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MAIN ARTICLE

Head and neck tuberculosis in KwaZulu-Natal, South Africa

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Abstract

Objective: To describe the clinical features of head and neck tuberculosis in KwaZulu-Natal, South Africa.

Study design: Retrospective, observational study.

Method: The study included 358 patients who received a histopathologically and/or microbiologically confirmed diagnosis of tuberculosis in the head and neck region between 1 January 2007 and 31 December 2011.

Results: A total of 358 new cases of head and neck tuberculosis were identified during the study period, involving 196 males (54.7 per cent) and 162 females (45.3 per cent). These patients had a median age of 31 years (range, 3 months to 83 years). Testing for human immunodeficiency virus was positive in 233 (65.1 per cent) and negative in 125 (34.9 per cent). Right-sided cervical lymphadenitis was the commonest form of presentation of head and neck tuberculosis.

Conclusion: In this study, right-sided cervical lymphadenopathy was the commonest presentation of head and neck tuberculosis in both human immunodeficiency virus infected and non-infected individuals. Head and neck tuberculosis should not be excluded solely based on a normal chest X-ray, nor on the absence of constitutional symptoms.

Key words: Tuberculosis; Lymph Nodes; Lymphadenitis; Retropharyngeal Abscess; Human Immunodeficiency Virus

Introduction

Tuberculosis (TB) is one of the oldest diseases known to mankind, and still remains the leading single infectious cause of death among adults.[1] One in every three people in the world is believed to be infected with *Mycobacterium tuberculosis*[1,2] and/or to carry the risk of developing the disease.[2,3]

More than 90 per cent of all TB cases and deaths occur in developing countries,[4,5] where TB is currently responsible for 20 per cent of all deaths in adults. Countries with a high prevalence of human immunodeficiency virus (HIV), particularly those in sub-Saharan Africa, have witnessed a great increase in the number of TB cases, with reported incidence rates increasing two- or three-fold in the 1990s.[5]

The incidence of head and neck TB has increased markedly in association with HIV infection, with 25 per cent of HIV-positive cases occurring without pulmonary involvement or constitutional symptoms.[5]

Although TB can affect any organ, only one of every five cases of TB is extrapulmonary.[6] Yang *et al.* noted that approximately half of patients co-infected with both HIV and TB have extrapulmonary involvement, and this figure can reach 80 per cent if there is severe immunosuppression.[7] Patients with HIV infection often present with persistent generalised lymphadenopathy (also known as reactive nodes), mainly in the cervical region.[7] The features distinguishing adenopathy secondary to TB from adenopathy related to HIV are not clear. It is in the setting of isolated head and neck involvement that the diagnosis of TB is most difficult.

In head and neck TB patients, the leading manifestation of TB is cervical lymphadenopathy, which accounts for 95 per cent of presentations.[8] Cervical lymphadenopathy is the most frequent type of tuberculous lymphadenopathy, constituting 60–80 per cent of all such cases.[9,10] Causes of tuberculous lymphadenopathy include *M tuberculosis*, *M bovis* and other non-tuberculous mycobacteria.

Tuberculous lymphadenopathy has a specific pattern.[11] Affected lymph nodes are usually multiple, unilateral, predominantly involving deep channels, and generally 1.5 to 5 cm in size.[11,12] In 20 per cent of cases, they are bilateral, non-tender and have discharging sinuses.[13] Cleary and Batsakis reported that cervical lymphadenopathy due to non-tuberculous

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mycobacteria most often occurs without general symptoms, pulmonary involvement or skin inflammation around the lymphadenopathy; furthermore, most cases have unilateral involvement and a weakly positive Mantoux reaction.[13]

Cervical lymphadenitis often involves the supraclavicular (posterior triangle) region and is frequently associated with axillary lymphadenitis. Infectious cervical lymphadenopathy may be due to mycobacteria other than *M tuberculosis*, and such bacteria can only be identified by culture in an appropriate medium.[14] Hence, fine needle aspiration cytology (FNAC) with standard mycobacterial culture may not be helpful in all patients with cervical lymphadenopathy. Furthermore, different mycobacteria may have different clinical presentations: constitutional symptoms, such as fever, weight loss, fatigue, anorexia and night sweats, only occur in 15–20 per cent of TB cases.[15,16]

The present study was conducted to describe the clinical features of head and neck TB in KwaZulu-Natal, South Africa, and to compare our data with internationally published literature. The study also compared the clinical features of isolated head and neck TB in patients with and without HIV disease.

