

Histopathology of lymph nodal tuberculosis – University Hospital experience

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Abstract

Fifty-nine cases of tuberculous cervical lymphadenitis were analysed histologically. Characteristic epithelioid cell granulomas were seen in all the cases with central areas of caseation necrosis in 96.6% (57/59) of these cases. The diagnosis of tuberculosis was further established by the demonstration of acid-fast bacilli (AFB) in the tissue sections in 29 cases. These AFB, although occasional, were found more frequently within the epithelioid cells as compared with other zones of the granuloma. There was no significant association between necrosis and bacillary content. We conclude that light microscopical assessment is still a useful screening method to diagnose tuberculosis in cases of cervical lymphadenopathy.

Key words: Cervical lymph node, tuberculosis, acid-fast bacilli.

INTRODUCTION

Tuberculosis is still a public health problem in Malaysia and is one of the ten major causes of death in Government hospitals. Extrapulmonary tuberculosis constitutes about 9.4% of the total number of cases of tuberculosis.¹ Although tuberculous lymphadenitis is one of the most common forms of extrapulmonary tuberculosis,² very few studies on the histopathology of this condition have been done.^{3,4} The purpose of our paper is to study the pathological spectrum of lymph nodal tuberculosis as encountered in the University Hospital.

MATERIALS AND METHODS

During the period January 1987 to July 1992, a total of 455 consecutive lymph node biopsies were received by the Department of Pathology. Of these 455 cases, 252 cases showed malignancy. A review of the remaining 203 cases of nonneoplastic lymph nodes was done. Ziehl-Neelsen staining for acid-fast bacilli (AFB) and Periodic acid-Schiff staining for fungal organisms were done in all the cases. The diagnosis of tuberculosis was made on the criteria of well formed epithelioid cell granuloma with or without caseation necrosis and or demonstration of AFB.

There were 63 cases of tuberculous lymphadenitis, 59 involving cervical group lymph nodes, 3 axillary group lymph nodes and 1 involving a hilar lymph node. Patients who had axillary tuberculous lymphadenitis were infants who developed lymphadenitis following BCG

vaccination. We studied only cases of tuberculous cervical lymphadenitis. The pathological features noted included the nature of the granuloma, amount of necrosis, types of giant cells, presence of fibrosis and perinodal granulomatous inflammation. Necrosis was considered massive when caseation was present in more than 50% of the area of lymph node, submassive when it occupied less than 50% and focal when scattered microscopical foci were noted. Furthermore, histological analysis of all cases of tuberculosis involving the other organs in order to find the comparative frequency of tuberculous lymphadenitis was done.

Mycobacterial isolation at the time of undertaking biopsy was done in only 9 cases. Direct smear for AFB was made before the lymph node tissue was inoculated onto Lowenstein-Jensen medium. The latter was examined on alternate days for any growth.

Clinical data was based on relevant information provided in the request form accompanying each biopsy.

RESULTS

Lymph node tuberculosis is the most common form of tuberculosis diagnosed histologically in the University Hospital (Table 1). The distribution of organ involvement in the order of frequency is given in Table 1. Tuberculous lymphadenitis constituted 13.8% of all cases of lymphadenopathy (Table 2).

The ages of patients ranged from 4 to 78 years with a mean of 32 years. There were 36 females

TABLE 1: Distribution of histologically diagnosed cases of tuberculosis by organ involvement between January 1987 and December 1992

Site	No. of cases
Lymph nodes	63
Pleura	42
Bone and soft tissue	23
Lung	12
Genitourinary tract	12
Gastrointestinal tract	12
Skin	3
Vocal cord	2
Adrenal gland	1
Breast	1
Pericardium	1
Total	172

and 23 males. Tuberculosis was suspected clinically in 47 patients, while in 4 patients a differential diagnosis of lymphoma was considered. An initial clinical diagnosis of lymphoma was made in 3 patients. Pyogenic infection and a branchial cyst was considered in 2 and 1 patient respectively.

Among the 9 cases from whom AFB culture was undertaken, *Mycobacterium tuberculosis* was grown only in 2 cases (22%). Atypical mycobacteria was isolated in one case. Even though the culture was negative in 6 cases, direct smear for AFB was positive in 2 cases.

