

Follow-up results in tuberculous cervical lymphadenitis

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Abstract

Objective: To investigate the efficacy of medical antituberculous treatment in patients with tuberculous cervical lymphadenitis (TCL).

Methods: In the period 1996–2002, 73 TCL patients were reviewed and the results of clinical and laboratory testing were documented. The efficacy of a four-drug chemotherapy regimen was investigated.

Results: Purified protein derivatives (PPD) skin test results were positive in 58 (79 per cent) patients. Chest X-rays revealed changes consistent with tuberculosis in nine (12.3 per cent) patients. The mean duration of medical treatment was 10.04 months. In follow-up evaluation, 14 (20 per cent) patients were considered suspicious for resistant TCL and total excision of all nodes was performed. Histopathology confirmed TB in only 10 of these cases.

Conclusion: The high incidence of residual disease in our study indicates that medical treatment (at least nine months of four combined antituberculous drugs) did not seem to be effective. If lymphadenopathy persists, total surgical excision of lymph nodes should be the treatment of choice.

Key words: *Mycobacterium Tuberculosis*; Neck; Lymph Nodes; Follow-Up Studies

Introduction

Tuberculosis (TB) is still a major health hazard in the developing countries, infecting approximately one-third of the world's population.¹ In 1990, TB killed between 2.6 and 2.9 million people worldwide. The incidence is enhanced by many factors such as poverty, lack of antituberculous chemotherapy, poor compliance and resistant organisms. In addition, the extrapulmonary type of TB is on the rise in many regions of the world.² This is of special concern to otolaryngologists since tuberculous cervical lymphadenopathy (TCL) is the most common extrapulmonary manifestation of tuberculosis.³

Although the mortality and morbidity of mycobacterial disease has been reduced considerably by improved sanitation, nutrition and medical treatment, a slight increase in its incidence has been observed in the last two decades in Turkey, as in other parts of the world.⁴ This resurgence reflects delay in diagnosis and ineffectiveness in management of the disease, the latter compounded by the emergence of multidrug-resistant organisms.^{2,5–7}

In this study, our objective was to investigate the efficacy of medical antituberculous treatment in

patients with TCL and also to discuss the clinical presentation, diagnosis and treatment of TCL.

Material and methods

Between 1996 and 2002, 73 patients with cervical TB who were diagnosed and treated at Dicle University Hospital, Diyarbakir, Turkey, were reviewed. The following data were collected: age, sex, presentation and site of involvement, results of purified protein derivatives (PPD) testing, chest X-ray, fine-needle aspiration biopsy (FNAB), and histopathological results. In all cases, the inclusion criterion for diagnosis was caseating granuloma consistent with TB. The diagnosis was obtained mostly by FNAB and excisional biopsy of the lymph nodes, and in some patients with fluctuation by curettage and biopsy of the abscess wall or superficial parotid lobectomy. When excisional biopsy was performed to obtain tissue for diagnosis, if there were multiple lymph nodes then no attempt was made to excise all those involved. All patients were treated with a four-drug combined chemotherapy regimen. The initial treatment comprised isoniazid, rifampicin, pyrazinamide,

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and ethambutol or streptomycin, for two months and then maintenance with isoniazid and rifampicin for the next seven months. After the completion of treatment, if any lymph nodes remained, isoniazid and rifampicin were given for an additional three to six months. After this therapy all the patients recovered and there was no evidence of cervical disease. For the follow-up examination, all patients were invited to the hospital (by telephone) to investigate the efficacy of treatment. Clinical examination and laboratory tests, such as chest X-ray, PPD testing, cervical and abdominal ultrasonography (USG), and FNAB, were repeated. In cases in which TCL was thought to have recurred, total surgical excision of the lymph nodes was performed. The general follow-up results were summarized.