Materials and methods

We retrospectively reviewed all 358 cases of head and neck TB which had received a histopathologically and/or microbiologically confirmed diagnosis within an ENT department in Durban, KwaZulu-Natal between 1 January 2007 and 31 December 2011. The study was performed in three tertiary care hospitals in Durban, namely the Inkosi Albert Luthuli Central Hospital, the King Edward VIII Hospital and the Addington Hospital. Patients' head and neck TB diagnoses were confirmed by referring to local radiology, histopathology, virology and microbiology databases.

The following was also extracted from hospital records: demographic information (i.e. age, ethnicity and gender), clinical information (i.e. HIV status, presenting symptoms and mode of disease presentation) and diagnostic information (e.g. chest X-ray (CXR), FNAC and biopsy results).

Characteristic features of head and neck TB were documented and compared with the international literature. The study also compared the clinical features of head and neck TB in patients with and without HIV infection.

Full ethical approval was obtained from the KwaZulu-Natal Department of Health and the University of KwaZulu-Natal Bio Research Ethics and Medical Law Department, prior to commencement of the study.

Statistics

Recorded data were analysed using the SPSS 21 software program (SPSS Ltd, Chicago, Illinois, USA). Descriptive statistics such as frequencies, percentages, means and standard deviations were used to summarise the data. The Pearson chi-square test or Fisher's exact test was used to test for association between HIV status and TB presentation site. The Kruskal–Wallis one-way analysis of variance test was used to test the relationship between age and TB presentation site. The level of significance was set at 0.05.

Results

Gender

There were 358 new cases of head and neck TB diagnosed and notified by ENT departments in Durban, KwaZulu-Natal, over the 5-year study period. Patients comprised 196 males (54.7 per cent) and 162 females (45.3 per cent), giving a male to female ratio of 1.2:1. The median patient age was 31 years (range, 3 months to 83 years).

Ethnicity

The patients' ethnic origin was mainly black ($n = 345$; 96.4 per cent), followed by Indian (9; 2.5 per cent), white (2; 0.6 per cent) and coloured (2; 0.6 per cent).

Human immunodeficiency virus status

Of the 358 study patients, 233 (65.1 per cent) tested positive for HIV and 125 (34.9 per cent) tested negative.

Sites involved

The distribution of head and neck TB sites is shown in Table I. The leading manifestation of head and neck TB was cervical lymphadenopathy, found in 302 patients (84.4 per cent), followed by TB of the ear (15 patients, 4.2 per cent), TB of the larynx (11 patients, 3.1 per cent), nasal TB (9 patients, 2.6 per cent) and TB of the tongue (3 patients, 0.8 per cent). Eighteen patients (5 per cent) presented with head and neck abscesses.

Cervical lymphadenopathy and laterality

Of the 302 patients with cervical lymphadenopathy, 177 (58.6 per cent) had right-sided lymphadenopathy,

TABLE I
DISTRIBUTION OF HEAD AND NECK TUBERCULOSIS

Site	Patients	
	n	%
Nose	9	2.6
Ear	15	4.2
Abscess		
– Neck	6	1.7
– Retropharyngeal	3	0.8
– Submandibular	4	1.1
– Parotid	3	0.8
– Thyroid	1	0.3
– Peri-tonsillar	1	0.3
Tongue	3	0.8
Larynx	11	3.1
Lymph nodes	302	84.4
Total	358	100

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73 (24.2 per cent) had left-sided lymphadenopathy and 52 (17.2 per cent) had bilateral cervical lymphadenopathy. This difference was statistically significant ($p < 0.001$). No patient had midline lymphadenopathy (Figure 1).

