

Evaluation of the patients with lymph node tuberculosis

M. Fatih Garca^{a,*}, Mehmet Aslan^b, Guner Demir^c, Suayip Bilgen^d, Muhsin Uysal^d

^aDepartment of Otorhinolaryngology, Yuzuncu Yil University Medical Faculty, Van, Turkey

^bDepartment of Internal Medicine, Yuzuncu Yil University Medical Faculty, Van, Turkey

^cDepartment of Radiology, Ercis Capa Medical Center, Ercis, Van, Turkey

^dErcis Tuberculosis Control Dispensary, Ercis, Van, Turkey

Abstract. Lymph node tuberculosis (LNT) is chronic granulomatous inflammation of the lymph nodes. The aim of the present study is to review the epidemiologic, clinical and laboratory features of patients with LNT retrospectively.

The records of 138 patients admitted to tuberculosis dispensary between 2005 and 2010 with the diagnosis of tuberculosis were reviewed retrospectively and LNT cases were investigated.

Twenty one cases were identified with LNT. 13 patients were female (61.9%), 8 (38.1%) were male and mean age was 41 ± 21 years. The female to male ratio of LNT cases was 1.625 (13/8). The most common complaint was palpable mass on neck. Just cervical lymph nodes were the most frequently involved; in 15 (71.5%) patients. Only 2 cases have contact history with tuberculosis cases (9.5%) and two cases had a history of pulmonary tuberculosis (9.5%). After confirmation of diagnosis all patients were treated with combined anti-tuberculous therapy for at least six months.

LNT is seen more frequently in females than males. It should be considered in the differential diagnosis of the neck masses.

Key words: Extrapulmonary tuberculosis, lymph node tuberculosis, neck mass

1. Introduction

Tuberculosis has recently resurged as a worldwide public health concern in spite of the recent advances in its diagnosis and management (1). This is thought to be because of the poor hygiene conditions, the greater prevalence of acquired immune deficiency syndrome (AIDS) and depression of the immune system (2). Tuberculosis is an infectious disease caused by *Mycobacterium tuberculosis*, an acid-fast bacillus that is transmitted primarily through the respiratory tract and undergoes lymphohematogenous dissemination (1). Tuberculosis chiefly affects the pulmonary system but it can also involve extrapulmonary sites including the cervical and supraclavicular lymph nodes (3). Lymph node tuberculosis (LNT)

also known as tuberculous lymphadenitis, is commonly seen in underdeveloped countries, and with the spread of AIDS, tuberculous lymphadenitis is now frequently encountered in developed countries and accounting for about 4.0–5% of all tuberculosis cases and 20.3–50.0% of extrapulmonary tuberculosis (4-6). The target organ of *Mycobacterium tuberculosis* is the bronchopulmonary apparatus, and the head and neck is usually second area of involvement. Cervical lymph nodes are the most common affected lymph nodes by this disease-classically termed as “scrofula” (7). Lymphadenitis due to *Mycobacterium tuberculosis* generally presents with enlarged, painless neck lesions at 4 to 12 months after infection. The diagnosis in this region can be difficult, because it can mimic various other conditions.

The aim of this study was to investigate the epidemiologic, clinical and laboratory features of patients diagnosed with LNT retrospectively.

2. Material and methods

The records of 138 patients admitted to our dispensary between 2005 and 2010 with the diagnosis of tuberculosis were reviewed

*Correspondence: Dr. M. Fatih Garca

Department of Otorhinolaryngology, Yuzuncu Yil University Medical Faculty, Van, Turkey

Tel: 90 432 2150470

Fax: 90 432 2167519

E-mail: fatihgarca@hotmail.com

Received: 10.01.2013

Accepted: 19.02.2013

retrospectively after institutional review board approval was obtained and 21 lymph node tuberculosis cases were identified.

The patients' medical records were reviewed for details relating to presenting signs and symptoms, site and appearance of the lesions, chest x-ray findings, sputum smear, age and sex breakdown, status of contact with active tuberculosis cases, BCG scar status, results of tuberculin test, diagnostic procedures and treatment duration. The features of LNT were discussed and compared to other reports. The chest radiography of all cases was evaluated by the same radiologist.

All patients gave a detailed medical history and received a physical examination. Fine needle aspiration biopsy (FNAB) was performed for all involved nodes. The criteria for a diagnosis of LNT were histopathologic evidence of granulomatous inflammation with epithelioid cells. Specimens were routinely sent for acid-fast bacilli (AFB) staining and pathology.

After the confirmation of diagnosis, all patients were treated with medical therapy for a minimum of 6 months. In the first two months isoniazid (5 mg/kg), rifampicin (10 mg/kg), pyrazinamide (15 to 20 mg/kg), and ethambutol (25 mg/kg), or streptomycin (1gr/day) was given followed by isoniazid and rifampicin for the next months.

