

Sp 14: Management of a patient not responding clinically to anti-tubercular therapy - Should second line drugs be started or a repeat biopsy needed to confirm resistance to primary drugs?

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Recommendation: The patients of TB spine not responding clinically and radiologically to 4 months antitubercular therapy should be submitted for biopsy to ascertain the diagnosis of tuberculosis and drug resistance by subjecting the tissue obtained for Histology, AFB culture (phenotypic DST) and GeneXpert and Line probe assay (Genotypic DST).

Level of Evidence: Moderate

Delegate Vote

Rationale:

Globally, an estimated 410,000 people developed multidrug-resistant (MDR) or Rifampicin-resistant (RR) TB in 2022.(1) The first National anti-Tuberculosis Drug Resistance Survey (NDRS) revealed that 28% of TB patients were resistant to any drugs (22% among new, 36.82% among previously treated (PT)) and 6.19% had MDR-TB (2.84% among, 11.62% among PT). Isoniazid (H) resistance (16% in all with 11.6% in new, 25% in PT) is a driver for RR-TB.(2).

Various studies are published where cases of proven drug resistance on culture/GeneXpert are treated for drug resistant (DR) spinal TB. Bhosale reported that 150/275 (55%) showed growth on MGIT culture out of which 43 demonstrated drug resistance. (3) Pawar reported 25 cases of culture-proven drug-resistant cases. (4) Mohan reported 111 culture-proven drug-resistant cases out of 686 culture-positive cases. (5) Li et.al reported a series where tissue from 249 spinal TB cases were submitted for culture. 127/249(51%) showed culture growth . 39/127 were drug resistant cases which were treated by second line ATT and/or surgery. 35/39 are reported with minimum 18 months follow up. (6) These all studies reported drug-resistant spinal TB cases who showed drug resistance on TB culture.

Jain et al. reported the validation of criteria to label a case as presumptive drug resistance (therapeutically refractory disease) and analysed the tissue samples by histology and phenotypic and genotypic DST. It was recommended to treat proven drug resistance cases by individualised second-line ATT, and the remaining cases were labelled as clinical drug resistance and treated by the MDR protocol.

DR-TB is labelled when Mycobacterium is cultured and DR is demonstrated.

Presumptive(suspected) drug resistance (PDR-TB) can be labelled when a patient of bone/spine TB on ATT for 4 months or more show poor clinic-radiological treatment response as worsening of lesion, increased spinal deformity, persistent discharging sinus/ulcer, appearance of fresh lesion, recurrence of previous lesion and wound dehiscence of post-operative surgical scar. In all such cases, the diagnosis of TB is to be ascertained by histology/PCR. The phenotypic/genotypic TB culture can establish drug resistance and be treated accordingly. (7,8)

In three studies by Abhimanyu (9), Yadav (10) and Gain (11) et.al, the diagnostic accuracy for TB and establishing the diagnosis of drug resistance was evaluated. The diagnostic accuracy for TB was 100% when tissue was submitted in tandem to AFB smear, TB culture, Histology and CBNAAT and LPA; thus, inclusion of molecular methods not only increases diagnostic

accuracy for TB, but also demonstrates the demonstration of DR in presumptive drug resistant cases. If tissue is insufficient, histology and CBNAAT can ascertain TB with RIF sensitivity in 100%. (9,10,11) Genotypic and phenotypic DST will be useful to prove (in 90% of instances) the type of drug resistance. The remaining patients on strong clinical suspicion of DR and yet inconclusive on phenotypic/genotypic DST (< 10%) may be treated as clinical drug resistance (CDR) by MDR protocol of ATT. (7) Gupta et.al. reported a retrospective analysis of 37 such cases, which were labelled as presumptive drug-resistant cases, and tissue was submitted for AFB smear, TB culture, histology and molecular methods (GeneXpert and LPA). The cases were treated as proven drug resistance and clinical drug resistance. (12) Finally, based on 6 studies, Jain et.al proposed an algorithm to identify presumptive drug-resistant cases (failure to respond clinically or radiologically to first-line ATT). Such cases are to be subjected to guided/open biopsy and the tissue is to be subjected to AFB smear, histology and genotypic and phenotypic DST. The cases with proven drug resistance are to be treated with individualised second line ATT, and the rest are to be treated as clinical drug resistance. (8)

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