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## International Journal of Pediatric Otorhinolaryngology

journal homepage: <http://www.ijporlonline.com/>

# Tuberculous lymphadenitis of the head and neck in Canadian children: Experience from a low-burden region



Jason J. Xu <sup>a,\*,1</sup>, Shazia Peer <sup>a,1</sup>, Blake C. Papsin <sup>a</sup>, Ian Kitai <sup>b,2</sup>, Evan J. Propst <sup>a,2</sup>

<sup>a</sup> Department of Otolaryngology – Head & Neck Surgery, University of Toronto, 190 Elizabeth St., Rm 3S-438, Toronto, ON, M5G 2N2, Canada

<sup>b</sup> Division of Infectious Diseases, Department of Paediatrics, Hospital for Sick Children, Toronto, ON, M5G 1X8, Canada

## ARTICLE INFO

### Article history:

Received 22 May 2016

Received in revised form

24 September 2016

Accepted 26 September 2016

Available online 28 September 2016

### Keywords:

Tuberculosis

Children

Extra-pulmonary

Head and neck

Scrofula

## ABSTRACT

**Background:** Children are more likely than adults to develop extra-pulmonary tuberculosis (EPTB), which often presents as cervical lymphadenopathy. The role of surgery in management is uncertain. We reviewed all head and neck EPTB cases presenting to our tertiary care pediatric institution over a twelve-year period.

**Methods:** All children 18 years of age and younger with EPTB involving the head and neck were included. We recorded clinical data and age at diagnosis, birth country, BCG vaccination status, as well as radiographic, surgical, histological, and microbiological results.

**Results:** All 16 patients presented with cervical lymphadenopathy. Fourteen were born outside of Canada in TB endemic areas and all had foreign-born parents. Diagnosis was confirmed microbiologically from lymph node biopsies in 14 cases. Multi-drug resistant TB was identified in two cases: both had previous excisional node biopsies that had not been cultured. Two patients had culture negative suppuration despite adequate anti-tuberculous treatment that required surgery for cure.

**Conclusion:** Ongoing suppuration despite appropriate drug therapy is seen in a minority of patients. We found that excisional lymph node biopsy of diseased cervical lymph nodes is diagnostic, and also therapeutic in some cases with ongoing suppuration despite appropriate drug therapy. Mycobacterial culture of lymph nodes is important for diagnosis and determination of drug resistance patterns.

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## 1. Introduction

Tuberculosis (TB) is the second most common infectious cause of death worldwide [1]. In Canada, the majority of reported cases occur in immigrants and refugees born in high TB-incident areas [2]. Tuberculosis in children is often a sentinel event implying transmission of infection from an adult with pulmonary TB [2,3].

Children have higher rates of extra-pulmonary TB (EPTB) than adults [4]. Most cases manifest as lymphadenopathy, which is a nonspecific finding. This makes diagnosis challenging and often delayed [5]. Cervical lymph nodes are most commonly involved and can be the sole manifestation of tuberculosis in 25–35% of cases [5]. Persistent lymphadenitis may result in abscess and chronic sinus formation – termed scrofula – and may persist despite appropriate

anti-tuberculous treatment [6]. In adult patients, some authorities recommend excisional surgery as the primary approach for diagnosis and cure [6].

In low burden countries, clinicians should be cognizant of this rare disease to ensure prompt diagnosis and optimal management [7]. There are many published series of adults with head and neck TB from TB-endemic areas [8–11], but there is little data about this condition in children from low-burden countries such as Canada, where the incidence of TB is less than 5 per 100,000 [12]. In contrast, clinicians are more likely to encounter nontuberculous mycobacteria lymphadenitis in the pediatric population, which has an incidence of 107 per 100,000 [13]. The aim of this study was to review our experience with TB of the head and neck at a large pediatric tertiary-care center in a low-burden region to learn more about this rare condition in order to improve diagnosis and treatment.

## 2. Methods

We reviewed all patients with TB younger than 18 years of age

\* Corresponding author.

E-mail addresses: [jasonji.xu@mail.utoronto.ca](mailto:jasonji.xu@mail.utoronto.ca) (J.J. Xu), [ian.kitai@sickkids.ca](mailto:ian.kitai@sickkids.ca) (I. Kitai).

<sup>1</sup> Both authors contributed equally.

<sup>2</sup> Both authors contributed equally.

managed by the Tuberculosis program at The Hospital for Sick Children in Toronto, Canada, from January 1, 2002 to June 1, 2014. Inclusion criteria were the presence of significant cervical lymphadenopathy or other disease of the head and neck, and a positive culture or Nucleic Acid Amplification Test (NAAT) for *Mycobacterium tuberculosis* from any site. Patient information was obtained from patient records and a prospectively populated database obtained at entry to our TB clinic. We recorded: 1) date of birth; 2) age at diagnosis; 3) place of birth of patient and parents; 4) duration of time living in Canada prior to diagnosis; 5) BCG (Bacillus Calmette–Guérin) vaccination status; 6) chest x-ray (CXR) findings; 7) tuberculin skin test (TST) results; 8) surgical, histopathological and microbiological reports. This study was approved by The Hospital for Sick Children Research Ethics Board.

