

Anna Maria Pajor¹, Magdalena Józefowicz-Korczyńska¹, Maria Korzeniewska-Koseła²,
Sylwia Kwiatkowska³

¹Department of Otolaryngology, Medical University of Lodz, Poland

²Department of Tuberculosis Epidemiology and Surveillance, National Tuberculosis and Lung Diseases Research Institute, Warsaw, Poland

³Pneumology Ward, Medical University of Lodz, Poland

A clinic-epidemiological study of head and neck tuberculosis — a single-center experience

Abstract

Introduction: Extrapulmonary tuberculosis (EPTB) accounts for less than 6% of all tuberculosis (TB) cases in Poland, although in other countries (European in particular) this proportion is much higher. The study was undertaken to evaluate the clinical and epidemiological differences in patients hospitalized in one of Otolaryngology Departments in Poland during 36 years.

Material and methods: In a retrospective study, 71 patients were identified and divided into three groups according to the study period: I — 1978–1989 (30 patients, 42%), II — 1990–2001 (19 patients, 27%) and III — 2002–2013 (22 patients, 31% of all cases). In each case histological examination of biopsy specimens was available.

Results: Larynx TB (54.9%) was most common, followed by cervical lymph nodes TB (29.6%) and auris TB (8.5%). In laryngeal TB, glottic region was most often affected (76.9%). Patients with larynx TB were mainly men (87.2%), 10 years older than women in each study period. However, in lymph nodes TB group, women constituted 66.7% of cases and were twice as old as men (64.0 vs. 34.7 yrs). Bacteriological confirmation was made in only one patient.

Conclusions: The number of patients diagnosed in our center declined in the first period of 12 years and remained stable over the last 24 years, as were the common sites of head and neck EPTB (larynx and cervical lymph nodes).

In patients with head and neck TB the biopsy specimens should be examined not only histologically but also for the presence of *Mycobacterium tuberculosis*.

Key words: extrapulmonary tuberculosis, larynx, lymph nodes, neck, auris

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Introduction

In Poland, like in the many countries over the world, the incidence rate of tuberculosis (TB) has been systematically declining during the last decades. World Health Organization (WHO) estimated that in 2013, nine million people developed TB and 1.5 million died of that disease [1]. Looking to the past, in 1978 the incidence rate in Poland was 76.6 per 100,000 population, while in 2013 it was only 18.8 per 100,000 population. But, quite unlike in other countries, extrapulmonary tuberculosis (EPTB) has been diagnosed relatively

seldom [2–6]. National Tuberculosis and Lung Diseases Research Institute, that keeps the TB register, has been gathering epidemiological data on tuberculosis in Poland since 1957. From that time, both forms of tuberculosis, pulmonary and extrapulmonary, have been notified. Reporting on tuberculosis is obligatory in Poland. Pulmonary tuberculosis has been over the years in great predominance in Poland. The complete data on EPTB, according to the WHO classification indicated that in 2013 EPTB accounted for only 5.7% (415 cases) of all 7250 TB cases, so it makes 1.1 EPTB case per 100,000 population [7].

Address for correspondence: Anna Maria Pajor, Department of Otolaryngology, Medical University of Lodz, Poland, e-mail: anna.pajor@umed.lodz.pl

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Studies conducted in developed countries have revealed that, while the overall incidence of TB has been declining, the proportion of EPTB has increased [2, 4]. Also Wang *et al.* [8] in their comprehensive study from Tianjin, the fourth largest city in China with 13 million inhabitants, reported 10% EPTB between 2006 and 2011. Similar result, 13.3%, was noted in Taiwan by Lin and coworkers [9]. However, according to descriptive analysis of EPTB in the European Union and European Economic Area from 2002 to 2011 [10], although the proportion the of EPTB increased from 16.4% to 22.4%, this was mainly due to the decreased notification of pulmonary TB (PTB). It is worth noting that the absolute number of EPTB cases remained stable over the study period. High incidence of EPTB was reported especially in some populations: those immunosuppressed like HIV-positive, treated with monoclonal antibody against TNF, in individuals of foreign origin or with genetic predispositions [11].