TABLE 2: Lymph node pathology by rank order

Diagnosis	No. of cases	%
Metastatic tumour	139	30.6
Reactive lymphadenitis	115	25.3
Lymphoma	113	24.8
Tuberculosis	63	13.8
Miscellaneous	25	5.5
Kikuchi's lymphadenitis (8)		
Dermatopathic lymphadenitis (5)		
Suppurative lymphadenitis (4)		
Non-specific (4)		
Castleman's disease (2)		
Histiocytosis-X (1)		
Sarcoidosis (1)		
Total	455	100

() = number of cases

Pathology

Haematoxylin and eosin stained sections of lymph nodes revealed distinct and well-formed epithelioid cell granulomas in all biopsies (Figure 1). There was partial or complete effacement of lymph node architecture by these granulomas. Variation in the size of the granuloma was observed in 50 biopsies (Figure 2). In 9 biopsies, the variation in size could not be assessed because of wide areas of caseation and compressed granulomas with or without fibrosis. Perinodal and perivascular granulomas were seen in 5 and 1 biopsies respectively. The capsule in all biopsies was intact and showed thickening. Pericapsular fibrosis and fibrosis within the granuloma were noted in 7 and 19 biopsies respectively.

Giant cells within the granuloma were seen frequently (55/59). Both foreign body as well as Langhans' type giant cells were noted. The proportions of these giant cells were equal in 21 biopsies, while Langhans' type giant cells was more than the foreign body giant cells in 12 biopsies. Typical caseation necrosis in the centre of the granuloma was observed in 96.6% of the biopsies (Figure 3). The necrosis was focal in 7 biopsies, submassive in 22 biopsies and massive in 28 biopsies.

In spite of meticulous search, AFB could be detected only in 29 out of 59 biopsies (49%). The bacilli were found mainly in the epithelioid cells. In the majority of biopsies (25/29), scanty and only occasional AFB were observed (Figure 4). In two cases numerous bacilli were noted in the epithelioid cells and both had noncaseating granuloma. Culture of the lymph node was done in one of these two cases and it showed atypical mycobacteria. There was no significant correlation between the presence of necrosis and AFB (Table 3). The site and number of bacilli are given in Table 4. In this study, there was no AFB positive lymph node detected which histologically lacked characteristic granuloma.

DISCUSSION

Tuberculosis remains a major health problem in South East Asia.¹ Tuberculous pleurisy is the commonest form of extrapulmonary tuberculosis.² However, in our study the lymph node is the most frequent site of histologically-proven tuberculosis. This is probably due to the fact that, in some cases of tuberculous pleurisy, the diagnosis was based on culture of AFB without tissue diagnosis. Cervical lymphadenopathy is the most common form of