Statistical analysis

Numeric values were determined as percent or mean \pm SD. Non parametric Kruskal-Wallis test was used for qualitative results and chi-square test was used for qualitative results between features. p value of less than 0.05 was regarded to indicate the statistical significance.

3. Results

Twenty one cases with LNT were identified. Thirteen were female (61.9%), 8 (38.1%) were male and mean age was 41 ± 21 years. The female to male ratio of lymph node tuberculosis cases was 1.625 (13/8). Coughing, night sweats, weight loss and weakness were found in 3 patients (14.3%). Two cases had a history of tuberculosis contact inside family (9.5%) and two case had a history of pulmonary tuberculosis (9.5%) (Table 1).

Table 2. Lymph node distribution

Node group	Patients	Unilateral	Bilateral
Cervical	15	15 (71.5%)	-
Cervical and Axillary	4	4 (19%)	-
Cervical and Supraclavicular	2	2 (9.5%)	-

The most common complaint was palpable lymphadenopathy. Just cervical lymph nodes were most frequently involved in 15 (71.5%) patients. Cervical and axillary lymph nodes were involved in 4 (19%) patients. Cervical and supraclavicular lymph nodes were involved in 2 (9.5%) patients (Table 2).

Tuberculin skin test was performed to 15 (71.5%) cases and found positive (≥ 10 mm) in all of them. Eighteen (85.7%) cases had BCG scar. Associated chest lesions on radiography were evident in only five cases (23.8%): local pulmonary lesions in four cases, hilar tuberculosis lymphadenopathy without local paranchymal lesions in one case. The chest radiography were normal in other patients (76.1%).

All the patients were treated with daily combined anti-tuberculous therapy for at least six months and progress was assessed by clinical examination. None of the patients has shown any recurrence of local or systemic disease with minimum follow up of six months after completion of therapy. Mean duration of treatment was 8.6 ± 2.7 months in our patients.

4. Discussion

Infection with Mycobacterium tuberculosis occurs primarily by inhalation of airborne droplet nuclei containing organisms. It has been reported that tuberculosis can affect almost every organ in the body. The bacilli spreads through lymphatic

Table 1. Demographic and clinic features in patients with lymph node tuberculosis

Patients (n)	21
Age (year)	41 \pm 21
Sex (F/M)	13/8
Treatment duration (month)	8.6 \pm 2.7
Main symptom (n/%)	
Coughing	3 (14.3 %)
Night sweats	3 (14.3 %)
Weight loss	3 (14.3 %)
Weakness	3 (14.3 %)
Previous history for LNT	2 (9.5%)
Family history for LNTT	2 (9.5%)

F, Female; M, Male; LNT. Lymph node tuberculosis.

channels to regional lymph nodes and through the bloodstream potentially to seed any distant organ, including kidneys, joints, meninges and parotid gland. Nodal disease is one of the most common manifestations of extrapulmonary tuberculosis. Tuberculosis that affects the cervical lymph nodes represents about 20.3–50% of extrapulmonary tuberculosis. Lymphadenitis is the commonest extrapulmonary manifestation of tuberculosis occurring in more than 25% of all cases of tuberculosis (5,6).

In recent years, the incidence of cervical mycobacterial infection has been increasing. The pathogenesis of cervical lymphadenitis has been a controversial aspect of tuberculosis. Some authors believe that this is a localized disease process. Others state that cervical lymphadenitis is probably a generalized lymphohematogenesis dissemination and hence spreads to the cervical lymph node. So far there is no basis to support this suggestion, and this may emphasize the primary nature of tuberculous cervical lymphadenitis (8). Cervical lymphadenitis has many etiological factors. In endemic areas, tuberculous infection is a frequent cause of cervical lymphadenitis. Differentiation between tuberculous and other inflammatory causes of lymphadenitis is important, because the treatments are very different. Patients with tuberculous lymphadenitis were often described as having nodes that were painless and matted, in addition to constitutional symptoms of fever, malaise, weight loss, and night sweats (9).

A high index of suspicion is needed for the diagnosis of LNT. A thorough history and physical examination, tuberculin test, staining for acid-fast bacilli, radiologic examination, and FNAB will help to reach the early diagnosis of LNT which will allow early institution of treatment before a final diagnosis can be made by biopsy and culture (3,4,6,9). The differential diagnosis is extensive and includes infections (viral, bacterial or fungal), and neoplasms (lymphoma or sarcoma, metastatic carcinoma), non-specific reactive hyperplasia, sarcoidosis, toxoplasmosis, cats-scratch fever, collagen vascular diseases and diseases of reticuloendothelial system.