Human immunodeficiency virus and cervical lymphadenopathy

Of those patients diagnosed with cervical lymphadenopathy, 191 (63.2 per cent) tested HIV-positive and 111 (36.8 per cent) tested HIV-negative; this difference was not statistically significant ($p = 0.090$). Cervical lymphadenopathy was seen in 168 males (55.6 per cent) and 134 females (44.4 per cent); this difference was not statistically significant ($p = 0.437$).

Chest X-ray and cervical lymphadenopathy

In patients diagnosed with head and neck TB, the CXR was noted to be normal in 222 (62.0 per cent) and suspicious in 136 (38.0 per cent); in patients with cervical lymphadenopathy, the CXR was noted to be normal in 222 (73.5 per cent) and suspicious in 80 (26.5 per cent) (Figure 2). This difference between the two patient groups, regarding the proportion of normal versus suspicious CXRs, was statistically significant ($p < 0.001$).

Diagnostic method used

Fine needle aspiration biopsy was the most commonly used diagnostic method for patients with cervical lymphadenopathy. Of the 302 such patients, 277 (91.7 per cent) demonstrated positive results (Table II). Cervical lymphadenopathy patients were also diagnosed using core biopsy (23 patients, 7.6 per cent) and excisional biopsy (2 patients, 0.7 per cent). This difference in the prevalence of diagnostic methods was statistically significant ($p < 0.001$).

Annual tuberculosis diagnoses

The number of head and neck TB diagnoses increased year on year throughout the study period, with 54 of the total 358 patients (15.1 per cent) diagnosed in 2007, 62 (17.3 per cent) in 2008, 66 (18.4 per cent) in 2009, 79 (22.1 per cent) in 2010 and 97 (27.1 per cent) in 2011 (Figure 3).

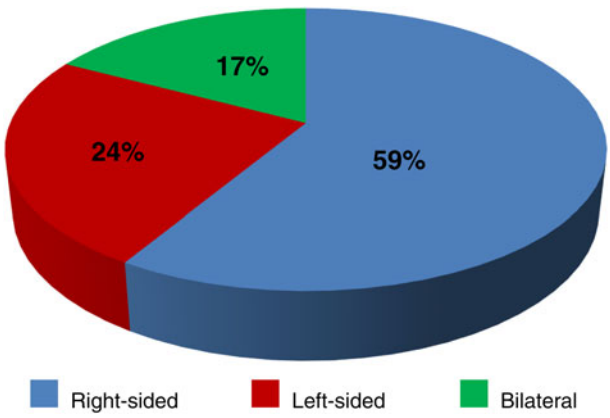

FIG. 1
Distribution of cervical lymphadenopathy.

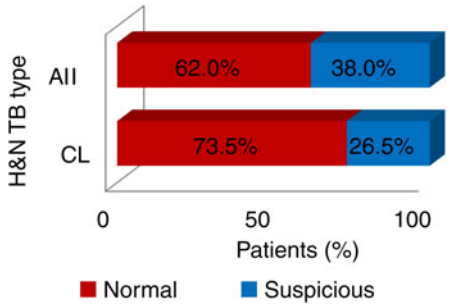

FIG. 2
Chest X-ray findings in head and neck tuberculosis (H&N TB) cases. CL = cervical lymphadenopathy