Lodz region for years has belonged to the places with the highest TB prevalence in our country. In 2013, our region was fourth among those with the highest incidence rates (22.8 vs. 18.8 overall in Poland) and the first when classified according to mortality rate (2.3 vs. 1.4 overall in Poland), however, for EPTB, the incidence rate was lower than overall in Poland (0.8 vs 1.1). Typical of this region was also a relatively high proportion of infantile TB as well as the high percentage of the most infectious forms of TB (fibrocavernous and TB pneumonia) and relatively few cases with bacteriological confirmation (about 60%) [7].

The aim of our study was to analyze epidemiological and clinical data of patients with extrapulmonary head and neck tuberculosis diagnosed in a single institution, the Otolaryngology Department in Medical University of Lodz between 1978 and 2013.

Material and methods

Seventy one patients, diagnosed with head and neck tuberculosis in the Otolaryngology Department, Medical University of Lodz during 36 years (between 1978 and 2013), were evaluated retrospectively. The mean age of patients was 53.9 ± 17.1 years (range 20–86 yrs), 43 men and 28 women. In all cases of tuberculosis, histological examination of biopsy specimens was available. The TB notification and pulmonary status was checked by National Tuberculosis Register. Patients were divided into three groups, depending on the study period: I — 1978-1989 (30 patients, 42%), II — 1990–2001 (19 patients, 27%), III — 2002–2013 (22 patients, 31% of all cases). Characteristics of the study population are shown in table 1. The study design was approved by the Ethics Committee of the Medical University of Lodz.

In statistical analysis data for age are expressed as means \pm standard deviation (SD). A comparison between mean age of male and female patients in laryngeal and cervical lymph nodes TB was performed using t-Student test. The differences were considered as significant at $p < 0.05$.

Results

Larynx was the most common site of TB involvement — 39 patients (54.9%), followed in the descending order of frequency by cervical lymph nodes — 21 patients (29.6%) and ear — 6 patients (8.5%); other organs were affected very seldom (Table 1).

In laryngeal TB group, 87.2% of patients were men, with mean age 10 years older than women in each study period (Table 2). All patients were referred to hospital with initial diagnosis that

Table 1. Study population — demographic data according to localization of head and neck tuberculosis

TB localization	n (%)	Age (yrs) — mean \pm SD	Sex male/female
Larynx	39 (54.9%)	53.6 ± 14.5	34/5
Lymph nodes	21 (29.6%)	54.2 ± 21.2	7/14
Ear	6 (8.5%)	44.8 ± 12.1	2/4
Pharynx	3 (4.2%)	59.7 ± 30.4	0/3
Salivary glands	1 (1.4%)	47	0/1
Nasal cavity	1 (1.4%)	80	0/1
Total	71 (100%)	53.9 ± 17.1	43/28

Table 2. Patients with laryngeal TB diagnosed in Otolaryngology Department between 1978 and 2013

Total	Laryngeal TB			
	1978–1989 n (%)	1990–2001 n (%)	2002–2013 n (%)	
Patients	39	18	11	10
Sex M	34 (87.2%)	16 (88.9)	10 (90.9)	8 (80)
Sex F	5 (12.8%)	2 (11.1)	1 (9.1)	2 (20)
M/F ratio	6.8	8:1	10:1	4:1
Age groups M/F				
20–39		0/1	1/0	1/1
40–59		10/0	5/1	6/1
≥ 60		6/1	4/0	1/0
Mean age M/F (yrs)	55.2/43.2	56.1/45.5	58.4/48.0	49.6/38.5
p	0.09	0.29	0.63	0.21



Figure 1. Laryngoscopic image — infiltration of both vocal folds (patient M.K. 40 years old)