Posterior, anterior and supraclavicular cervical regions are usually involved. The submandibular, submental, axillary, and inguinal lymph nodes are less frequently affected. The involved lymph nodes are typically firm, non-tender, and painless, with non-erythematous overlying skin. Lymph node involvement typically occurs between six to nine months following the initial infection (10). In our study, we found that

unilateral involve of cervical lymph nodes in 15 patients prevailed (71.5%), as in other series (11).

In our study, we found that twenty one patients with LNT were identified. Thirteen were female (61.9%), 8 (38.1%) were male. Although tuberculosis is seen in men more often than women in the literature, in our study, the female to male ratio was 1.625 (13/8). Various recent studies have also reported a higher incidence in females (12,13).

Our findings are agree with the findings of other authors (14,15). Women usually have a quiescent presentation or report multiple, vague, and atypical constitutional symptoms. These observations reflect biological, hormonal, social, environmental, or behavioral differences between men and women. Biologically there is a fundamental difference in the immune systems of men and women (16). Ramanathan et al. (17) suggest a hormonal influence on immunity as the underlying cause for the different pattern of disease in women.

Socially, in developing countries women often have a low socioeconomic and nutritional status, which can affect the immune response to the disease. Others have suggested that women are more conscious of their appearance and attend healthcare facilities earlier, while men ignore their disease until it is at a more advanced stage (8,17). In addition, in our study, the majority of cases occurred between 20 and 62 years of age: this is similar to other reports (18).

Lung disease is common with cervical tuberculosis, and frequently the lung on the same side of the neck lymph node was found to be involved (19). In our study, according to patients' records, we found that only two patients had a history of pulmonary tuberculosis in patients with cervical tuberculosis. The common radiological findings were nodular shadows in the upper and middle zones as reported by William et al. (20).

In our study, we found that tuberculin skin test was performed to 15 (71.5%) cases. It was positive (≥ 10 mm) in all cases. Tuberculin skin test does not measure immunity. It also does not indicate the presence of disease; it only indicates infection. This test is unreliable in the diagnosis of latent TB, because of immunosuppression and because of the regular vaccination with Bacillus Calmette Guerin in childhood. Serologic diagnosis (ELISA) has a high specificity and sensitivity for the detection of antibodies in fluids from infected areas (10). It is known that microbiologic diagnostic methods are the gold standard for diagnosis of extrapulmonary manifestation of tuberculosis, as in cases in pulmonary tuberculosis (19). Culture of

mycobacteria is time consuming, requiring 5 to 6 weeks to produce results. The yield is also low. In the literature, cultures are reported to be positive in 50% to 70% of patients (20).

FNAB plays an important role not only in diagnosing cervical malignancies but it can also be used for the diagnosis of tuberculosis cervical adenitis. To avoid surgery, it is logical to initiate antituberculous therapy on the basis of positive PPD and positive histopathologic FNAB results. If the culture result confirms the diagnosis or if the mass is responding to medical therapy, the treatment should be continued until final resolution. FNAB has been increasingly used to diagnose tuberculous infection in endemic areas; FNAB has been shown to be sensitive, specific, and cost effective (21). Although this is less invasive and cheap procedure that is useful for tuberculosis cervical adenitis diagnosis, definitive diagnosis of tuberculosis cervical adenitis can be established by positive culture or with the identification of AFB. Therefore, FNAB should be regarded as a screening test for mycobacterial adenitis (22).

Recently, other techniques have shown to promise in the more rapid and accurate diagnosis of tuberculous lymphadenitis. The use of polymerase chain reaction with FNAB has been found to be a fast and accurate method to identify M tuberculosis, with a sensitivity and specificity of 76.4% and 100%, respectively (22). This method also has an additional advantage of differentiating tuberculous from other granulomatous lymphadenopathy and non tuberculous mycobacterial disease.

Tuberculosis cervical lymph node is a medical disease. Surgical intervention is considered only when excision is needed for biopsy purposes or when a node remains enlarged after antimicrobial therapy. Residual disease in the nodes after complete therapy is uncommon and irrespective of the size of the nodes. Regimen suitable for using in DOT's (Directly Observed Therapy) include isoniazid (H), rifampicin (R), and pyrazinamide (Z) for the first 2 months where there was a low risk of isoniazid resistance (23) followed by isoniazid and rifampicin for 4 months (HRZ 2; HR 4). Like others, we believe that it was highly satisfactory and offered a cure to approximately 80% to 90% of treated patients for cervical LNT (24). All our patients received anti-tuberculous therapy for a minimum of 6 months and showed a good response. No drug resistance was seen even in cases who had an incomplete course of anti-tuberculous therapy a year before. The treatment was continued for a minimum of 6 months in all cases.

