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Directly observed treatment short-course in management of peripheral tubercular lymphadenitis

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ABSTRACT

Background: Tuberculosis (TB) is a major public health problem worldwide. It is one of the main causes of infectious disease and mortality, especially in the developing countries, and has been recognized as one of the top ten causes of death worldwide by the World Health Organization. **Aims and Objectives:** The aims of this study were to assess clinical pattern and efficacy of Directly Observed Treatment Short-Course (DOTS) in management of peripheral tubercular lymphadenitis. **Materials and Methods:** This was a prospective, observational study among pediatric peripheral tubercular lymphadenitis patients to assess the clinical pattern, investigations, and treatment outcome. **Results:** In this study, 72 patients having peripheral tubercular lymphadenitis were enrolled. Most cases had cervical node involvement (81%). Discharging sinus was found in 28.98% cases. Acid-fast bacillus (AFB) was detected by fine needle aspiration and cytology (FNAC) in 21 cases (30.43%). Among them, pulmonary TB was found in two cases (9.52%), one patient being sputum positive. After treatment completion, lymph node(s) enlargement persisted in 6 (8.69%) cases, of which two patients (2.89%) had persistent discharging sinus. On repeat FNAC, acid-fast bacilli were seen in two patients. Success rate was 91.3% confirming the efficacy of DOTS in the management of tubercular lymphadenitis. **Conclusions:** Cervical lymphadenitis was found to be most common type of peripheral lymphadenitis. Cytopathology from the suspected lymph nodes had better success rate than AFB detection or CBNAAT of FNAC samples for diagnosing tubercular etiology in the study. DOTS strategy was effective for peripheral tubercular lymphadenitis with high success rate in this study.

Key words: AFB; CBNAAT; DOTS; Peripheral lymphadenitis; Tuberculosis

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INTRODUCTION

In recent years, it was estimated that approximately 10 million individuals had tuberculosis (TB) each year, of which almost one-third were not diagnosed or reported. This detection gap has further increased in 2020 as reported cases fell from 7.1 million to 5.8 million, with an estimated 4.1 million cases thought to be unreported.[1] In children, the case detection gap is larger than in other age groups, with up to 69% of missed cases projected to occur in children under 5 years of age.[2] While the data on prevalence of pediatric TB in India is unknown, regional data from the World Health Organization (WHO) indicate that sputum smear-positivity is 0.6–3.6% of all reported cases in children (<14-years-old).[3]

Incidence of extrapulmonary tuberculosis varies from 10% to 15% worldwide among all HIV negative TB patients. Among all the extrapulmonary TB cases, the proportion of lymph-node TB is highest.[4] Lymph node TB can occur at any age with a higher incidence in female patients and most commonly infected by *Mycobacterium tuberculosis* and sometimes by atypical mycobacteria.

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Directly observed treatment short-course (DOTS) under Revised National Tuberculosis Control Program (RNTCP) yielded a remarkable success rate of 86% in newly diagnosed sputum positive pulmonary TB cases.[5] Although sputum conversion from sputum positive to sputum negative for acid-fast bacilli is a very good parameter to assess the success of treatment in sputum positive cases, in extrapulmonary TB, there is no such parameter and we have to depend mainly on clinical improvement. Sometimes appearance of new gland, abscess formation, increases in the size of gland during treatment, and residual enlarged gland after completion of treatment creates problem to the physician. Sometimes systemic diseases or malignancies present with lymphadenopathies, and therefore, a better understanding of the differential diagnosis is important in guiding the clinician for timely evaluation and management.