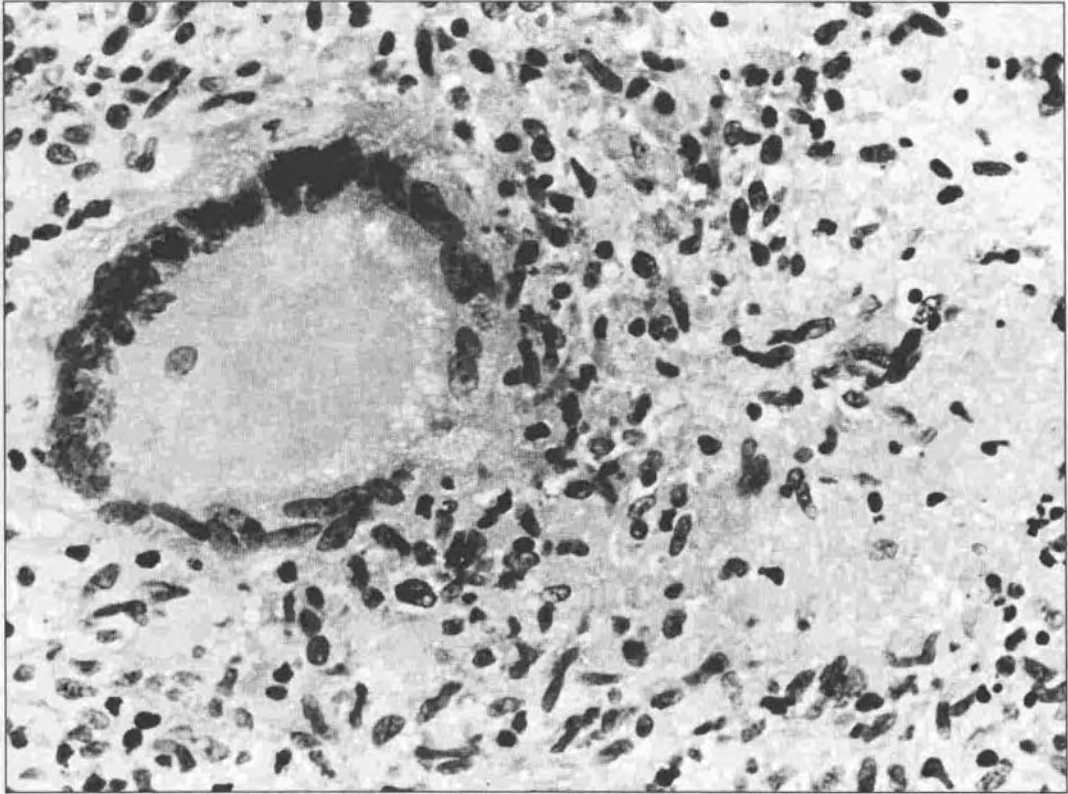


FIG. 1: Epithelioid cell granuloma with Langhans' giant cell. Haematoxylin and eosin x 250.

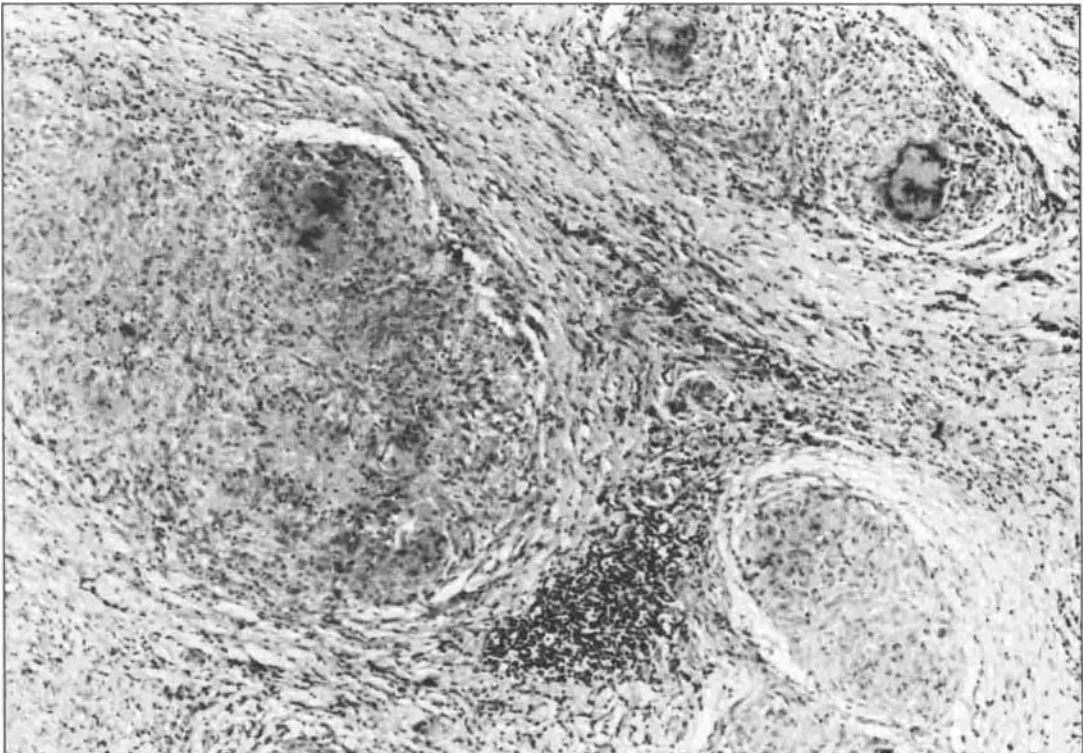


FIG. 2: Histology showing granuloma of varying sizes. Haematoxylin and eosin x 125.

