Cervical Node Tuberculosis in Adults of an Urban Middle Class Community: Incidence and Management

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Abstract The aim of this study is to estimate the incidence of cervical node tuberculosis (TB) in an urban middle class population and to describe an effective protocol for management of cervical lymphadenopathy. The present study is a prospective observational study conducted over two years (2007–2009) in a community hospital in Mumbai, India. All adults (age ≥ 14 years) presenting with cervical lymphadenopathy, not resolving were included and their details of history and examination were noted. All patients were subjected to fine needle aspiration cytology (FNAC) and biopsy was done selectively as indicated. The response at 1, 3 and 6 months of starting anti tuberculous treatment (ATT) were noted. A total of 191 patients were included in this study. The mean age was 41 years and male to female ratio was 1:1.1 in patients with cervical lymphadenopathy. A history of contact with a patient of TB was the most significantly associated history seen in patients diagnosed to have TB of cervical nodes ($p < 0.001$). TB (38.7%) followed by

reactive nodes (37.6%) were the most common etiologies. A 90.6% response rate was seen in patients taking 6 months ATT for cervical node TB. The incidence of adult (≥ 14 years) cervical node TB was 52/100,000 people in an urban middle class community in Mumbai. A single swelling in the neck without other associated symptoms or signs was the commonest mode of presentation of TB of the neck nodes. A history of contact with TB, demonstrated an association with the final diagnosis of tuberculous lymphadenopathy.

Keywords Cervical lymph node · Tuberculosis · Incidence · Adults

Introduction

Lymph node tuberculosis (TB) is the most common site of extra pulmonary TB in India [1, 2]. Amongst these sites, cervical nodes are the most commonly affected [3]. While many Indian studies have discussed the clinical presentations and management of cervical node TB, the burden of tuberculous cervical lymphadenopathy is not known in Indian population [1, 2, 4–6]. The aim of this study is to estimate the incidence of cervical node TB in an urban middle class population and to describe an effective protocol for management of cervical lymphadenopathy.

Materials and Methods

Study Setting

The study population consists of 85,000 urban middle-class people, with Universal Health Coverage (UHC) for all their

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health needs. The UHC is delivered through an equitable and accessible health scheme, to the employees and their dependents of the Government's Department of Atomic Energy, from birth to death. The scheme is implemented through a pyramid of 14 satellite "Primary Care" dispensaries in and around suburban Mumbai. The primary care physicians refer patients with cervical lymphadenopathy, who have not responded to the initial conservative management to a single central hospital for secondary care. The diagnostic and therapeutic services are provided at a single central laboratory, free of cost. There are electronic records available for the entire study population, which makes it an ideal setting for patient tracking and long term follow ups. Defaulters are traced to their homes, by community-level social workers.

Study Design

Prospective observational study conducted over two years (2007–2009). This study was approved by Department review board.

Inclusion Criteria

All patients who presented with acutely enlarged nodes in the neck, received initial conservative management with antibiotics and were followed up after two weeks. The longstanding or chronic cervical nodes and unresolved acute cervical nodes after conservative treatment were included in the study and further investigated and diagnosed as per the flowchart (Fig. 1).

Exclusion Criteria

Pediatric patients (age <14 years) which constituted 15.4 % of the total population, were excluded. The presentation, etiology and management of cervical lymphadenopathy in children are different from that in adults.

All fine needle aspiration cytologies (FNACs) were reported by two cytopathologists at a single laboratory. A single observer followed up the patients till the nodes resolved completely or for a period of, at least, six months. Patients with metastatic nodes on cytology underwent further investigation for the site of primary tumor. Those with lymphomas were referred to a tertiary cancer centre for further treatment.

Patients diagnosed with cervical node TB received anti-tuberculosis treatment (ATT) regimen, as per the World Health Organization guidelines [7]. This consisted of an intensive phase with four drugs i.e. Isoniazid, Rifampicin, Pyrazinamide and Ethambutol for 2 months followed by a continuation phase of Isoniazid and Rifampicin for 4 months.

Response was noted in terms of change in the size of the node. Those with decreasing size of node were termed as 'responders' and those with no decrease or increase in the size were termed as 'non-responders' at follow up. Patients who did not respond to ATT after 3 months of treatment underwent biopsy for confirmation of diagnosis and mycobacterium culture and sensitivity to rule out multi-drug resistant tuberculosis (MDR TB). Demonstration of caseating necrosis and granulomas on histology was considered diagnostic of TB.