Developing countries like India more commonly have infectious causes of lymph node enlargement in comparison to developed nations, where a neoplastic etiology is more common.[6] In general, extrapulmonary TB in children can be treated with the same regimen as pulmonary disease. Most cases of the pediatric TB, both pulmonary and extrapulmonary TB, are treated as drug-sensitive TB. However, once treatment fails, microbiological data comes usually positive for multi-drug resistant TB (MDR-TB). They must be treated with second-line drugs. MDR-TB therapy in children is complex, because data regarding drug regimen, dosage, safety, and therapy duration are scant and extrapolated from adult data.[7]

Aims and objectives

By keeping in view, this study was designed to determine the clinical pattern of peripheral lymph-node TB and its response to DOTS under RNTCP.

MATERIALS AND METHODS

A prospective, observational, single center, and hospital-based study was done in a teaching hospital of eastern India from November 2018 to October 2019 among pediatric TB patients with tubercular lymphadenitis.

Study group

Patients with lymphadenitis admitted in the study institute during the study period.

The clinical symptoms suggestive of TB were fever and/or weight loss and lymph node enlargement. Informed written consent from parents was obtained for different diagnostic interventions. TB workup including sputum for acid-fast bacilli was done for 3 consecutive days and fine-needle aspiration and cytology (FNAC) was done in patients who gave consent for the intervention. The patients who were diagnosed with tubercular lymphadenitis were enrolled in the study. They were treated with DOTS under revised national TB control Program and were followed up.

A total of 72 pediatric patients with matted lymph node enlargement (lymph node size >2 cm in transverse diameter) in one or more sites, with or without discharging sinuses were enrolled in our study.

Inclusion criteria

Seventy-two pediatric subjects' up to 12 years of age with having peripheral tubercular lymphadenitis were included in the study.

Exclusion criteria

Guardians of the pediatric patients not willing to participate in the study were excluded from the study.

Sample collection

Fine-needle aspiration was performed on the suspected lymph nodes using sterile, disposable 23 gauge needles and 10-cc syringes were collected in 10% formalin container for histopathological examination. Microscopic examination of the smear for Acid-fast bacillus (AFB) by Ziehl Neelsen's method as well as cartridge-based nucleic acid amplification (CBNAAT) of pus from discharging sinuses/aspirate from lymph node was done in every case. Besides FNAC, sputum examination (spot-morning-spot) for 3 consecutive days for AFB was also done in those patients who had symptoms specific to respiratory system (i.e., cough for 3 weeks or more with or without fever and/or hemoptysis).

Diagnosis

Diagnosis was confirmed if the pus/aspirate from FNAC show: (i) *M. tuberculosis* detected by CBNAAT, (ii) Ziehl Neelsen stain positive for AFB, and/or (iii) cytological picture consistent with tubercular lymphadenitis (epithelioid cell granuloma, caseaous necrosis, and Langhan's giant cells).

Treatment

All confirmed cases of tubercular lymphadenitis were treated with DOTS regimen WHO category I and II. Patients were treated in their nearest DOTS center and monthly follow-up was done. At the end of 6 months of anti-tubercular therapy, if any significant lymph node (Lymph node size >1 cm in transverse diameter) remains palpable or any sinus is present, repeat FNAC from the enlarged lymph node was done and microscopic examination of the smear was done for AFB.

Data were maintained and analyzed using Microsoft Excel software.

RESULTS

Among 398 patients admitted with lymphadenitis during the study period of 1 year, parents of 143 patients gave consent for the study. Out of those, 72 patients were diagnosed with lymphadenitis due to tubercular etiology and they were enrolled for the study after obtaining proper informed consent of the parents of the cases. They were put on anti-tubercular therapy with DOTS regimen under RNTCP. Out of 72 patients enrolled in the present study, three patients were lost to follow-up due to travel constraints. There was no death among them. Therefore, 69 patients, who completed the treatment and follow-up were included in the final analysis, among them 30 were male and 39 were female. (Figure 1)

The mean age of the study population was 7.8 years with ranges from 1 year to 12 years. The most common age group in this study was 5–7 years 41 (59.42%) patients followed by 7–12 years (22; 31.88%) and 1–5 years (6; 8.69%).

