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RESEARCH ARTICLE

Histopathological Review of Granuloma in Diagnosis of Tuberculosis Lymphadenitis (TBL)

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Abstract

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis and is the second leading cause of death from an infectious disease. Indonesia has the highest TB cases in West Java, East Java, and Central Java. Tuberculosis lymphadenitis (TBL) represents about 30–40% of cases of extrapulmonary tuberculosis. The study aimed to study the clinical and histopathological characteristics of TBL patients. The research design in this study used an exploratory, descriptive method. Data was taken from Al Islam Hospital Bandung as medical records from January 2019 to December 2020. The result showed that TBL primarily affects patients aged 6–11 years (28%), male gender (57%), patients not working (25%), and those residing in the East Bandung area (34%). Histopathological appearance showed granulomas of caseous necrosis, epithelioid cells, and Langhan's cells, indicated by types 1, 2, and 3. The most common type was type 1 (47%), which was more widely distributed in the right neck (46%) with size 1–3 cm. In conclusion, the frequency of TBL is higher in boys aged 6–11 years, residents of the East Bandung area, and patients who did not work. Well-formed granuloma of enlarged lymph nodes in the right neck with size 1–3 cm is most commonly found in TBL.

Keywords: Histopathological review, lymphadenitis, tuberculosis

Introduction

Tuberculosis (TB) is an infectious disease caused by *Mycobacterium tuberculosis*. According to the World Health Organization, in 2021, an estimated 10 million people developed TB, resulting in 1.6 million deaths, making it the second leading cause of death from an infectious disease after COVID-19. Southeast Asia accounted for almost half of TB cases, reaching 4.82 million (45.4%). Eight countries are responsible for 66% of global cases, and Indonesia ranks second after India (9.2%).[1]

There are 450,000 new tuberculosis cases in Indonesia, with a death rate of 175,000 yearly. According to the Global Tuberculosis Report 2022, there were 969,000 TB cases reported in Indonesia, and 144,000 died because of TB. The highest TB cases were found in the most populous regions, including West Java, East Java, and Central Java.[2,3]

The two types of TB are pulmonary and extrapulmonary. Extrapulmonary TB constitutes about 15–20% of all TB patients. Tuberculosis lymphadenitis (TBL) is the most common form of extrapulmonary TB and represents about 30–40% of cases. In developing countries, the incidence of TB is high. TBL is often located in the cervical lymph nodes; many benign and malignant conditions mimic the disease.[4]

Diagnosis of TBL still faces many challenges because each diagnosis method has limitations. Clinically, TBL may be challenging to distinguish from other causes of lymphadenitis due to its nonspecific clinical presentation and overlap with granulomatous lymphadenopathy.[5] Diagnosis TBL should be combined between clinical findings, histopathological staining, and culture as the gold standard. Histopathology remains one of the most important methods for diagnosing TBL, and in a high TB area, histopathology is the reliable diagnostic method. In the histopathological picture of TBL, granulomas, caseous necrosis, epithelioid cells, and Langhan's cells will usually be found.[6,7]

Lymphadenitis TB is still a public health problem. Although TBL is one of the most common forms of extrapulmonary TB, few studies on approaching diagnosis of the clinical and histopathology of TBL in Bandung have been

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done. Therefore, this study aimed to study the clinical and histopathological characteristics of TBL patients at Al Islam Hospital Bandung.

Methods

This type of research is exploratory, descriptive research. The data obtained is secondary from the medical records of TBL patients treated at Al Islam Hospital Bandung from January 2019 to December 2020. The sampling method used the total sampling method with 76 cases that fit the inclusion criteria. The inclusion criteria are the patients who have yet to be treated based on medical records. The exclusion criteria is a patient diagnosed with other diseases. The ethical clearance of the study is No. 021/KEPPIN-RSAI/10/2021.

Results

Demographic characteristics of TBL patients at Al Islam Hospital Bandung can be seen in Table 1. TBL is more common in patients with an age range of 6–11 years, with as many as 21 people (28%). Based on gender, men were more often affected by TBL, with 43 patients (57%).

In this study, histopathology diagnosed 76 patients with enlarged lymph nodes as having TBL. These patients were further divided into three groups according to the granuloma histopathological pattern. TBL patients in Table 2 show the grouping of granulomas based on three types: type 1 shows a well-formed granuloma consisting of necrosis caseous, epitheloid cells, and Langhan's cells. Type 2 indicates the presence of one of the structures of necrosis caseous, epitheloid cells, and Langhan's cells. Type 3 shows no granuloma features. Histopathological features in patients mainly were in type 1, namely 36 patients (47%), and the least in type 2, namely 19 patients (25%).

Clinical manifestation of TBL patients in Table 3 shows symptoms of enlarged lymph nodes in TBL patients, more often distributed in the right neck in as many as 35 patients, and distribution is rare in preauricular, submental, inguinal, subclavicular, and chin, only one patient. The most enlarged lymph nodes were 1–3 cm in size in 25 patients. The number of enlarged lymph nodes was, at most, two enlarged lymph nodes in 15 patients.