In conclusion, our data suggest that lymph node tuberculosis is seen frequently in female than male. Clinicians, it should be always considered in the differential diagnosis of the neck masses. Hence, early diagnosis and effective treatment of LNT are important.

Acknowledgments

The authors would like to thank friendly assistance during the collection of the data of this study.

References

1. WHO. Global tuberculosis control: surveillance, planning, financing. WHO report 2007 (WHO/HTM/TB/2007.376).
2. Miziara ID. Tuberculosis affecting the oral cavity in Brazilian HIV-infected patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2005; 100: 179-182.
3. Jha BC, Dass A, Nagarkar NM, et al. Cervical tuberculous lymphadenopathy: Changing clinical pattern and concepts in management. *Postgrad Med J* 2001; 77: 185-187.
4. Shapiro AL, Pincus RL. Fine-needle aspiration of diffuse cervical lymphadenopathy in patients with acquired immunodeficiency syndrome. *Otolaryngol Head Neck Surg* 1991; 105: 419-421.
5. Pehme L, Hollo V, Rahu M, et al. Tuberculosis during fundamental societal changes in Estonia with special reference to extrapulmonary manifestations. *Chest* 2005; 127: 1289-1295.
6. Ilgazli A, Boyaci H, Basyigit I, Yildiz F. Extrapulmonary tuberculosis: clinical and epidemiologic spectrum of 636 cases. *Arch Med Res* 2004; 35: 435-441.
7. Grzybowski S, Allen E. History and importance of scrofula. *Lancet* 1995; 346: 1472-1474.
8. Lau SK, Kwan S, Lee J, et al. Source of tubercle bacilli in cervical lymph nodes: a prospective study. *J Laryngol Otol* 1991; 105: 558-561.
9. Sloane MF. Mycobacterial Lymphadenitis. In: Rom WN, Garay SM, eds. *Tuberculosis*. Boston/New York/Toronto/London: Little, Brown and Company; 1996. p. 577-583.
10. Cruz AT, Starke JR. Clinical manifestations of tuberculosis in children. *Paediatr Respir Rev* 2007; 8: 107-117.
11. Hooper AA. Tuberculous peripheral lymphadenitis. *Br J Surg* 1972; 59: 353-359.
12. Al-Sherhani AM. Mycobacterial infections of the head and neck: presentation and diagnosis. *Laryngoscope* 2001; 111: 2012-2016.
13. Polesky A, Grove W, Bhatia G. Peripheral tuberculous lymphadenitis: epidemiology, diagnosis, treatment, and outcome. *Medicine (Baltimore)* 2005; 84: 350-362.
14. Long NH, Diwan VK, Winkvist A. Difference in symptoms suggesting pulmonary tuberculosis among men and women. *J Clin Epidemiol* 2002; 55: 115-120.
15. Matsushita Y, Ikeda N, Kurasawa T, et al. The characteristics of clinical features of pulmonary tuberculosis in female. *Kekkaku* 1996; 71: 391-398.

16. Ammari FF, Bani Hani AH, Ghariebeh KI. Tuberculosis of the lymph glands in the neck: a limited role for surgery. *Otolaryngol Head Neck Surg* 2003; 128: 576-580.
17. Ramanathan VD, Jawahar MS, Paramasivan CN, et al. A histological spectrum of host responses in tuberculous lymphadenitis. *Indian J Med Res* 1999; 109: 212-220.
18. Dean K. Self-care components of lifestyles: the importance of gender, attitudes and the social situation. *Soc Sci Med* 1989; 29: 137-152.
19. Bothamley G. Sex and gender in the pathogenesis of infectious tuberculosis. A perspective from immunology, microbiology and human genetics. In: Diwan VK, Winkvist A, editors. *Gender and tuberculosis*. NHV report. Goteborg, Sweden: Nordic School of Public Health; 1998, p. 41-53.
20. Williams RG, Douglas-Jones T. *Mycobacterium* marches back. *J Laryngol Otol* 1995; 109: 5-13.
21. Martin PD. The tuberculin skin test. *N Z Med J* 1994; 107: 310-311.
22. Davis SD, Yankelevitz DF, Williams T, Henschke CI. Pulmonary tuberculosis in immunocompromised hosts: epidemiological, clinical, and radiological assessment. *Semin Roentgenol* 1993; 28: 119-130.
23. Ibekwe AO, Al Shareff ZA, Al Kindy S. Diagnostic problems of tuberculosis cervical adenitis (scrofula). *Am J Otol* 1997; 18: 202-205.
24. Dasgupta A, Ghosh RN, Poddar AK, et al. Fine needle aspiration cytology of cervical lymphadenopathy with special reference to tuberculosis. *J Indian Med Assoc* 1994; 92: 44-46.