The duration of symptoms varied from 3 weeks to 10 months. Less than 1 month two patients (2.89%), 1–2 months seven patients (10.14%), 2–3 months 21 patients (30.43%), and 3–10 months 39 patients (56.52%). (Table 1)

Cervical lymph nodes were most commonly affected as was observed in 50 cases (72.46%); bilateral involvement was noted in four cases (5.79 %), followed by axillary lymph node involvement in seven cases (10.14%). In three cases (4.35%, n=69), inguinal lymph node involvement was noted. Both cervical and axillary lymph node involvement was found in four cases (5.79%). Sinus was most commonly found in patients with cervical lymph nodes involvement 28.98 % of cases (n=20) followed by in one case each (1.44%) with inguinal and right sided axillary lymph node involvement. (Table 2)

Out of 69 cases, Mantoux test positivity was found in 49 cases (71.01%; n=69). Acid-fast bacillus AFB found in smear in FNAC from lymph node in 21 cases (30.43%), whereas associated pulmonary TB was seen in 13 cases, of which sputum for acid-fast bacilli was positive among nine (13.04%) cases. Lymph node cytology was consistent with TB in all cases (100%).

Constitutional symptoms were improved by the end of 1 month of treatment with anti-tubercular drugs in 63 (91.3 %) cases. At the completion of 6 months of DOTS treatment, lymph gland remained enlarged (lymph node size >1 cm in transverse diameter) in 6 (8.69%) patients. Repeat FNAC revealed a picture suggestive of persistent tuberculous lesions in two patients (4.34%). Persisting sinus was found in two patients (2.90%) and AFB was found in smear of FNAC in 2 patients (2.90%). Hence, the overall success rate in direct observation therapy under RNTCP was 91.3%. (Table 3)

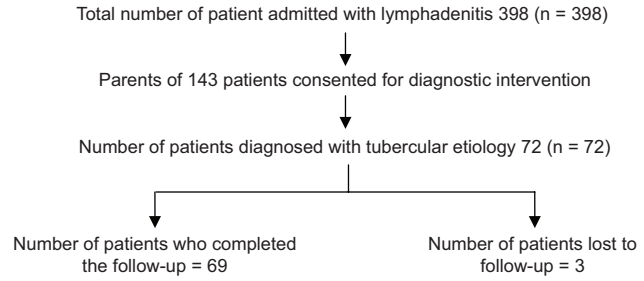

Figure 1: Distribution of patients according to symptoms, consent, diagnosis and follow-up

DISCUSSION

DOTS is the WHO recommended strategy for TB control and is accepted in over180 countries in the world. Unlike pulmonary TB where sputum conversion (Sputum AFB positive to negative) is a definite parameter for assessment of success of treatment of TB, in case lymph node TB, clinical improvement, and follow-up FNAC in remaining

Table 1 : Distribution of patients according to presenting symptoms

Symptom	Number of patients	Percentage (n=69)
Fever	18	26.08
Cough	6	8.69
Weight loss	8	11.59
Discharging sinus	16	23.18
Cold abscess	5	7.24
Abdominal distension	1	1.44
Diarrhea	2	2.90
Loss of appetite	17	24.63
Painless cervical swelling	22	31.88

Table 2: The sites of lymph nodes involved

Site	Total number	Percentage	Discharging Sinus (n=69)
Cervical			
Right	29	42.03	11 (15.94%)
Left	21	30.43	8 (11.59%)
Both	4	5.79	1 (1.45%)
Axillary			
Right	3	4.35	1 (1.45%)
Left	4	5.79	
Both	1	1.44	
Mesenteric	7	10.14	
Hilar	4	5.79	
Inguinal	3	4.35	1 (1.45%)
Para tracheal	3	4.35	
Periportal	2	2.89	

Table 3: Distribution of cases according to the investigational findings (n=69)