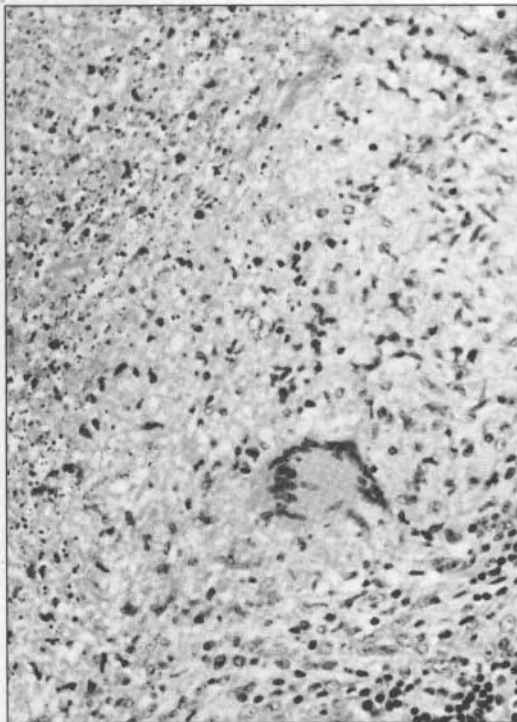


FIG. 3: Granuloma with central caseation necrosis. Haematoxylin and eosin x 125.

lymph node tuberculosis noted in our analysis and this finding was similar to other studies.^{6,7} The preponderance of cervical node tuberculosis could be possibly the result of lymphoid tissue in the tonsils, adenoids and Waldayer's ring facilitating an easy entry to mycobacteria.⁸

Tuberculosis of lymph nodes can present at any age. It was observed most frequently in the third decade of life in our study as in other published reports.^{8,9} We have also found that tuberculous lymphadenitis is more commonly seen in females, a similar experience recorded by others.^{2,10} The reason for this is not clear.

Although several studies on the role and utility of fine needle aspiration cytology in establishing the diagnosis of tuberculous lymphadenitis have

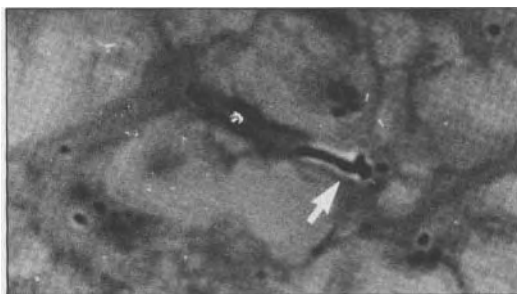


FIG. 4: Ziehl-Neelsen stain demonstrating a single acid-fast bacillus (arrow) x 1250.

TABLE 3: Correlation between presence of necrosis and acid-fast bacilli

Caseation	Acid-fast bacilli	
	Positive	Negative
Present	27	27
Absent	2	3
Total	29	30

p = 1.0 (not significant)

been published,^{11,12,13} surprisingly only two publications elucidated the histopathological aspects of lymph nodal tuberculosis.^{2,3} Among the various pathological features of tuberculosis analysed in our study, a number of interesting observations have emerged. The two histological features which are useful in the diagnosis of tuberculosis are variation in the size of the granulomata and the presence of caseation necrosis. None of the cases in the present study had granuloma of uniform size. Sarcoidosis has to be ruled out in the presence of isomorphic granulomata. Caseation necrosis is an important microscopical feature noted in 57 out of 59 cases in the study. However, there was no correlation between necrosis and AFB demonstration (p=1.0), unlike in an earlier study by Das et al.¹¹ In the latter study, bacilli were seen more frequently in those cases with caseation necrosis. We have specifically looked at the different zones of the granuloma for the detection of AFB and they were more frequently observed in the epithelioid cells compared to necrotic area. This is perhaps due to the fact that bacilli in the necrotic area are either highly fragmented or completely disintegrated and thus not identifiable in routine Ziehl-Neelsen stained sections. The

TABLE 4: Bacillary content versus different zones of the granulomata

Site of bacilli	No.	Bacillary content	
		Scanty	Numerous
Epithelioid cells	13	11	2
Borderzone			
(Epithelioid cells/necrosis)	6	6	0
Caseation necrosis	8	7	1
Epithelioid cells and necrosis	2	1	1
Total	29	25	4

overall AFB positivity of 49% in our study is similar to other published data.^{14,15}

Culture of the lymph node was undertaken only in nine cases. *Mycobacterium tuberculosis* and atypical mycobacteria were grown in culture only in 2 and 1 case respectively. The reason for the low yield was probably due to the small number of live bacilli in the lymph node. The positive yield for AFB in the literature varies from 18% to 90%.^{16,17} Fibrosis in the lymph node was seen in 19 cases indicating chronicity. However in all these cases caseation necrosis was also present suggesting activity.