Discussion

Approximately 50 per cent of TB cases in developed countries have an extrapulmonary presentation.[17] Tuberculous lymphadenopathy is the most frequent presentation in the head and neck region.[17] The source of cervical lymph node infection is controversial. The initial tubercular infection is thought to start in the tonsillar crypts and then spread to the cervical lymph nodes.[17] Lymph node involvement typically occurs six to nine months after the initial infection. Cervical tuberculous lymphadenopathy, especially in its isolated form, needs to be differentiated from lymphadenopathy due to other causes. These include: reactive hyperplasia; bacterial, viral and fungal infection; toxoplasmosis; sarcoidosis; Hodgkin's disease and non-Hodgkin's lymphomas, as well as other primary disease of the lymphoid and reticuloendothelial tissue; metastatic carcinoma; cat scratch disease; and Kawasaki disease.[17,18]

In the earliest stage of the disease, tuberculous lymph nodes have been described as rubbery, non-tender, non-fluctuant, affecting deep channels, often unilateral, smaller than 2 cm, and well circumscribed with non-erythematous overlying skin.[18] With time, they can gradually harden, become multiple and increase in size. Cervical lymphadenopathy has been noted to usually involve the right side of the neck. The present study had similar findings. Caseation of the lymph nodes occurs during the advanced stage of the disease, with subsequent formation of fistulae to the skin surface.[18]

TABLE II
CERVICAL LYMPHADENOPATHY*: DIAGNOSTIC METHODS

Method	+ve result (pts; % (*n*))	*p*
Fine needle aspiration	91.7 (277)	<0.001
Core biopsy	7.6 (23)	
Excision biopsy	0.7 (2)	

*n = 302 patients (pts). +ve = positive

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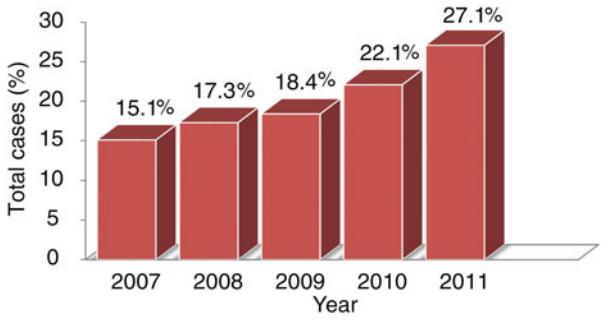

FIG. 3
Percentage of the total 358 newly diagnosed head and neck tuberculosis cases presenting in each year of the study period.

The radiological features of tuberculous lymphadenitis, as seen on computed tomography scans, include the presence of necrosis with rim enhancement, confluent and matted lymph nodes, and calcification. In the present study, the majority of patients with cervical lymphadenopathy (73.5 per cent) had a normal CXR. Thus, a normal CXR in the presence of cervical lymphadenopathy cannot be used to exclude extrapulmonary TB.

Gandhi *et al.* reported an association between tuberculous lymphadenitis and HIV infection, solid organ transplantation and/or immunosuppressive therapy. This association was thought to be due to failure of the immune response to contain *M tuberculosis,* thereby facilitating early haematogenous dissemination and subsequent spread to single or multiple non-pulmonary sites.[19] In the present study, there was no statistically significant association between cervical lymphadenopathy and HIV infection.

Fine needle aspiration cytology is the diagnostic test most commonly used to evaluate patients with neck masses. Liatjos *et al.* observed three patterns of tuberculous lymphadenitis on cytological examination: granulomatous lymphadenitis, necrotising granulomatous lymphadenitis and necrotising lymphadenitis.[20] Satyanarayana *et al.* described a fourth pattern seen in tuberculous lymphadenitis, termed a reactive pattern with acid-fast bacilli positivity.[21] In their study of HIV-infected and non-infected children, Jeena *et al.* found no difference regarding tuberculous lymphadenitis biopsy findings.[22] In HIV-positive patients with head and neck TB, an absence of constitutional symptoms of TB often delays the diagnosis; patients are often incorrectly diagnosed as having persistent generalised lymphadenopathy of HIV.

The advantages of FNAC include low cost, time savings and fewer complications (compared with other diagnostic methods such as core biopsy and excisional biopsy). However, its disadvantage is that it can theoretically seed the infection into the skin.