Investigations	Number of patients	Percentage
Mantoux Test (Positive)	49	71.01
Chest X-ray findings		
Cavity	1	1.45
Lung infiltrate	4	5.79
Pleural Effusion	1	1.45
Para tracheal lymph node	3	4.35
Hilar lymph node	4	5.79
Ultrasonography		
Mesenteric lymph node	7	10.14
Periportal lymph node	2	2.89
Sputum for AFB (Positive)	9	13.04
FNAC of lymph glands showing AFB	21	30.43
CBNAAT of FNAC samples	52	75.36
Cytopathology from FNAC samples	69	100

enlarged lymph gland is considered to evaluate treatment success.

In our study, 69 patients were followed up throughout the treatment period for 6 months. The number of female patients was higher than male (M: F=1:1.3). A study conducted by Das et al., in a tertiary care center among 69 patients also found a higher incidence in females (60.3%),[8] low nutritional status and overcrowding suggested to be the cause for higher incidence in females in our male dominated society. In our study, the most common age group was 5–7 years followed by 7–12 years. Although lymph node TB can affect patients of any age, in our study, we found that 41 (59.42%) of all children were in the 5–7-year-old age group. In the older age group, 7–12 years predominance of cervical gland involvement had been established, similar to the studies by Shah and Dani,[9] which may be due to infection in tonsil, adenoid and Waldeyer's ring providing early entry and extension from TB in lung and mediastinal glands. In the present study also, cervical lymph node involvement is the highest (72.46%) followed by axillary lymph node involvement (10.14%), inguinal lymph node involvement (4.35%), and hilar lymph node involvement (5.79%). Discharging sinus was found in 20 cases (28.98 %) which was quite high in this study which might be due to delayed presentation to health-care facilities resulting in delayed diagnosis and treatment.

Similar findings were seen in the study by Purohit et al.,[10] where discharging sinuses were seen among 1.4% cases.

In this study, all patients were diagnosed by FNAC, AFB in FNAC smear was found in 21 cases (30.43%). In other studies, incidence was between 21% and 30%.[11] CBNAAT of FNAC samples was positive in 75.36% cases. In a study by Singh et al.,[12] CBNAAT was positive for *M. tuberculosis* in 77% of patients with cytologically and histopathologically proven TB lymphadenopathy. The incidence of associated pulmonary TB was found only in 18.84 % patients, of which nine cases (13.04%) were sputum positive. This is lower compared to a study conducted by S Dasgupta et al.,[13] where the incidence of AFB positivity was 49% in TB lymphadenitis patients, and can be explained by development of immunity due to environmental exposure to *M. tuberculosis*.

After treatment for 6 months with DOTS under RNTCP, there was remarkable improvement in constitutional symptoms. However, lymph node remains enlarged in six cases (8.69%), among which discharging sinus and AFB were present in two cases (2.9%) each. Hence, overall success rate was 91.3%. This is comparable to the findings of Sharma et al., where the overall success rate of DOTS therapy was 95.4 %, in a study conducted among 1,098 cases of pediatric TB.[14] Hence, this study shows that DOTS is very much effective in the management of peripheral lymph node TB.

Limitations of the study

The limitation of our present study is that it was conducted in a single center, hospital-based among pediatric TB patients with tubercular lymphadenitis. Therefore, further studies should be conducted with bigger sample sizes and hospitals in rural and urban areas.

CONCLUSIONS

The study shows that DOTS, under RNTCP, is very much effective in the management of peripheral lymph node TB in pediatric patients. The take home message from the present study may be helpful for management and arriving at clinical decision making regarding completion of therapy.

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Ethical approval

The study was approved by the Institutional Ethics Committee.

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BKK, AKR- Involved in the diagnosis and management of the cases; **AKR, MS-** Interpreted the results; reviewed the literature and manuscript preparation; **BKK, BKG-** Concept, coordination, statistical analysis and interpretation, preparation of manuscript, and revision of the manuscript

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