Mycobacterial lymphadenitis in the cervical region can be confused with many other conditions clinically which include malignancy, infections and reactive conditions. The histological differential diagnosis is granulomatous lymphadenitis due to sarcoidosis, foreign body granuloma and fungal infection. Clinical features as well as microscopical findings such as noncaseating granulomata in the absence of AFB suggest sarcoidosis. Fungal infection is diagnosed by the identification of the organisms in the Periodic acid-Schiff stain. Where history and tuberculin test are noncontributory and culture techniques are not easily available, a histological assessment of the excised lymph node is a simple procedure to establish the diagnosis and commence antitubercular therapy. In our study the microscopical features are quite typical in most cases and thus histology can be a reliable diagnostic tool. In our study AFB were seen only in 49% of biopsies, even after a careful search. In the majority of these cases (89%), only an occasional bacillus was found. We recommend that bacilli should be looked for especially in the epithelioid cells and in the borderzone (interface of epithelioid cell and necrosis) of the granulomas to further substantiate the diagnosis of tuberculosis. Ideally culture must be undertaken not only for detection of AFB but also subclassification of the various types of mycobacteria especially the atypical forms. Such an effort is imperative in view of rising incidence of HIV infection in Malaysia.

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REFERENCES

1. Ministry of Health Malaysia Annual Report 1989; 69-74.
2. Tan KK. Tuberculous lymphadenitis in Singapore. Singapore Med J 1988; 29: 441-4.
3. Krishnaswami H, Koshi G, Kulkarni KG, Job CK. Tuberculous lymphadenitis in South India – A histopathological and bacteriological study. Tubercle 1972; 53: 215-20.
4. Reid JD, Wolinsky E. Histopathology of lymphadenitis caused by atypical mycobacteria. Am Rev Resp Dis 1969; 99: 8-12.
5. Lim VKE. The resurgence of tuberculosis. Med J Malaysia 1991; 46: 298-300.
6. Priel I, Doley E. Tuberculous lymphadenitis: A survey of 94 cases. J Inf Dis 1982; 146: 710.
7. Cantrell RW, Jensen JH, Reid D. Diagnosis and management of tuberculous cervical adenitis. Arch Otolaryngol 1975; 101: 53-7.
8. Gale GL. Tuberculosis of superficial lymph nodes. Can Med Assoc J 1953; 69: 303-9.
9. Kent DC. Tuberculous lymphadenitis not a localized disease process. Am J Med Sci 1967; 254: 866-74.
10. Castro DJ, Hoover DL, Castro DJ, Zuckerbraun L. Cervical Mycobacterial Lymphadenitis. Medical vs Surgical Management. Arch Otolaryngol 1985; 111 :816-9.
11. Das DK, Pant JN, Chachra KL *et al.* Tuberculous lymphadenitis: Correlation of cellular components and necrosis in lymph node aspirate with A.F.B positivity and bacillary count. Indian J Pathol Microbiol 1990; 33 : 1-10.
12. Rajwanshi A, Bhamhani S, Das DK. Fine needle aspiration cytology in diagnosis of tuberculosis. Diagnostic Cytopathol 1987; 3: 13-6.
13. Patra AK, Nanda BK, Mohapatra BK, Panda AK. Diagnosis of lymphadenopathy by fine needle aspiration cytology. Indian J Pathol and Microbiol 1983; 26: 273-8.
14. Metre MS, Jayaram G. Acid-fast bacilli in aspiration smears from tuberculous lymph nodes: An analysis of 255 cases. Acta Cytol 1987; 31: 17-9.
15. Margileth AM, Chandra R, Altman RP. Chronic lymphadenopathy due to mycobacterial infection. Am J Dis Childhood 1984; 138: 917-22.
16. Ehring F. Tuberculosis of the peripheral lymph nodes. Fortchr Med 1978; 96(1): 438-42.
17. Lau SK, Kwan S, Lee J, Wei WT. Source of tubercle bacilli in cervical lymph nodes; a prospective study. J Laryngol Otol 1991; 105: 558-61.