Results

Clinical features

The study group consisted of 73 patients (24 men and 49 women) with TCL. Their ages ranged from 13 to 67 years (mean: 32.2 years) (Figure 1). The adenopathy was unilateral in 56 (77 per cent) of the 73 patients. Forty-three (59 per cent) of the 73 patients had nodes only in the anterior chain and 22 (30 per cent) had nodes in the posterior chain. Eight patients (11 per cent) had nodes in both the anterior and posterior chains. Seven patients had nodes only in the supraclavicular region.

A history of contact with an infected individual was given in 13 (18 per cent) patients.

The PPD skin test result was positive (i.e. more than 12 mm induration) in 58 (79 per cent) patients. Pre-operative chest X-rays revealed fibrocalcific changes consistent with inactive tuberculosis in nine (12.3 per cent) cases; however, 87.7 per cent of patients showed a normal chest X-ray. Active lesions were not found on chest X-ray examination in any patients.

The diagnosis of TB lymphadenitis was based on: FNAB in five patients; curettage and biopsy of the abscess wall in 14 cases; superficial parotidectomy

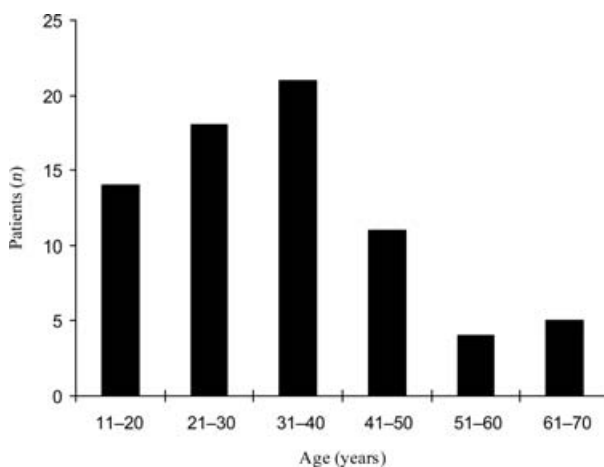


FIG. 1

Age distribution of patients with tuberculous cervical lymphadenopathy.

TABLE I

DIAGNOSTIC METHODS USED IN CASES WITH TUBERCULOUS CERVICAL LYMPHADENOPATHY*

Diagnostic method	Patients (%)
Excisional lymph node biopsy	48 (66)
Curettage and/or biopsy of abscess wall	14 (19)
FNAB	5 (7)
Superficial parotid lobectomy	6 (8)
Culture	0 (0)

*n = 73. FNAB = fine-needle aspiration biopsy

in six patients; and excisional biopsy in 48 patients (Table I).

Follow-up results

Sixty-nine out of the 73 patients were accessible for follow-up evaluation. Of these 69 patients, the duration of medical treatment was nine months in 49 (71 per cent) patients, 12 months in 16 (23 per cent) patients and 15 months in four (6 per cent) patients. The mean duration of medical treatment was 10.04 months. The follow-up period after completion of treatment was between 21 and 66 months (mean: 28 months).

Fourteen (20 per cent) of the patients were considered suspicious for resistant TCL according to their clinical and radiological findings, and PPD testing and total excision of all nodes was performed. Histopathologic evaluation of the specimens confirmed caseating granuloma in only 10 of these cases. Of those patients, seven received treatment for nine months, one received treatment for 12 months and two received treatment for 15 months. In one patient, in spite of a normal cervical examination, extensive mesenteric lymphadenopathy was observed, with highly positive PPD testing, and active mesenteric tuberculous lymphadenopathy was diagnosed. In total, treatment was considered to have failed in 11 of 69 (16 per cent) patients. Another four patients with enlargement of cervical lymph nodes were considered to have nonspecific inflammatory lymphadenopathy. The characteristics of these resistant cases are illustrated in Tables II and III.

