ORIGINAL ARTICLE

Tuberculous lymphadenopathy: Experience from the referral center of Northern India

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ABSTRACT

Background: Lymphadenopathy is the common form of extrapulmonary tuberculosis (TB) in the developing country like India. The aim of the study was to assess the clinical and the pathological features of tuberculous peripheral lymphadenopathy along with the effect of the antitubercular drugs on its clinical course. **Materials and Methods:** A prospective study was carried out in the department of pulmonary medicine from July 2013 to June 2014. Clinico-demographical and pathological characteristics of the patients of tuberculous lymphadenopathy were studied. **Results:** Two and four cases, 84 (41.2%) male and 120 (58.8%) females were diagnosed as the cases of tuberculous lymphadenopathy. Mean age of the patients were 28.45 ± 12.83. Palpable mass (100%) was the most common presenting feature. Cervical lymphadenopathy (92.6%) was the most common presentation of peripheral tuberculous lymphadenopathy. Most common cytological pattern seen was epithelioid granuloma with caseous necrosis (32.84%) followed by epithelioid granuloma without caseous necrosis on fine needle aspiration cytology (FNAC). Directly observed treatment short course (DOTS) for TB was effective in treating tuberculous lymphadenopathy. **Conclusion:** Tuberculous lymphadenopathy affects female more often than males. FNAC is the effective mean in diagnosing tuberculous lymphadenopathy. DOTS is the effective mean for treating tuberculous lymphadenopathy.

Key words: Epitheloid granuloma, lymphadenopathy, tuberculosis

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INTRODUCTION

Tuberculosis (TB) is the oldest disease in the history of mankind. It is still the major health problem worldwide. According to the World Health Organization (WHO), 9 million people fell ill with TB in 2013, including 1.1 million cases among people living with HIV.[1] There were estimated 1.5 million deaths worldwide due to TB. The WHO considered TB as one of the top killers of women of reproductive age group. The TB mortality rate has decreased 45% since 1990.[1]

Primarily, TB is considered the pulmonary disease. However, it can affect almost any part of the body. Tubercular lymphadenitis is the most common form of extrapulmonary TB. It has been also called as "scrofula." In Europe, it was known as "Kings Evil," where the royal touch was believed to cure the disease until the 18th century.[2] Bollinger, May, and Demme in the mid to late 19th century was the first to define the microbiological association of scrofula with *Mycobacterium bovis*.[3] However, pasteurization of milk has substantially eliminated this source of human infection. However, risk continues with the consumption of unpasteurized milk.[4] At present, *Mycobacterium tuberculosis* is the usual cause of tuberculous lymphadenitis. Fine needle aspiration cytology (FNAC) is the widely accepted and cost-effective and safe procedure to diagnose the tuberculous lymphadenopathy.

This study was conducted to examine the clinical features and sociodemographic profile of the tuberculous peripheral

Access this article online	
Quick Response Code:	Website: www.nigeriamedj.com
	DOI: 10.4103/0300-1652.182077

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How to cite this article: Singh SK, Tiwari KK. Tuberculous lymphadenopathy: Experience from the referral center of Northern India. Niger Med J 2016;57:134-8.

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lymphadenopathy and to describe various cytological pictures of tuberculous lymphadenitis with their relative frequency. The effect of directly observed treatment short course (DOTS) for TB in the management of tuberculous lymphadenopathy was also evaluated.

MATERIALS AND METHODS

This study was conducted at Department of Pulmonary Medicine Gajra Raja Medical College, Gwalior, India. It is a tertiary care teaching hospital. It was the prospective and descriptive study conducted during the time span of 1 year from July 2013 to June 2014. Ethical clearance was taken from the Ethical Committee of the College. All the patients of age more than 12 years who were referred or diagnosed at our Department of Pulmonary Medicine with tuberculous peripheral lymphadenitis were included in the study. Consent from the patients was taken before inclusion in the study. Study was approved by the Ethical Committee of our institution.

History was taken in full details regarding particulars of the patient and complaints including cough, weight loss, fever, hemoptysis, and anorexia, history of contact with TB, and history of any other systemic illness. The previous history of antitubercular drug intake was noted. Modified Prasad classification was used to assess the economical status of the study population.[5] Chest X-ray (posterior-anterior view) was done in all the cases to assess the pulmonary involvement due to TB.