### 3. Results

Sixteen cases of EPTB of the head and neck were included. All patients presented with symptomatic cervical lymphadenopathy and one child presented with concurrent meningitis. All children were otherwise healthy and none had known exposure to TB. HIV (human immunodeficiency virus) screening was performed for 10 children and was negative in all cases. No cases of sinus, ear, or laryngeal TB were identified in our review.

#### 3.1. Demographics

The mean (standard deviation, SD) age at time of diagnosis was 13.4 (4.0) years (range 1–17 years). Fifteen (94%) children were ten years of age or older. Fourteen (88%) children were born outside of Canada. Six (38%) of these were born in South Asia, 4 (25%) in Africa, and 4 (25%) in East Asia. The mean (SD) duration in Canada prior to diagnosis was 4.46 (3.4) years (range 0.1–10 years). Nine children (56%) lived in Canada for 5 years or less before being diagnosed. Of the 2 (12%) Canadian-born children, 1 was diagnosed at 1 year of age and the other at 17 years of age. The one-year-old child presented with meningitis in addition to cervical lymphadenopathy. Both had parents born in TB-endemic countries. BCG vaccination was documented in nine (56%) children.

#### 3.2. Diagnostic tests

Results of diagnostic testing are detailed in Table 1. Abnormal chest radiography was present in 7 children: 4 with mediastinal or hilar lymphadenopathy, 2 with pulmonary infiltrates, and 1 with a small pulmonary nodule. Interferon-gamma release assays are not routinely used at our institution and were not used for any case in this series. Spoligotyping is performed but the results are collected for a provincial database and were not available for this review.

#### 3.3. Biopsy results

Tissue biopsies were obtained from either cervical (94%) or parotid lymph nodes (6%). Twelve children (75%) had excisional biopsies, 3 (19%) had incisional biopsies, and 1 (6%) had a core

needle biopsy. The type of biopsy performed was determined by the otolaryngologist-head & neck surgeon or general surgeon involved. Biopsy results are detailed in Table 2.

Two patients had nodes that were culture negative but showed histologic evidence of granulomatous inflammation. For one of these patients, TB was diagnosed based on a concurrent positive NAAT of induced sputum. In the other patient, culture-positive drug sensitive TB had been diagnosed 2 years previously and the patient was treated with 9 months of anti-TB therapy at that time; the lymphadenitis was thought to be a late granulomatous reaction.

Twelve of the 14 (86%) culture-positive specimens were sensitive to ethambutol, isoniazid (INH), rifampicin and pyrazinamide. Two (12%) were multi-drug resistant (MDR), implying resistance to both INH and rifampicin (Table 3). Both of these patients had prior excision of cervical nodes at community hospitals with negative TB cultures, but received empirical TB treatment based on histology results and strongly positive TST. They both were well following treatment for approximately 1 year before presenting to our institution with recurrent lymphadenopathy. Subsequent excisional biopsy cultures were both positive for the MDR organism.

#### 3.4. Treatment and follow-up

Fifteen out of the 16 patients received anti-tuberculous treatment. The one patient thought to have had a late granulomatous reaction had no further therapy after lymph node biopsy. One patient emigrated 3 months after starting treatment, with appropriate arrangements made for ongoing care. For the remaining patients, the mean (SD) follow-up duration was 24.4 (13.7) months (range 11–53 months). There was no recurrence of disease in any patients including those with MDR disease.

All 12 patients with a positive node culture for drug sensitive TB and the patient with a negative node culture but NAAT-positive sputum were treated with a combination of ethambutol, INH, rifampicin and pyrazinamide based on standard regimens. Treatment was directly observed by municipal public health departments. Excluding the one patient who emigrated, the treatment duration for the remaining cases was typically 12 months (mean (SD) = 12.5 (4.1)), however duration ranged from 6 to 24 months. One patient who received a total of 24 months of treatment had ongoing suppuration that developed 1 year after initiating treatment. Four of these 13 patients (31%) experienced significant medical adverse effects (3 hepatotoxicity, 2 gastrointestinal intolerance) that required temporary cessation of medication or admission to hospital. Therapy was successfully completed in all.

The two patients with MDR TB received over 18 months of therapy (Table 3), which included a four-month course of amikacin, and a fluoroquinolone (either moxifloxacin or ofloxacin). One child experienced significant vestibulotoxicity secondary to amikacin, which was replaced with cycloserine and clofazamine. The same child also developed hypothyroidism and iron-deficiency anemia. Both MDR cases also experienced significant gastrointestinal intolerance.

Two children with drug-sensitive TB (13%) developed a draining

**Table 1**  
Ancillary test results.

Ancillary test	N (percentage)
Positive tuberculin skin test (TST)	10/10 (100%)
Abnormal chest x-ray	7/16 (44%)
Positive sputum culture	6/10 (60%)
Positive gastric aspirate culture	5/6 (83%)
HIV test	0/10 (0%)

**Table 2**  
Lymph node biopsy results.

Biopsy results	N (percentage)
Histopathology: necrotizing granulomatous inflammation	14/14 (100%)
Positive node culture	14/16 (87.5%)
Positive acid-fast bacillus stain	3/13 (23.1%)
Positive nucleic acid amplification test (NAAT)	7/8 (87.5%)
MDR TB	2/16 (12.5%)

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