Discussion

The most common manifestation of mycobacterial infection encountered in otolaryngologic practice is cervical lymphadenitis.^{8,3} Mycobacterial cervical lymphadenitis remains a diagnostic and therapeutic challenge because physical and laboratory findings are inconsistently reliable, it mimics other pathologic processes, and it may necessitate both medical and surgical treatments.^{2,9}

Patients with cervical mycobacterial disease due to nontuberculous mycobacteria can also present in an identical fashion and with similar histologic appearances. However, the clinical course and treatment in these cases are quite different. Differentiation is only possible via culture and identification of the organism.¹⁰ However, culture of mycobacteria is

TABLE II
CLINICAL FEATURES OF RESISTANT CASES WITH TUBERCULOUS CERVICAL LYMPHADENOPATHY

Case	Duration of treatment (months)	Unilateral/bilateral	Site of involvement	PPD (mm diameter)	Chest X-ray
1	15	Unilateral	SC	8	Normal
2	12	Unilateral	SC, PC	11	Normal
3	9	Unilateral	AC	16	Normal
4	9	Unilateral	SM	14	Normal
5	6	Unilateral	PC, AC	15	Apical fibrocalcific changes
6	15	Bilateral	SM, AC	16	Normal
7	9	Unilateral	PC	8	Normal
8	6	Unilateral	SC, AC	14	Apical fibrocalcific changes
9	6	Bilateral	AC	11	Normal
10	9	Unilateral	SM	13	Normal
11*	12	–	–	15	Normal

*Case with mesenteric tuberculous lymphadenopathy. PPD = purified protein derivatives test; SC = supraclavicular lymph nodes; PC = posterior cervical lymph nodes; AC = anterior cervical lymph nodes; SM = submandibular lymph nodes

time-consuming, requiring five to eight weeks to produce results, and the yield is low.⁹ On the other hand, mycobacterial lymphadenopathy involving nontuberculous mycobacterium occurs almost exclusively in children under 12 years of age, especially between the ages of one and three years.^{3,11} Patients over 12 years of age almost always have tuberculous lymphadenopathy; the exception to this rule is the human immunodeficiency virus (HIV)-infected patient.^{10,12,13} In Turkey, HIV infection is very rare¹⁴ and all the patients in our study were over 12 years of age and apparently immunocompetent. Therefore, they were considered as TCL. In Turkey, histopathology of the lymph nodes is very suggestive of tuberculosis.¹⁵ All of our patients in the present series were diagnosed on the basis of a histopathological finding of caseating granuloma consistent with TB alone, which was confirmed in all biopsies.

Most of our patients had progressive enlargement of neck lymph nodes, without any other symptoms at presentation. Many studies have suggested a typical pattern of involved nodes in TCL: multiple, matted, bilateral and (usually) posterior adenopathy.^{16–18} In our cases, most of the adenopathies were unilateral or anterior in location. Our findings, along with those of other studies,^{2,8,11,19} suggest that there is no typical nodal location in patients with TCL.

In many reports, most adult, immunocompetent patients with *Mycobacterium tuberculosis* infection had a positive PPD test.^{2,10,19} Our results concur; we obtained 79 per cent positive PPD testing at the time of diagnosis. The PPD test is simple and has a fairly high positive rate in tuberculosis infections.

TABLE III

DURATION OF MEDICAL TREATMENT IN OVERALL AND RESISTANT CASES

Duration of medical treatment (months)	Overall cases (%) (n = 69)	Resistant cases (%) (n = 11)
9	49 (71)	7 (63)
12	16 (23)	2 (18)
15	4 (6)	2 (18)

However, a positive PPD test result is common in many healthy individuals in Turkey because of the Bacillus Calmette-Guerin (BCG) vaccination programme. Therefore, the PPD test does not provide sufficient evidence to confirm the diagnosis of TCL. Ucan *et al.* found a mean induration diameter of 11.95 mm in a large, healthy Turkish population; the PPD test produced induration of greater than 10 mm in 63 per cent and greater than 12 mm in 54.2 per cent of the general Turkish population.²⁰

In our study, the chest X-ray was positive for TB in 12.3 per cent of patients. Although in earlier literature pulmonary involvement was reported to be more common in TCL,¹¹ recent reports have showed less pulmonary involvement, indicating that TCL is a localized disease.⁸ Similarly, few patients presented with the classic constitutional symptoms of fever, chills, night sweats, anorexia, weight loss and haemoptysis seen in pulmonary involvement.