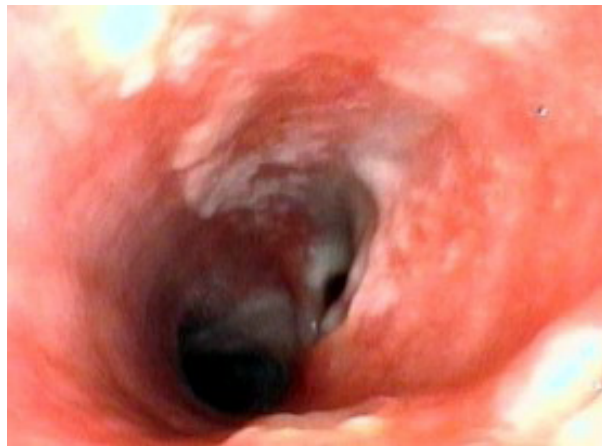


Figure 2. Bronchoscopic image showing redness and purulent sputum in trachea and bronchi (same patient as in Fig. 1)

was different from the final one. Patients with laryngeal TB were mostly suspected of malignancy or nonspecific chronic inflammation. Sometimes other comorbidities masked the main disease and delayed the correct diagnosis. One patient (40 yr. old woman), who presented with dysphonia, but without any visible laryngeal changes, was diagnosed with hypofunctional voice disorder and was rehabilitated by a speech therapist. She complained also of chronic cough, which was attributed to bronchial asthma as she had been treated for 3 years by pulmonologist. Then, after 2 months, the patient developed laryngeal lesions on both vocal folds (Fig. 1) with pulmonary involvement (Fig. 2). In laryngeal EPTB patients, glottic region (vocal folds, false vocal folds, anterior and posterior commissures) was most often affected (30 patients, 76.9%) (Fig. 3),



Figure 3. Laryngoscopic image — infiltration of left vocal fold and anterior commissure (patient J.G. 44 years old)

followed by supraglottic region (epiglottis, aryepiglottic folds, 7 patients), and subglottic region (2 patients).



Figure 4. Cervical lymph nodes tuberculosis with purulent fistula (patient Z.J. 64 years old)

Cervical lymph nodes TB in our patients were initially misdiagnosed as nonspecific lymphadenitis (5 cases), neck cyst (1 case), abscess with skin fistula (3 cases) (Fig. 4) and suspicion of neoplasm metastasis (5 cases). In one patient, neck tuberculosis coincided with laryngeal cancer. Contrary to larynx TB, in cervical lymph nodes TB group, women constituted 66.7% of cases and were on average about twice as old as men (64.0 vs. 34.7 years) (Table 3). Tuberculosis was confirmed bacteriologically in one case.

The aural TB mostly affected middle ear (5 patients), in two of them with involvement of external meatus and only one patient had

external ear TB with preauricular skin fistula. The diagnosis of aural TB typically was delayed as mostly patients with middle ear TB presented with chronic otitis media.

According to the data of National TB Register, from 1994 13 out of 16 (81.3%) subjects with larynx TB had also pulmonary one, in 75% of cases (12/16) it was bacteriologically confirmed. Also in one patient pharynx TB was associated with culture positive pulmonary TB. In the rest of patients: only one case out of nine patients with lymph nodes TB was culture positive for *Mycobacterium tuberculosis*, 3 cases with aural TB and one case with nose TB were culture negative.

Discussion

During the study period, seventy one patients were diagnosed with TB in Otolaryngology Department in Lodz. It is worth noting that none of the patients had been suspected of TB on admission. In patients with laryngeal lesions malignancy was the main initial diagnosis, while subjects with unilateral enlarged cervical lymph nodes were considered to have typical bacterial infection or metastatic disease. However, no effect of antibiotic treatment and development of fistula made mycobacterial etiology more probable. In all our patients, the diagnosis was established by histological examination where typical granuloma formations of epithelioid and giant Langhans cells with caseous necrosis were found.

