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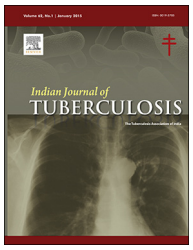

Original Article

Patterns of granulomatous responses in TB lymphadenitis and their correlation with treatment outcomes

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ABSTRACT

Introduction: Four patterns are noted in aspirates of TB lymphadenitis with or without concomitant HIV. They are granulomatous, necrotizing granulomatous, predominantly necrotizing and necrotizing suppurative designated pattern 1, 2, 3 and 4, respectively. The present study attempted to correlate granulomatous patterns, Acid Fast Bacilli (AFB) density with treatment outcomes.

Materials and methods: The MGG and Papanicolaou stained slides of 56 lymphadenitis patients, 38 TB and 18 TB with seropositive HIV were studied for two years. The AFB were stratified into: 0 – nil (1 – ≤1 AFB, 2 – >1 but <10 AFB, 3 – ≥10 AFB)/10 fields.

Results: There were 35 males and 21 females. Eleven aspirates demonstrated AFB. TB+HIV lymphadenitis displayed a higher AFB score. TB+HIV lymphadenitis aspirates significantly showed higher grade granulomas and AFB. TB+HIV lymphadenitis required ≥8-month treatment. Granulomas (pattern 3 or 4) but not high AFB scores required longer treatment (>6 months). Treatment of AFB (≥1) often extended to >6 months.

Conclusion: TB with seropositive HIV, possibly due to defective immune regulation exhibited granulomas (pattern 3 or 4) necessitating treatment for ≥8 months. Pattern 3 or 4 granulomas irrespective of HIV status demanded >6-month treatment.

1. Introduction

The cytomorphology of TB lymphadenitis in AIDS patients falls principally into either of four patterns: necrotizing, necrotizing suppurative, necrotizing granulomatous and granulomatous lymphadenitis.[1] Of these, necrotizing suppurative is the most confusing since any pointer to the TB infection is missing, this pattern being largely non-specific and can be seen in fungal infections, destructive metastases and other inflammatory conditions. The ill-formed granulomas of the necrotizing and necrotizing suppurative patterns are largely realized with very low CD4 counts.[2]

In a seminal article by Rao et al., these four patterns, albeit with a little difference were correlated with CD4 counts. The necrotizing and necrotizing suppurative with Acid Fast Bacilli (AFB) grade 3+ were clubbed into pattern 1. The granulomatous pattern was divided into pattern 4 without necrosis, AFB 1+ and pattern 3 with minimal necrosis and AFB 1+. The necrotizing and necrotizing suppurative pattern were

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associated with the lowest CD4 counts. The CD4 counts increased in quantum leaps as the granulomas became more defined and AFBs lessened. Thus, it was concluded that pattern 1 suffered from the most severe disease and pattern 4, the least.[3]

Even, in non-HIV patients with TB lymphadenitis, the gamut of the granulomatous responses is not too different from that of HIV positive cases, though necrotizing suppurative may be very occasionally encountered. The treatment outcome of these patients may then be correlated with the cytomorphological pattern. This would test the clinical implications of the patterns encountered in TB lymphadenitis and envisage the likelihood of therapeutic consequence should a particular pattern be faced, conditional upon significant concordance or the absence of such being established between the pattern and the treatment result. Such a study has so far not been undertaken in the literature.

2. Materials and methods

2.1. Study setting

The patients studied were recruited from the patients subjected to Fine Needle Aspiration Cytology (FNAC) of a lymph node. All the patients demonstrating granulomatous inflammation in their aspirates were checked for infection with *M. Tuberculosis*. The patients proven by culture positive *M. Tuberculosis* on their lymph node aspirates were taken up for this study. Since all the patients were included, the sampling method so used was opportunity sampling.

2.2. Method of data collection and duration of study

The archival FNAC slides were collected from the department of pathology which are already diagnosed with TB lymphadenitis. The patient's clinical data included the age and gender, duration of illness, blood counts and mycobacterial culture report. The treatment regimen prescribed by the physician was noted and record of periodic visits by the patient to document his/her disease status was also checked. *Retrospective study was continued for 2 years*. Completed records remained deficient in most cases and thus were not able to be incorporated in the study. Prior to two years, the slides were faded.