It is generally agreed that tuberculous cervical lymphadenitis is a medical condition and that anti-tuberculous chemotherapy is the definitive treatment modality for tuberculous lymph nodes. Deitel *et al.*¹⁷ have shown complete TCL remission with prolonged medical treatment alone, reserving surgery for confirmation of the diagnosis via lymph node biopsy. However, Huhti *et al.*¹³ reported a 73 per cent treatment success rate using chemotherapy alone.

When combining both surgery and antituberculous medication for a duration of between 12 and 18 months, the success of treatment has been reported to be 89–95 per cent,^{13,19,21} however, after total excision of lymph nodes, Alleva *et al.*,¹¹ Castro *et al.*⁸ and Kanlikama *et al.*¹⁰ reported successful treatment in all their patients. These studies confirm that excisional biopsy followed by long term chemotherapy constitute curative therapy. In our study, following nine to 15 months of antituberculous medication (10.04 months mean), 11 (16 per cent) patients had persistent evidence of TB due to residual TCL disease.

Atypical mycobacterial disease, drug-resistant tuberculosis bacilli and duration of treatment seem

to be important contributors to residual lymph node disease. When the ages and clinical and laboratory results of our cases are considered, treatment failure seems more likely to be related to the duration of the treatment and the presence of drug-resistant tuberculosis bacilli rather than to atypical mycobacterial disease. Development of drug-resistant strains is becoming a major problem in the treatment of tuberculosis. It is sometimes difficult to guide the initial treatment according to culture and antibiotic susceptibility tests because these results are not readily available.²² On the other hand, drug resistance operates differently in different countries. In a large, meta-analytic, Turkish study, significant increases were found in multi-drug resistance in 1990–1995 compared with 1980–1985. Total resistance values for streptomycin, rifampicin, isoniazid and ethambutol were found to be 17.9 per cent, 22.1 per cent, 23.8 per cent and 7.7 per cent, respectively.²³

One interesting finding of our study, a case of active abdominal mesenteric lymphadenopathy, occurred in a 34-year-old woman who had taken antituberculous therapy for 12 months and was responding well. Tuberculous mesenteric lymphadenitis is usually treated with a 'short course' of chemotherapy, with good response; concomitant occurrence with TCL is rare in literature.⁸ Since TCL may be considered a systemic disease, its follow-up evaluation should include abdominal lymph node assessment via abdominal ultrasonography, as well as checking for superficial lymph nodes.

In our study, after surgery, four patients showed histologically evident reactive lymphadenitis that was clinically considered as residual TCL. Clinical and laboratory testing, including FNAB, were not able to identify these cases before surgical excision. In follow-up evaluation, the clinician should consider these 'false positive' cases before the surgical procedure.

- **This study looks at the efficacy of antituberculous chemotherapy in tuberculous cervical adenitis**
- **Despite aggressive, four-drug combination chemotherapy, residual lymphadenopathy suspicious of residual disease occurred in 20 per cent of the 73 patients**
- **Surgical removal of residual lymph nodes following antituberculous chemotherapy should be undertaken**

References

- 1 Ibekwe AO, al Shareef Z, al Kindy S. Diagnostic problems of tuberculous cervical adenitis (scrofula). *Am J Otolaryngol* 1997;**18**:202–5
- 2 Al-Serhani AM. Mycobacterial infection of the head and neck: presentation and diagnosis. *Laryngoscope* 2001;**111**:2012–16
- 3 Munck K, Mandpe AH. Mycobacterial infections of the head and neck. *Otolaryngol Clin North Am* 2003;**36**:569–76