Systemic features like fever more often accompanied patients with TBL in five patients, cough in four patients, and manifestation that rarely occurred was weight loss in one patient.

Table 1 Demographic Characteristics of TB Lymphadenitis Patients

Characteristics	n=76 (%)
Age (years)	
0–5	9 (12)
6–11	21 (28)
12–16	10 (13)
17–25	15 (20)
26–35	9 (12)
36–45	8 (11)
46–55	2 (3)
56–65	2 (3)
Gender	
Male	43 (57)
Female	33 (43)
Residence	
East Bandung	26 (34)
South Bandung	17 (22)
Central Bandung	2 (3)
Bandung regency	21 (28)
Out of Bandung	10 (13)
Occupation	
Laborer	4 (5)
Housewife	7 (9)
Private sector employee	11 (14)
Student	18 (24)
Self-employed	2 (3)
Not working or not yet working	19 (25)
Etc.	15 (20)

Discussion

Tuberculosis has been a major health problem worldwide since the discovery of *Mycobacterium tuberculosis* in 1882. Each year, there are more than eight million new cases of tuberculosis and 1.3 million deaths—extrapulmonary forms of tuberculosis as its relative frequency increases. Among extrapulmonary organs, TBL is the

Table 1 Histopathological Pattern of TB Lymphadenitis Patients

Histopathological Pattern	n=76 (%)
Type 1	36 (47)
Type 2	19 (25)
Type 3	21 (28)

Table 3 Clinical Manifestation of TB Lymphadenitis Patients

Clinical Manifestation	n=76	%
Lymph node enlargement		
Distribution	(54)	
Right cervical	35	46
Left cervical	8	11
Submandibular	5	7
Preauricular	2	3
Submental	1	1
Inguinal	1	1
Subclavicular	1	1
Axilla	2	7
Mentum	1	1
Size (cm)	(30)	
<1	2	
1–3	25	
>3	3	
Number of enlarged lymph nodes	(18)	
1	2	
2	15	
3	1	
Fever	(76)	
Yes	5	
No	71	
Cough	(76)	
Yes	4	
No	72	
Weight loss	(76)	
Yes	1	
No	75	

most common. Their diagnosis is often difficult based on clinical, radiological, bacteriological, and histological findings.[8] All the study subjects (n=76) were previously diagnosed with TBL, depending on the presence of variable histological TB evidence. Demographic features of TBL in various ages, genders, residences, and occupations were evaluated. It was found that TBL is more prevalent in children in the age group range of 6–11 years. This finding is similar to the previous study by Yang and Du;[9] TBL represents about 30% of cases with an average of children. TBL was found to be more common in children, 78%, compared to adults, around 65%. Tuberculosis is a common illness for vulnerable populations in resource-limited settings, with the latest figures showing an annual incidence of 10 million, including 1 million children. Gender distribution in this study found men were more often affected. It was quite consistent with the study conducted by Ali et al.;[10] the frequency of TBL is higher in the male gender. Most patients came from the East Bandung area, and patients did not work or had not worked. The demographic profiles of this study were consistent with studies of Southeast Asian regions, where most of the subjects were from rural areas.[11–13]

The right cervical lymph node was the most common predilection in our study (46%), a consistent survey of Kamal et al.,[14] but much higher in north India (67.8%). Gautam et al.[15] study found that cervical lymph nodes are the most common site of tuberculous lymphadenopathy in 60%–90% of cases. The involvement of the cervical region nodes is dominant due to enriched lymphatics in this area and close communication with the pulmonary system. The most common enlarged lymph nodes were 1–3 cm with multiple lymph nodes, mostly around two lymph nodes. Jha et al.[16] found multiple lymph nodes in 57% of the cases. Clinical manifestations like fever more often accompanied patients with TBL in five patients, cough in four patients, and weight loss in one patient. While evaluating these kinds of patients, an adequate physical examination and diagnostic studies should be done. In instances like this study, where systemic signs and symptoms seldom appear, identification of TBL can become challenging.[17]

We assess the histopathology by grouping the granulomas' histological features depending on the histomorphology features of TBL. The histological tissues that showed the presence of a well-formed granuloma consisting of necrosis caseous, epithelioid cells, and Langhan's cells were considered as type 1 in 47% of cases, followed by type 2 in 25%, and type 3 with no granuloma, which was 28% case. The Huda et al.[7] study found that well-formed granuloma is detected in 68% of cases, which is higher than in this study. Granuloma formation and necrosis caseous are two specific pathology criteria for identifying TBL. Necrosis caseous is more specific and sensitive.[18] In the present study, 68 lymph nodes were of caseating granuloma type, and 32 were noncaseating granuloma type.[3] This is in correlation with Lake and Oski,[19] who reported 76% caseating granuloma and 24% noncaseating granuloma, and Fatmi and Jamal,[20] who reported 62% caseating granulomas and 38% noncaseating granuloma. In endemic countries, the majority of granulomatous lesions without necrosis are considered to be TBL.[21,22]

Conclusions

The frequency of TBL is higher in males and children aged 6–11 years, residents of the East Bandung area, and patients who did not work. Type 1 histopathologic features of well-formed granuloma, necrosis caseous, epithelioid cells, and Langhan's cells are most commonly found in TBL. Clinical symptoms of enlarged lymph nodes in the right neck with size 1–3 cm.

