopsy (inconclusive biopsy would be defined as those which donot show any findings in histopathological exam, geneXpert or culture) but high clinical suspicion for tuberculosis, advanced diagnostic modalities should be considered in order to try to come to an conclusive result. In those patient who still prove to be inconclusive, there is a need for high quality prospective randomised control trial to conclude as to whether an emperical therapeutic trial or repeat biopsy should be advocated. Untill such time, the decision should be left to the judgement of the physician deliberating on pros and cons relevant to the particular patient and involving the well informed patient in decision making.

Level of Evidence: Low

Delegate Vote:

Rationale:

In patients with clinical suspicion of tuberculosis (TB) but an inconclusive biopsy, there is ongoing debate regarding the appropriate next step in management. Tuberculosis remains a significant global health threat, and early diagnosis and treatment are crucial to prevent disease progression and transmission.[1] When a biopsy yields inconclusive results, clinicians are faced with the challenge of deciding whether to initiate empirical anti-tuberculosis therapy or to pursue repeat biopsy or alternative diagnostic approaches.

Clinical Presentation and Epidemiological Risk Factors:

- In developing countries with high prevalence of TB, spinal TB is often diagnosed and treated empirically based on the clinical and radiological criteria. But radiography cannot diagnose it until there is more than 50% decalcification of the vertebra. The magnetic resonance imaging (MRI) on the other hand is a very sensitive tool in identifying the typical features of spinal tuberculosis including bone marrow oedema, endplate erosion, vertebral destruction, paravertebral collection, cord compression and cord changes but its specificity is very low.[2] The decision to initiate an empirical anti-tuberculosis trial should be based on patient's clinical presentation (e.g., prolonged fever, weight loss, night sweats, or localized symptoms suggestive of TB), epidemiological risk factors (e.g., history of TB exposure, travel to endemic areas, immunocompromised status) and radiological findings.[3] High clinical suspicion, radiological suspicion and in conjunction with relevant risk factors, may warrant an empirical therapeutic trial of anti-tuberculosis drugs.
- In regions with high TB prvalence or when TB is strongly suspected, a decision to initiate an empirical trial of anti-tuberculosis therapy may be justified, even in the absence of a conclusive biopsy.[4] Early initiation of

treatment could be lifesaving, particularly in immunocompromised patients or those with severe disease.

Repeat Biopsy Consideration:

- If clinical suspicion for TB remains high, and empirical therapy is not immediately warranted (due to concerns about drug side effects, potential resistance, or other underlying conditions), a repeat biopsy is often necessary. This is especially true in cases where the initial biopsy is non-diagnostic or when other causes (e.g., malignancy, granulomatous inflammation) have not been definitively excluded based on atypical radiological or clinical findings.[5]

Diagnostic Limitations:

- Biopsy specimens may be inadequate for a definitive diagnosis due to insufficient tissue, contamination, or the absence of granulomas or acid-fast bacilli (AFB).
- As mentioned above, the empirical treatment maybe started based on the demography, clinical suspicion and radiological findings.
- However, if there is deterioration of the clinical conditions after inititation of the therapy or no improvement in blood markers, a repeat biopsy could be considered. A repeat biopsy should ideally be combined with advanced diagnostic modalities, such as molecular testing e.g., PCR for Mycobacterium tuberculosis, liquid culture, metagenomic next-generation sequencing (mNGS), CT guided biopsy.[6]
- Also with socioeconomic development and decreasing incidence of TB, ruling out non-tubercular pathologies like primary and secondary malignancies, fungal and bacterial infections, spondyloarthropathies and other granulomatous lesions of spine are becoming more important.[7]

References:

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