- 4 Suoglu Y, Erdamar B, Colhan I, Katircioglu OS, Cevikbas U. Tuberculosis of the parotid gland. *J Laryngol Otol* 1998;**112**:588–91
- 5 Williams RG, Douglas-Jones T. Mycobacterium marches back. *J Laryngol Otol* 1995;**109**:5–13
- 6 Maher D, Raviglione MC. The global epidemic of tuberculosis: a World Health Organization perspective. In: Schlossberg D, ed. *Tuberculosis and Nontuberculous Mycobacterial Infections*, 4th edn. Philadelphia: WB Saunders, 1999;104–15
- 7 Cleary KR, Batsakis JG. Mycobacterial disease of the head and neck: current perspective. *Ann Otol Rhinol Laryngol* 1995;**104**:830–3
- 8 Castro DJ, Hoover L, Castro DJ, Zuckerbraun L. Cervical mycobacterial lymphadenitis. Medical vs surgical management. *Arch Otolaryngol* 1985;**111**:816–19
- 9 Kanlikama M, Mumbuc S, Bayazit Y, Sirikci A. Management strategy of mycobacterial cervical lymphadenitis. *J Laryngol Otol* 2000;**114**:274–8
- 10 Lee KC, Schechter G. Tuberculous infections of the head and neck. *Ear Nose Throat J* 1995;**74**:395–9
- 11 Alleva M, Guida RA, Romo T 3rd, Kimmelman CP. Mycobacterial cervical lymphadenitis: a persistent diagnostic problem. *Laryngoscope* 1988;**98**:855–7
- 12 Lai KK, Stottmeier KD, Sherman IH, McCabe WR. Mycobacterial cervical lymphadenopathy. Relation of etiologic agents to age. *JAMA* 1984;**251**:1286–8
- 13 Huhti E, Brander E, Paloheimo S, Sutinen S. Tuberculosis of the cervical lymph nodes: a clinical, pathological and bacteriological study. *Tubercle* 1975;**56**:27–36
- 14 Yenen OS, Ekinci E, Aydilek R, Baydar I. HIV infection and tuberculosis in Turkey. *Chest* 1988;**94**:674
- 15 Karaöz T, Şenol T, Bekçi TT. Tuberculous lymphadenitis. *Toraks Dergisi* 2001;**2**:74–9
- 16 Domb GH, Chole RA. The diagnosis and treatment of scrofula (mycobacterial cervical lymphadenitis). *Otolaryngol Head Neck Surg* 1980;**88**:339–41
- 17 Deitel M, Saldanha CF, Borowy ZJ, Ronald AC, Krajden S. Treatment of tuberculous masses in the neck. *Can J Surg* 1984;**27**:90–3
- 18 Kanlikama M, Gokalp A. Management of mycobacterial cervical lymphadenitis. *World J Surg* 1997;**21**:516–19
- 19 Levin-Epstein AA, Lucente FE. Scrofula – the dangerous masquerader. *Laryngoscope* 1982;**92**:938–43
- 20 Ucan ES, Sevinc C, Abadoglu O, Arpaz S, Ellidokuz H. Comment on the tuberculin test results: Standards of our country and new requirements. *Toraks Dergisi* 2000;**1**:25–9
- 21 Wong ML, Jafek BW. Cervical mycobacterial disease. *Trans Am Acad Ophthalmol Otolaryngol* 1974;**78**:ORL75–87
- 22 Yuen AP, Wong SH, Tam CM, Chan SL, Wei WI, Lau SK. Prospective randomized study of thrice weekly six-month and nine-month chemotherapy for cervical tuberculous lymphadenopathy. *Otolaryngol Head Neck Surg* 1997;**116**:189–92
- 23 Yolsal N, Malat G, Disci R, Orkun M, Kilicaslan M. The resistance problems for antituberculous drugs comparison with 1984–1985 years. *Klinik Dergisi* 1998;**1**:6–9

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