Before HIV patients are diagnosed with persistent generalised lymphadenopathy, FNAC (at least) must be done to exclude head and neck TB. In cases where the FNAC result is ambiguous, lymph node biopsy provides definitive proof. Node excision may also physically decrease the mycobacterial load. Excisional biopsy is generally avoided due to the higher risk of surgical complications (e.g. nerve injury and fistula formation).

In the international literature, laryngeal TB is the second most common type of extrapulmonary TB.[23] In the present study, laryngeal TB was the third commonest form of presentation (after cervical lymphadenopathy and ear TB). Laryngeal TB is classified into one of four subtypes: granulomatous, polypoid, ulcerative and non-specific pattern.[23] Granulomatous lesions are more common in patients with pulmonary TB.[24] Laryngeal TB has been reported to coexist with active pulmonary TB in 50 per cent of cases.[24–26] This may explain why we encountered fewer patients with laryngeal TB, as most of our patients (62.0 per cent) had no radiological signs of pulmonary TB. Laryngeal involvement affects the posterior portion of the true vocal folds, the arytenoids and the inter-arytenoid space.[26] The predominant posterior location of TB in the larynx is probably due to spread from lung lesions via the accumulation of respiratory secretions in the posterior larynx when the patient is in the decubitus position.[26] Patients with laryngeal TB often present with dysphonia, and less frequently with cough and odynophagia, and are highly contagious.[27]

Oropharyngeal TB is the third most common form of extrapulmonary TB according to the international literature.[28] However, in the present study oropharyngeal TB was rare, and retropharyngeal TB accounted for only 0.8 per cent of head and neck TB presentations. Oropharyngeal TB usually occurs in younger patients with cervical tuberculous lymphadenopathy, appearing as a painless lesion within the oral cavity.[28,29] Secondary oropharyngeal TB is due to auto-inoculation from the sputum in patients with pulmonary TB.[29] Oral TB manifests itself as single or multiple lesions in the form of nodules, superficial ulcers, indurated plaques or sluggishly progressive lesions which can appear as fissures, blisters or masses.[30]

- **Cervical lymphadenopathy is the commonest presentation of head and neck tuberculosis (TB)**
- **It is usually right-sided**
- **Patients with tuberculous cervical lymphadenopathy often have a normal chest X-ray, and may have no constitutional symptoms**
- **Human immunodeficiency virus (HIV) positive patients with head and neck TB may have no constitutional symptoms, delaying correct diagnosis**
- **HIV-positive patients should undergo fine needle aspiration biopsy to exclude head and neck TB, before persistent generalised lymphadenopathy is diagnosed**

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Tuberculosis of the ear usually manifests as chronic, painless otorrhoea.[31] It may also present with a polypoid lesion within the external auditory canal or middle ear, and sometimes with multiple perforations of the tympanic membrane.[31] As it progresses, otic TB often produces irreversible hearing loss, and if it extends to the mastoid it may induce facial paralysis and erosion of the temporal bone.[31]

Nasal TB is also very rare. It can manifest as nasal obstruction, chronic rhinorrhoea, or ulcerative or excretive lesions of the nasal mucosa.[32] Butt *et al.* described the clinical features of nasal TB as being predominantly found amongst elderly women.[33] The most commonly affected site is the cartilaginous septum, followed by the inferior turbinates, while the most common presenting symptoms are nasal obstruction followed by nasal discharge.[33] Very rarely, nasal TB can also affect the paranasal sinuses, especially the maxillary sinuses, and manifest as chronic maxillary sinusitis.

Although various authors[28–32] have noted a steady decline in head and neck TB, the present study found a year on year increase in the number of new cases identified.

Conclusion

In this study, right-sided cervical lymphadenopathy was the commonest presentation of head and neck TB in both HIV-infected and non-infected individuals. Head and neck TB should not to be excluded based solely on a normal CXR, nor on the absence of constitutional symptoms. Fine needle aspiration remains the 'gold standard' when diagnosing tuberculous lymphadenopathy.

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