2.3. Laboratory methods, grading criteria and statistical methods

We collected and studied the Leishman/May-Grunwald-Giemsa (MGG) and Pap and Ziehl-Neelsen (ZN) stained slides already available in the FNAC laboratory. We grouped the granulomatous response into four patterns; the granulomatous and the necrotizing granulomatous effects occupying pattern 1 and 2 respectively; the necrotizing and necrotizing suppurative reactions occupying pattern 3 and 4 respectively. Pattern 1 granulomatous response should show well-formed granulomas composed of epithelioid cells, few Langhan's giant cells in a background of small lymphocytes or admixed with reactivated lymphoid cells with minimal caseous necrosis in the background. Pattern 2 granulomas likewise should show abundant caseous necrosis in the background with few epithelioid granulomas along with small lymphocytes. Pattern 3 granulomas should show no/occasional granulomas or scattered epithelioid cells with caseous necrosis largely ruling the aspirate picture. Pattern 2 and 3 should be differentiated by whether the granulomas can be found easily or have to be hunted for. Pattern 3 is ≤2 small granulomas in two well-spread slides with good material. Pattern 4 granulomas should not show granulomas at all, rather, very little necrotic material in the background with karyorrhectic debris, numerous neutrophils and scattered macrophages, not the epithelioid type should be the dominant aspirate representation. The number of AFB found were also stratified from numerous to absent into 4 grades; the absent scoring 0, 1 or less AFBs in 10 oil immersion fields (OI) scoring 1, more than 1 but less than 10 AFB per 10 OI awarded 2 and 10 or more AFBs in 10 OI notching a score of 3. The outcome of the treatment was correlated with the pattern of granulomas and the AFB score.

SPSS version 16 was used to analyze the data. Chi-square test was used to establish associations. A p-value of <0.05 was considered statistically significant.

3. Results and analysis

The duration for which slides could be studied spanned from December 2014 to January 2012. The total number of patients (n) were 56 of which 35 were males and 21, females.

Most patients (n = 23/56, 41.1%) belonged to the 20–29-year age group that consisted of 15 males and 8 females. The mean age of the patients was 33.23 ± 14.21 years, displaying a range starting at 10 up to 69 years.

Of all the patients, 38 suffered from TB only and 18, TB with HIV infection. The granulomas in majority of the cases (n = 15/18, 83.3%) of TB+HIV lymphadenitis showed pattern 3 or 4 granulomas. The TB lymphadenitis patients mostly displayed pattern 2 or 1 granulomas (n = 30/38, 78.9%) except 8 cases with pattern 3 or 4 granulomas. This difference in the granuloma patterns between TB and TB+HIV lymphadenitis patients was significant (Chi-square = 10.398, p = 0.0013). Of the 18 TB+HIV lymphadenitis cases, 5(27.78%) showed AFBs in their aspirate while 8(21%) of the TB lymphadenitis patients showed AFBs in their aspirate, the difference not being significant.

Most patients (n = 45/56, 80.4%) had an AFB grade of '0'. Of the 5 patients with AFB grades of 2 or 3, four belonged to the TB +HIV lymphadenitis and only one to TB lymphadenitis alone.

Most of the patients (n = 49/56, 87.5%) were prescribed Category I treatment. The mean duration of treatment was 6.98 ± 2.03 months. The duration of treatment taken by the patients ranged from 2 to 11 months.

The duration of treatment of TB lymphadenitis patients extended to less than 8 months, except 7 (18.42%) cases whereas most of the TB+HIV lymphadenitis patients (n = 12/18, 66.67%) were treated for 8 or more months. The difference in treatment duration between the two groups was significant (Chi-square = 12.69, p = 0.0004).

The granuloma pattern among all the patients was correlated with the final outcome vis-à-vis completed treatment versus discontinued/died and is shown in Table 1. The

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