The most common form of EPTB in our patients, irrespectively of the studied time period, was laryngeal TB. Similarly to the results pre-

Table 3. Patients with cervical lymph nodes TB diagnosed in Otolaryngology Department between 1978 and 2013

Total	Lymph nodes TB			
	1978–1989 n	1990–2001 n	2002–2013 n	
Patients	21	9	6	6
Sex M	7 (33.3%)	3	2	2
Sex F	14 (66.7%)	6	4	4
M/F ratio	0.5	1:2	1:2	1:2
Age groups M/F				
20–39		2/2	2/0	1/0
40–59		1/2	0/0	0/0
≥ 60		0/2	0/4	1/4
Mean age M/F (yrs)	34.7/64.0 *	30.7/53.7	32.0/72.8	43.5/70.8

* $p < 0.001$

sented by other authors, laryngeal TB occurred more often in males [12–14]. The male-to-female ratio of 6.8:1 for the whole period, decreased from 8:1 (1978–1989) to 4:1 at the end of the study. Also the age distribution changed, shifting over 30 years towards the younger age. Between 1978 and 1989 the maximum incidence in men was recorded in 40 to 59 yr. and above 60 yr. age groups, in the last period it was 40 to 59 yr. age group. While in 1978–1989 37.5% of men were above 60 yr. old, in the last period the proportion was only 12.5%. The same trend was observed in females, whose mean age was much lower than that of males. Moreover, the number of patients with laryngeal TB slowly decreased over the 30 years: from 18 at the beginning of the study to 10 in the last period. It should be stressed that since 1994, although the data is incomplete, 81.3% of patients with EPTB had also pulmonary TB, thus should be classified as pulmonary TB. Similar results were reported by Wang *et al.* [15] from Taiwan. In their study, out of 26 patients with laryngeal TB, 24 had concomitant pulmonary TB. In the report by Benwill *et al.* [12] among 126 cases of laryngeal tuberculosis from United States between 1970–2012, as much as 86% of the patients had pulmonary involvement. It is in line with theory of endobronchial mycobacteria spreading from the lungs [16]. Owing to such a way of dissemination, mycobacterial infections affected mainly the posterior part of the larynx due to pooling of infected sputum in recumbent subjects. The isolated laryngeal TB, mostly in epiglottic region, was considered as a result of hematogenous route of infection [12, 17]. According to many reports, especially from the developed countries, the clinical and pathological patterns of laryngeal TB have changed over the last decades. The most common symptoms shifted from odynophagia to hoarseness and dysphonia with minor predilection to upper and posterior part of larynx, lesser degree with pulmonary involvement and more often hypertrophic than ulcerative lesions [13, 14, 17]. In our study, laryngeal TB mainly affected the true vocal folds with still high co-existence with PTB, which is in line with other studies [13–15].

Cervical lymph nodes TB was the second most common EPTB. However, the study conducted in one of the Warsaw Hospital at almost the same time as our study found this form of EPTB the most popular followed by laryngeal TB [18]. In a large study on EPTB conducted in United States, cervical lymphatic TB accounted for more than 60% of lymphatic tuberculosis which was

the most common site of TB [4]. The high prevalence of cervical lymph nodes involvement in EPTB was reported also in other studies [3, 6, 19], in some of them this form of TB affected mainly immigrants of Asian or African origin [3, 19, 20]. In the study from UK, during 10 years out of all 128 head and neck TB cases, 111 patients had cervical TB lymphadenitis, but 89% of them were of Asian origin [3]. Peripheral lymph nodes TB is second most popular EPTB in Poland, also outnumbered only by the pleural TB. Tuberculous lymphadenitis mostly involves cervical nodes, then mediastinal and axillary nodes [20], but in the neck, different groups of nodes may be affected. In Menon *et al.* study [3] anterior triangle nodes (mostly jugulodigastric ones) were involved in 70% and posterior triangle nodes in 21% of cases. Also Oishi *et al.* [6] reported that supraclavicular nodes were affected in 60% while in a large study from India comprising 893 patients, posterior triangle nodes were involved in 43.8 %, followed by upper deep cervical nodes (33.9%) [21].