Data Collection and Analysis

A single surgical resident doctor entered the patient data prospectively, on a predesigned case proforma. Case files and electronic case records were checked for all the relevant clinical reports and notes. The patients were followed up at 1st, 3rd and 6th month for assessing the response to treatment. They were either given prior appointments or were telephonically invited to follow up. We recorded the response status on follow up visits. Case records were revisited for any missing clinical information. Data was then analyzed using SPSS version 17 (IBM Corporation, Somers, NY, USA).

Results

Over a two year period, 198 patients with clinically enlarged cervical nodes were evaluated. Seven patients were excluded from the final analysis (N = 191), as their cytology showed no lymph node characteristics. The male to female ratio was 1:1.1 with a mean age of 41 years. The commonest age group was 14–23 years (Fig. 2).

Size, Signs and Symptoms

The size of the cervical node on initial presentation was 1–2 cm in 58 % cases, 2–3 cm in 18.3 % and less than 1 cm in 16.6 % cases. Cervical swelling was present as the only symptom in 95 (49.7 %) patients. Fever and weight loss were the most common associated symptoms (24.6 % each) seen in patients presenting with cervical lymphadenopathy. A history of close contact with a diagnosed case of TB was a significant associated history, seen in patients with cervical node TB ($p < 0.001$). In 58.11 % (111/198) of patients, there was a single lymph node on presentation. Posterior triangle was the most common site accounting for 51 % of the cases.

Fine Needle Aspiration Cytology

Most common diagnosis on FNAC was reactive nodes (39 %) followed by 26 % with TB. Sixteen patients (8 %) were diagnosed to have metastasis and 4 (2 %) patients were diagnosed having lymphoma. Granulomatous disease not

Fig. 1 Recruitment protocol for cervical lymphadenopathy patients **Fig. 2** Age group wise distribution of cervical nodes in common etiologies. *NHL* non Hodgkin's lymphoma

otherwise specified was the diagnosis in 32 (17 %) patients and in 14 (7 %) patients, it was reported inconclusive on FNAC.

Biopsy

A total of 48 (25.1 %) patients were subjected to biopsy. Common diagnosis of histopathology and its correlation with the FNAC diagnosis have been shown in the Table 1. Other diagnoses on biopsy were toxoplasmosis (3), Kikuchi

Fujimoto node (1), sarcoidosis (1) and granulomatous disease not otherwise specified (6). The final results of this study showed the most common diagnosis as TB followed by reactive nodes (Table 2).

Tuberculosis Affecting Cervical Lymph Nodes

1. Incidence: The total no. of patients with cervical node TB, over the period of 2 years in this community was 74. The age group wise distribution of cervical nodes, population and age standardized rate in Indian urban population is as shown in Table 3.
2. The average age of patients with cervical node TB was 37. The commonest age group was between 34 and 43 years. There were more women (63.5 %) with TB than men (36.5 %).
3. The history of contact with a patient of TB was found to be very significant in patients with cervical node TB ($p < 0.001$), though the number of patients with this history were few (13/74).
4. Most common site in the neck was Level V group nodes (58.16 %). Single node (64.86 %) with TB was more common than matted nodes (22.97 %).
5. Response to ATT (Fig. 3)

Table 1 Correlation in FNAC diagnosis and common histopathology diagnosis

FNAC diagnosis	No. of patients in whom cytology done	Common histopathological diagnosis			
		Reactive nodes	Tuberculosis	Metastasis	Lymphoma
Reactive nodes/acute bacterial infection	9	5	2	0	2
Tuberculosis	6	0	6	0	0
Metastatic nodes	2	0	0	2	0
Non-Hodgkin lymphoma	1	0	0	1	0
Granulomatous disease not further categorized	16	0	15	0	1
Inconclusive	3	1	1	1	0
Total	37	6	24	4	3