Site of lymph node was noted in terms of cervical, axillary, and inguinal group of lymph nodes. Cervical group of lymph nodes was further divided into submental, submandibular, postauricular, jugulo-omohyoid, jugulodigastric, and supraclavicular lymph nodes.[6] Lymph node characteristics were noted in terms of number, tenderness, and mobility. Condition of lymph node nodes was defined as soft, firm, matted, fluctuant/abscess, or draining sinus.

All patients were subjected to FNAC. FNAC was done by 10 cc disposable syringes with 22-gauge needle. Alcohol-fixed slides were used for H and E and Papanicolaou stain. While the air fixed slides were used for Ziehl-Neelsen (ZN) stain. In case of two or more than two site involvement, FNAC was done from one site only. In cases of nonspecific findings in FNAC and persistence of lymphadenopathy after the course of antibiotics, biopsy was performed. Patients who were already diagnosed as a case of tuberculous lymphadenopathy and referred to our department for antitreatment were not undergone repeat FNAC. The cytology smears revealing features of tuberculous lymphadenitis were grouped into four categories: Epithelioid granulomas with caseous necrosis, epithelioid granulomas without necrosis, necrosis only without epithelioid granulomas, and polymorphs with necrosis with or without epithelioid granulomas.[7] HIV testing was not performed in all the cases. It was done when paradoxical upgrading reaction seen in lymph node during the course of therapy.

All the diagnosed cases of TB were undergone treatment under DOTS for TB according to Revised National Tuberculosis Control Program for India.[8]

Statistical analysis

Patients data were entered in Microsoft Access 2007. The data were analyzed by exporting into Microsoft Excel 2007. Descriptive analysis of demographic data, clinical parameters, and posttreatment outcome complications was carried out. Quantitative variables were summarized by mean and standard deviation.

RESULTS

Two hundred and fifty-five cases were assessed at our Department of Pulmonary Medicine for lymphadenopathy. Out of 255 cases, 204 (80%) were diagnosed as the cases of tuberculous lymphadenopathy. Rests of the cases were found to have reactive lymphadenitis, lymphoma, and metastasis. Females 120 (58.8%) were more affected than males 84 (41.2%). Ratio of male to female in peripheral lymphadenopathy was 1:1.43. Mean age of the patients was 28.45 ± 12.83. Maximum numbers of patients were in the age group of 21–30 years in both males and females [Table 1]. Palpable mass (100%) was the most common presenting feature followed by loss of appetite (32.4%). Chest X-ray suggestive of TB was found in 14.7% patients only [Table 2].

Cervical lymphadenopathy (92.6%) was the most common presentation of peripheral tuberculous lymphadenopathy. In 12 (5.9%) patient's more than one site involvement was seen. Cervical group of lymph node enlargement was seen in 189 (92.6%) cases. In cervical group of lymph node, more than one lymph node station was enlarged. Matting (32.8%) was the most frequent condition of lymph node followed by firm lymph node. Tenderness was noted in 62 (30.4%) patients. All of the patients with tender lymphadenopathy were having the fluctuant or draining sinus type of lymph node and their lymph node was nonmobile [Table 2]. Bilateral lymphadenopathy was noted in 50 (24.5%) patients. Supraclavicular group (29.4%) was the most frequent lymph node enlarged in cervical groups of lymph nodes [Table 3].

Table 1: Age distribution of cervical lymphadenopathies in males and females

	Male	Female	Total (%)
12-20 years	25	36	61 (29.9)
21-30 years	31	49	80 (39.2)
31-40 years	12	22	34 (16.7)
41-50 years	7	8	15 (7.4)
≥51 years	9	5	14 (6.8)
Total	84	120	204 (100)

Table 2: Sociodemographic and clinical characteristics of patients of tuberculous lymphadenopathy