Conflict of Interest

None declared.

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References

1. World Health Organization. Global tuberculosis report 2022. Geneva: World Health Organization; 2022.
2. Erida Y. Limfadenitis tuberculosis [Internet]. Jakarta: Direktorat Jenderal Pelayanan Kesehatan Kementerian Kesehatan Republik Indonesia; 2022 [cited 2023 August 23]. Available from: https://yankes.kemkes.go.id/view_artikel/204/limfadenitis-tuberculosis.
3. Abebe G, Bonsa Z, Kebede W. Treatment outcomes and associated factors in tuberculosis patients at Jimma University Medical Center: a 5-year retrospective study agenda. Int J Mycobacteriol. 2019;8(1):35–41.
4. Sharma SK, Mohan A, Kohli M. Extrapulmonary tuberculosis. Expert Rev Respir Med. 2021;15(7):931–48.
5. Lemus LF, Revelo E. Cervical tuberculous lymphadenitis. Cureus. 2022;14(11):e31282.
6. Ahmed HGE, Nassar AS, Ginawi I. Screening for tuberculosis and its histological pattern in patients with an enlarged lymph node. Patholog Res Int. 2011:2011:417635.
7. Huda MM, Taufiq M, Yusuf MA, Rahman MR, Begum F, Kamal M. Histopathological features of lymph nodes of tuberculous lymphadenitis patients: experience of 50 cases in Bangladesh. Bangladesh J Infect Dis. 2016;3(2):40–2.
8. Ketata W, Rekik WK, Ayadi H, Kammoun S. Extrapulmonary tuberculosis. Rev Pneumol Clin. 2015;71(2–3):83–92.
9. Yang JS, Du ZX. Comparison of clinical and pathological features of lymph node tuberculosis and histiocytic necrotizing lymphadenitis. J Infect Dev Ctries. 2019;13(8):706–13.
10. Ali S, Mubeen A, Javed M. Demographic features of tuberculosis lymphadenitis patients. J Sheikh Zayed Med Coll. 2014;5(4):730–2.
11. Bottineau MC, Kouevi KA, Chauvet E, Garcia DM, Galetto-Lacour A, Wagner N. A misleading appearance of a common disease: tuberculosis with generalized lymphadenopathy-a case report. Oxf Med Case Reports. 2019;2019(9):omz090.
12. Tahseen S, Ambreen A, Ishtiaq S, Khanzada FM, Safdar N, Sviland L, et al. The value of histological examination in diagnosing tuberculous lymphadenitis in the era of rapid molecular diagnosis. Sci Rep. 2022;12(1):8949.
13. Rana S, Bhat P, Bhat S, Bakshi V, Bisht RS. Clinico-pathological and demographic profile of patients of cervical tubercular lymphadenitis in the hilly region of Uttarakhand. Int J Health Sci (Qassim). 2022;6(Suppl 3):4232–9.
14. Kamal MS, Hoque MH, Chowdhury FR, Farzana R. Cervical tuberculous lymphadenitis: clinico-demographic profiles of patients in a secondary level hospital of Bangladesh. Pak J Med Sci. 2016;32(3):608–12.
15. Gautam H, Agrawal SK, Verma SK, Singh UB. Cervical tuberculous lymphadenitis: clinical profile and diagnostic modalities. Int J Mycobacteriol. 2018;7(3):212–6.
16. Jha BC, Dass A, Nagarkar NM, Gupta R, Singhal S. Cervical tuberculous lymphadenopathy: changing clinical pattern and concepts in management. Postgrad Med J. 2001;77(905):185–7.
17. Gulati HK, Mawlong M, Agarwal A, Ranee KR. Comparative evaluation of clinical, cytological and microbiological profile in abdominal vs. cervical lymph nodal tuberculosis with special emphasis on utility of auramine-O

staining. J Cytol. 2021;38(4):191–7.
18. Pagán AJ, Ramakrishnan L. Immunity and immunopathology of tuberculosis granuloma. Cold Spring Harb Perpect Med. 2015;5(9):a018499.
19. Lake AM, Oski FA. Peripheral lymphadenopathy in childhood. Ten-year experience with excisional biopsy. Am J Dis Child. 1978;132(4):357–9.
20. Fatmi TI, Jamal Q. A morphological study of chronic granulomatous lymphadenitis with the help of special stains. Pak J Med Sci. 2002;18(1):48–51.
21. Dasgupta S, Chakrabarti S, Sarkar S. Shifting trend of tubercular lymphadenitis over a decade – a study from eastern region of India. Biomed J. 2017;40(5):284–9.
22. Hemalatha A, Shruti P, Kumar MU, Bhaskaran A. Cytomorphological patterns of tubercular lymphadenitis revisited. Ann Med Health Sci Res. 2014;4(3):393–6.