Table 2 Final diagnoses of the all cervical nodes, after biopsy

Final diagnosis	No. of patients (%)
Reactive nodes/acute bacterial infection	72 (37.6)
Tuberculosis	74 (38.7)
Metastatic nodes	18 (9.4)
Non-Hodgkin's lymphoma	7 (3.6)
Granulomatous disease not further categorized	8 (4.1)
Inconclusive	7 (3.6)
Kikuchi Fujimoto	1 (0.5)
Sarcoidosis	1 (0.5)
Toxoplasmosis	3 (1.5)
Total	191

Discussion

Incidence

The spectrum of differential diagnoses for cervical lymphadenopathy makes it a clinical challenge for the treating physician. However, in India, TB remains the most common diagnosis. We have attempted to record incidence of cervical tuberculous lymphadenitis in the study population. The incidence calculated was 52 per 100,000 people of an urban middle class community in the city of Mumbai [8–

10]. This figure will add to the literature about disease burden and incidence of cervical node TB from India for urban communities. Sharma et al. in a review mentioned that lymph node TB forms 35 % of extra-pulmonary TB of which two third have cervical nodes [4]. TB, in general, is a communicable disease seen more in the low socioeconomic and crowded living conditions and this figure maybe an underestimation of the true Indian scenario as it was measured in the urban and middle class population.

FNAC

FNAC is a well-established diagnostic tool in the assessment of cervical nodes. It obviates the need for excision biopsy in majority of cases. Other studies have also described the benefits of FNAC in the protocol of cervical lymphadenopathy management, since it has high sensitivity and specificity in diagnosing of cervical lymphadenopathy and allows quick diagnosis [11, 12]. The sensitivity of this method in various studies ranged from 46 to 87 % for tuberculous cervical nodes which is similar to our study [13, 14]. Further, FNAC is also a good tool in diagnosing metastatic disease (an important differential diagnosis) with high sensitivity, specificity and positive predictive value [11, 14]. In the high-income countries (HIC) other diagnostic tools as ultrasonography and MRI, are used in

Table 3 Age group wise distribution of tuberculous cervical nodes, population and age standardized rates in Indian urban population

Age group	Count of cervical node TB over 2 years (a)	Population exposed	Population at risk over 2 years period (b)	Age specific incidence per 100,000 people $c = [(a \times 1,00,000)/b]$	Indian urban population [8] (d)	Expected age specific incidence in Indian urban population per 100,000 people $[(c \times d)/29,77,67,233]$
14–23	16	12,767	25,534	62.66	74,174,767	15.61
24–33	14	11,581	23,162	60.44	67,941,709	13.79
34–43	18	11,955	23,910	75.28	55,482,666	14.03
44–53	17	11,663	23,326	72.88	39,770,339	9.73
54–63	7	12,126	24,252	28.86	38,667,565	3.75
64 and above	2	11,456	22,912	8.72	21,730,187	0.64
Total	74	71,548	1,43,096	51.71	297,767,233	57.55

Fig. 3 Response to ATT and management in non-responders (TB tuberculosis, ATT anti tuberculous treatment)

conjunction with FNAC as they have a higher proportion of metastatic nodes, in their differential diagnosis. The unit price of FNAC in India's major metropolis cities would be around Rs. 1200–Rs. 1500 (\$25–\$40). The cost of histopathology would also be similar, but with added cost of surgery (excision biopsy) which would amount to Rs. 4500–Rs. 5500 (\$90–110). This cost is of a private pathology laboratory, non-subsidized and is borne by the patient. FNAC, being low in cost, an out-patient procedure and with low procedure related risks would be the recommended tool in India for diagnosing and starting treatment and the authors recommend its early use.

Age

Our results shows that cervical lymphadenopathy more commonly affects the young and middle aged adult group (mean age 41 years) and its occurrence decreases as age advances. Studies from Saudi Arabia and Nepal had their average age of patients with cervical lymphadenopathy between 36 and 39 years which was similar to ours [15, 16]. In our study malignant etiology group have their peak incidences between 55 and 65 years. This trend is also seen in studies done in Saudi Arabia [15, 17].

Size and Associated Symptoms

The size of the cervical node on initial presentation did not correlate well with the final diagnosis, in our study. However, the decreasing size was an important prognostic indicator. Our study shows a significant association between those with cervical node TB and having a history of contact with a patient already having TB ($p < 0.001$). Studies on constitutional symptoms of cervical node TB show a wide variability [2, 5]. These constitutional symptoms mimic other conditions with cervical node and cannot be attributed solely to TB.