	Male	Female	Total (%)
Age	29.45±14.01	27.75±11.94	28.45±12.83
Symptoms			
Palpable mass	84	120	204 (100)
Fever	12	16	28 (13.7)
Cough	10	15	25 (12.3)
Night sweats	20	27	47 (23.0)
Weight loss	21	36	57 (27.9)
Loss of appetite	28	38	66 (32.4)
Tubercular lesions on chest X-ray			
Present	12	18	30 (14.7)
Absent	72	102	174 (85.3)
Educational status			
Illiterate	15	18	33 (16.2)
Primary	18	30	48 (23.5)
High school	27	32	59 (28.9)
Intermediate	11	32	43 (21.1)
Graduate	11	4	15 (7.4)
Postgraduate	2	4	6 (2.9)
Modified Prasad classification			
Class 1	16	15	31 (15.2)
Class 2	19	24	43 (21.1)
Class 3	24	39	63 (30.9)
Class 4	20	30	50 (24.5)
Class 5	5	12	17 (8.3)
Marital status			
Married	52	78	130 (63.7)
Unmarried	32	42	74 (36.3)
Past history of tuberculosis			
Absent	76	108	184 (90.2)
Present	8	12	20 (9.8)
History of contact			
Present	36	35	71 (34.8)
Absent	48	85	133 (65.2)
Lymph node site			
Cervical	75	114	189 (92.6)
Axillary	12	10	22 (10.8)
Inguinal	2	3	5 (2.5)
Number of lymph node			
Single	51	70	121 (59.3)
2-4	23	32	55 (27.0)
≥5	10	18	28 (13.7)
Condition			
Soft	10	11	21 (10.3)
Firm	22	32	54 (26.5)
Matted	26	41	67 (32.8)
Fluctuant/abscess	18	25	43 (21.1)
Draining sinus	8	11	19 (9.3)
Tenderness			
Present	26	36	62 (30.4)
Absent	58	84	142 (69.6)
Mobility of nodes			
Mobile	58	85	143 (70.1)
Nonmobile	26	35	61 (29.9)

FNAC was performed in all the cases presented to the department with peripheral lymphadenopathy. Only 39 (19.1%) patients demonstrated acid-fast bacilli on ZN staining. Most common cytological pattern seen was epithelioid granuloma with caseous necrosis (32.84%) followed by epithelioid granuloma without caseous necrosis [Table 4]. In 14 (6.8%) cases, diagnosis of TB was confirmed by biopsy. DOTS category one treatment was given to 184 (90.2%) patients, whereas the rest received category two treatment. Only 20 (9.8%) patients showed the persistence of lymphadenopathy even after completion of treatment. They showed a reduction in the size of the lymph node to <5 mm. Although their treatment was not extended. These patients were advised to follow in OPD regularly every 2 monthly. After 6 months posttreatment, there was no increased in size of lymph node was noted. Twenty-four patients (11.8%) showed paradoxical increase in the size of the lymph node. Complete resolution of this enlargement was seen in these patients after the completion of treatment. HIV screening in all these cases was negative.

Table 3: Distribution of the involvement in cervical group of lymph nodes due to tuberculosis

	Male	Female	Total (%)
Submental	12	13	25 (12.5)
Submandibular	23	29	52 (25.5)
Postauricular	6	4	10 (4.9)
Jugulo-omohyoid	22	29	51 (25)
Jugulodigastric	22	33	55 (27)
Suprascapular	23	37	60 (29.4)

DISCUSSION

TB is a worldwide disease having the varied presentation. Extrapulmonary TB is a significant health problem worldwide. It poses a challenge in diagnosis and monitoring of the treatment.[9] Peripheral lymphadenopathy is the most common form of extrapulmonary TB.

Male to female ratio for peripheral lymphadenopathy in our study was 1:1.4. Fontanilla *et al*.,[4] in their study had found the same ratio. Similarly, male to female ratio of 1:1.2 was noted by Purohit *et al*.[10] and Nidhi *et al*.[7] in the studies done in Indian population. Male predominance was noted by Bezabih *et al*.,[11] where they found male to female ratio of 1.3:1. They found the peak incidence of tuberculous lymphadenitis in age group of 30–40 years. In our study, the peak incidence was in age group of 20–30 years. Although previously considered a disease of childhood, lymphadenitis has a peak age of onset of 20–40 years.[12] Our studies also showed that majority of the patients (55.9%) were in the age group of 20–40 years. Patients of age <12 years were not included in our study. Past history of TB was found in 20 (9.8%) cases. History of TB in past in the patients of TB of lymph node was reported 11.4% and 14.3% by Khan *et al*.[13] and Iguchi *et al*.[14] However, the Nidhi *et al*. found 27.3% of their patients having the past history