In our study, the number of diagnosed patients during the study periods was stable and they presented with unilateral cervical or submandibular group of involved lymph nodes. This localization of EPTB was more frequent in females, with the male to female ratio of 1:2, especially during the last two periods. Also, opposite to the subjects with laryngeal TB, the incidence of this form of TB was shifted to the older groups of patients. Such a trend was also noticed in the whole group of subjects with peripheral lymph nodes TB in our country [2, 7]. In all patients, the diagnosis was established by histological examinations of excised lymph nodes. Only in one case the bacteriological confirmation was obtained by culture. In our opinion, this is because, unfortunately, the available specimens had been very rarely tested for *Mycobacterium tuberculosis*. It is much lower than in other studies, although Menon *et al.* [3] also reported that only 39% of surgical biopsy specimens were examined for *M. tuberculosis*.

Only a few patients were diagnosed with pharyngeal TB, nasal cavity and salivary glands TB during the study period. In six subjects aural TB were found, presented mainly as otitis media with recurrent otorrhea and temporal bone destruction. These locations are also rarely found in other studies, and tuberculosis of the middle ear accounts for about 0.04–0.9% of chronic otitis media [22, 23]. It often mimics other chronic infections of middle ear and presents as aural

discharge, with granulation and multiple perforation of tympanic membrane, rapidly progressive hearing loss non-responding to typical antibiotic treatment [23, 24].

It should be stressed that less attention has been paid to EPTB, as that form of TB is not so communicable as PTB with exception of larynx and pharynx TB. That was the reason why EPTB was often perceived as a clinical problem mainly, insignificant to public health. Moreover, bacteriological confirmation of usually paucibacillary EPTB may be a great challenge. As positive culture result which is the reference standard for the diagnosis is time consuming, some genetic methods can be used. Thus, according to the recent WHO guidelines, molecular assay Xpert MTB/RIF with its high sensitivity and specificity also to the extrapulmonary tissue specimens can be implemented for EPTB diagnosis [25, 26].

The limitation of our study was the lack of clinical data as well as follow-up observation. It should be stressed that patients with TB histological diagnosis (of course not according to gold standard) were immediately sent with chest X-rays to the pulmonary department for further examination and treatment. So, their bacteriological sputum examination results and treatment regimes were mostly unknown for us. Moreover, after so many years also patients' records are not available.

Although our study is only a single center analysis, some trends can be noticed. Except for the first study period (1978–1989), the number of hospitalized patients was rather stable as well as the most common EPTB localizations (larynx and peripheral lymph nodes). However, unlike in the general Polish population, EPTB was more often diagnosed in males than females due to high prevalence of laryngeal TB. In the whole study group male to female ratio was lower than that in patients with PTB (1.5:1 vs. > 2:1), but quite similar to the ratio for all patients with EPTB in Poland (1.2:1). If the TB elimination process (1 TB case per 1 million population) should succeed till 2050 according to WHO prognosis, physicians must remember that the white plague, as TB was called in the past, with its old and new faces is still here.

Conclusions

1. The number of patients diagnosed of head and neck TB in Otolaryngology Department declined in the first period of 12 years and remained stable over the last 24 years.

2. The most common form was larynx TB followed by lymph nodes TB.
3. Head and neck TB slowly becomes a forgotten disease, as only one patient had bacteriological confirmation.
4. As patients with head and neck TB are still hospitalized in otolaryngology department, the biopsy specimens should be examined not only histologically but also for the presence of *Mycobacterium tuberculosis*.

Conflict of interest

The authors declare no conflict of interest.

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