The most common cause of persistent cervical lymphadenopathy was TB (38.7 %) followed by reactive and then malignancy in our study. In a recent study done in Saudi Arabia by Tawfiq et al. showed reactive lymph nodes to be commonest (52 %) followed by malignancy (32 %) followed by granulomatous disease (15.5 %) [15]. Studies done in Nepal showed the commonest cause for cervical node was TB, followed by reactive lymphadenitis and then malignancy [16]. In a study done in Mexico TB was seen in 48 % of individuals having cervical lymphadenopathy [18]. As we have dispensary based community healthcare delivery system, early insignificant reactive nodes are treated at primary care centre with antibiotics which may have been referred to the hospital in other healthcare systems, diluting the percentage of tuberculous nodes by adding more burdens of reactive nodes to the total numbers. Also we performed biopsies, on follow up in cervical nodes which were initially labeled on cytology as reactive but were persistent and did not resolve with antibiotic treatment. Malignancy, Non-Hodgkin's lymphoma and TB were diagnosed by these biopsies. The authors recommend an early course of antibiotics and the need of biopsy for persistent nodes labeled as reactive nodes on cytology. TB because of its high prevalence in developing nations and cervical nodes being the most common site of extra pulmonary TB should be the first differential in young adults.

Changing Trends in Presentation of Cervical Nodes of Tuberculosis

Nodal TB presenting as matted or sinuses has been discussed in many previous studies [5, 19, 20], however, in contrast to these studies, we found very few patients with presenting with these signs. Matted nodes were seen only in 17 (22.9 %) patients and sinus was seen in only one patient, who did not respond to treatment, and was later diagnosed to have MDR TB. Also, we found more patients presenting with a unilateral single node most commonly affecting the posterior triangle. Similarly, Oktay and colleagues in a recent study from Turkey have shown the most common presentation to be single node, without matting and sinuses [21]. Dharma et al. in their study found posterior triangle (51 %), unilateral (83 %) and involvement of a single group (68 %) of cervical nodes affected by TB to be the most common clinical picture [6]. This can be explained by our population seeking early treatment as they are under a UHC and as they belonged to an urban middle class community. Also, they may represent patients with better immunity but further studies are needed to compare with lower socioeconomic class and rural populations.

Response to Anti-tuberculosis Treatment

After 6 months of ATT, we found in our study 61 (90.6 %) patients who had responded to treatment. We had three patients of MDR TB and one case of atypical mycobacterium. M. S. Jawahar et al. studied efficacy of 6 months ATT. They recommended the 6 months course of ATT drugs in view of 96 % complete response observed in their study [1]. Arslan and Oktay et al. followed up results of 9 months ATT in tuberculous cervical lymphadenopathy patients. Complete response was seen in 65 % of the study group, partial response and drug resistance were seen in 15 and 20 % of the study group, respectively [21].

The chance of a patient seeking treatment outside the UHC system remains a possibility. However, the authors are confident that these patients with cervical lymphadenopathy, would have been captured or recaptured in this study, as the employees/dependents would have to report to the healthcare facility for; viz. 'absence from work' certification, record all private treatment for monetary reimbursement purposes, and for procurement of anti-tuberculous drugs (which are expensive and of long-duration). There is an unlikely chance that a patient, within a accessible and free healthcare system, will refuse or not seek treatment at all, and be allowed to fester an untreated cervical node, by his/her family.

The study population is middle class as defined by India's National Council of Applied Economic Research (NCAER) defines this as between Rs 2,00,000 and Rs 10,00,000 per family per annum, corresponding to the World Bank definition of a \$10 minimum per capita per day. This population is under a municipality, with greater than 75 % population in non-agricultural trades, qualifying to be an urban population. Therefore, the results of our study are not externally valid for other populations in India, for example, population below-the-poverty-line, or the rural populations.

Conclusion

The incidence of adult (≥ 14 years) cervical node TB was 52/100,000 people in an urban middle class community in Mumbai. A single swelling in the neck without other associated symptoms or signs was the commonest mode of presentation of TB of the neck nodes. A history of contact with TB, demonstrated a significant association with the final diagnosis of tuberculous lymphadenopathy.

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Conflict of interest None.

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