Table 4: Cytological features of patients of tuberculous lymphadenopathy

	Male (*n*=84)	Female (*n*=120)	Total (204) (%)
Epithelioid granuloma + caseous necrosis	29	38	67 (32.8)
Epithelioid granuloma no caseous necrosis	25	38	63 (30.9)
Necrosis only no epithelioid granuloma	18	29	47 (23.1)
Polymorphs with necrosis ± epithelioid granuloma	12	15	27 (13.2)
Total			204 (100)

of TB.[7] Chest X-ray suggestive of TB was seen in 14.7% of cases in our study. Priel *et al*. found 28.8% of lymph node TB having the evidence of pulmonary TB.[15] In another study, 22% of the cases showed features suggestive of active TB in chest X-ray in patients with lymph node TB.[16]

Cervical lymph nodes (92%) were the most common region affected by TB. This was in concordance with the other studies.[4,7,9-11] In the cervical region, supraclavicular group (29.4%) was the most common group enlarged due to TB. In the literature involvement of suprascapular group has been reported between 12% and 26% due to TB.[4] Single lymph node was found in 121 (59.3%) of patients. A study by Nidhi *et al*.[7] showed single lymph node enlargement in tuberculous lymphadenopathy in 63.3% cases, whereas Aggarwal *et al*.[17] found single lymph nodal enlargement in 48.6% patients. Aggarwal *et al*. also noted matting in 26.8% cases, whereas our study showed matting in 32.8% cases.

Most common cytological pattern noted was epithelioid granuloma with caseous necrosis (32.84%) followed by epithelioid granuloma without caseous necrosis (30.9%). Study by Handa *et al*. in patients of tuberculous lymphadenitis reported a combination of well-formed epithelioid cell granulomas, giant cells, and caseous necrosis in 34% cases, epithelioid cell granulomas but no caseous necrosis in 12% cases, and only caseous necrosis unassociated with granulomas in 26% cases.[3] While in a study by Gupta *et al*., epithelioid clusters with or without Langhans giant cells with necrosis was most commonly observed cytological pattern in 50.35% cases and epithelioid clusters with or without Langhans giant cells without necrosis in 32.14% cases.[18]

Acid fast staining for *Mycobacterium* of the slides showed positivity in only 39 (19.1%) cases. This lower rate may be due to the use of acid-fast stain only not a fluorescent stain for the detection of *Mycobacterium*. The overall positivity rate of FNAC for acid-fast bacilli ranges from 13.8% to 71.0%.[7,11,13,17,19,20] Highest positivity usually seen in smears showing necrosis, whereas the lowest seen in smears showing epithelioid granuloma only.[7]

Only 20 (9.8%) patients did not show complete resolution even after completion 6 months of completed treatment. There was a reduction in the size of the lymph node to <5 mm. These cases may be considered the cured case because the size of lymph node was reduced to <1 cm.[21] Still they were followed for 6 months to detect any relapse. There was no increase in the size of lymph node noted. In the study done by Jindal *et al*., it was shown that 6 months therapy of DOTS is sufficient, and there is no benefit of prolonging the treatment for 9 months in cases of tuberculous lymphadenopathy.[21] Our study showed paradoxical increase in the size of the lymph node in 24 (11.8%) patients. However, these patients after completion of treatment showed complete resolution of their enlarged lymph node. Enlargement of the size of the lymph node with the treatment is not the sign of treatment failure. All such patients may require further observation of the clinical course. Alternative diagnostic and treatment approaches including the surgery should be considered in such cases.[21] There is controversial role of steroid in the paradoxical upgrading reaction. Steroids had shown to reduce the paradoxical upgrading reaction. In our study, none of the patients received steroid for the paradoxical upgrading reaction.

CONCLUSION

TB of the lymph node is the most common form of extrapulmonary TB. It affects female more than that of male. FNAC is the effective mean to diagnose the TB of the lymph node in the resource-limiting setting. Six months of antitubercular treatment is sufficient to treat the cases of TB of the lymph node in the new cases. There is no need to extend the treatment for the residual tuberculous lymph nodes.

Financial support and sponsorship
Nil.

Conflicts of interest
There are no conflicts of interest.

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