CASE REPORT

Diversities in presentations of extrapulmonary tuberculosis

Shiba Neelakantan,¹ Preeti P Nair,¹ Roby V Emmanuel,² Kavita Agrawal¹¹Department of Oral Medicine and Radiology, People's College of Dental Sciences, Bhopal, Madhya Pradesh, India²Department of Periodontology and Oral Implantology, People's College of Dental Sciences, Madhya Pradesh, Bhopal, India**Correspondence to**
Professor Preeti P Nair,
shajihoss@gmail.com**SUMMARY**

The incidence of extrapulmonary tuberculosis (EPTB) has been increasing worldwide over the last few years. Tuberculous lymphadenitis is the most common form of the disease and is reported to occur in 25–60% of all EPTB cases. It is commonly seen in the cervical lymph nodes, but may also be in the larynx, pharynx, parotid and rarely, in the sinuses and petrous bone. The posterior triangle, supraclavicular and jugular nodes are most frequently affected. They are usually unilateral, although diffuse adenopathy may occur. TB involving cervical lymph nodes represents 50% of extrapulmonary TB. A series of six cases of tuberculous lymphadenitis with varying clinical features is documented here to alert one of its prevalence in developing countries.

BACKGROUND

Tuberculosis (TB) is still a major public health problem with a high death rate in developing countries. TB lymphadenitis ranks high in the differential diagnosis of cervicofacial lymphadenitis even in the presence of obvious odontogenic source of infection, thus posing a challenge to the oral medicine specialist. All the reported patients belonged to an urban setup and high socioeconomic status. Factors like closed crowded living conditions, exposure in family, fever, loss of appetite and weight were not present.

CASE PRESENTATION**Case report 1**

A 12-year-old man reported with a chief complaint of swelling in lower left jaw since 7 months. Three months previously he underwent incision and drainage and swelling partly regressed, but slowly reappeared and progressed to the current size. At the time of presentation there was pus and blood discharge from the swelling.

Extraoral examination showed multiple draining sinuses over the lower border of the mandible in relation to the left submandibular lymph node. Surrounding skin was erythematous at some areas and wrinkled along with scab formation. Upon palpation there was no local rise in temperature, the area was soft and tender (figure 1). Two right submandibular lymph nodes were palpable, soft, tender and mobile.

Intraoral examination revealed that there was a root piece of the lower left deciduous canine (figure 2). Patient also had mild degree of generalised gingivitis.

Figure 1 Swelling with pus discharge on the lower left side of face.

Case report 2

A 15-year-old woman presented with a chief complaint of swelling on left lower side of her face since 7 months. The patient had a history of frequent vomiting, evening rise in temperature and weight loss. She also complained of watery discharge mixed with pus from left ear since 2 years. Seven months back she noticed a small swelling 1 cm below the left angle of mandible, which slowly progressed to the current size. Examination revealed an enlarged left superficial cervical lymph node which was irregular in shape measuring about 1×0.5 cm, with no change of colour of overlying skin. On palpation it was soft, tender, mobile and fluctuant (figure 3).

Intraoral examination revealed deep caries with pulpal involvement on the lower right first molar and severely hypoplastic lower left first molar with destruction of crown involving pulp and was tender on percussion (figure 4).

Figure 2 Root stumps of 73.

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Figure 3 Swelling below left angle of mandible.

Case report 3

A 62-year-old woman presented with a chief complaint of small swelling in front of her left ear for 15 days. The swelling was sudden in onset and has remained without any change. She did not have any difficulty in opening the mouth or while chewing food. The swelling did not change in its size when she chewed food.

Upon clinical examination single left preauricular lymph node was enlarged, oval in shape, 2×1 cm in size, with no secondary changes on the overlying skin. On palpation the lymph node was non-tender, soft and mobile with no local rise in temperature (figure 5).

Case report 4

A 22-year-old man patient reported with a chief complaint of a swelling on the preauricular area since 5 days. The swelling was sudden in onset and has remained without any change. He did not have any difficulty in opening the mouth or while chewing food. The swelling did not change in its size when he chewed food. There was no associated fever or weight loss.

Upon clinical examination single left preauricular lymph node was enlarged, round in shape, 2×2 cm in size, with no secondary changes on the overlying skin. On palpation the lymph node was non-tender, soft and mobile with no local rise in temperature.

Case reports 5 and 6

Cases 5 and 6 were very similar in their age, sex and professions (healthcare workers). In clinical presentations too they were

Figure 4 Hypoplastic 36 and grossly decayed 46.

Figure 5 Swelling in left preauricular region.

alike in terms of sudden onset of swelling in the cervical lymph nodes and with no other associated features. Remarkably both were in good health and were well built and well nourished.

INVESTIGATIONS

Blood reports confirmed that none of the patients were suffering from any haematological abnormality. In Case 1, pus culture and sensitivity tests showed that the cultured microbes were sensitive to cephalothin, vancomycin, erythromycin, clindamycin and resistant to penicillin G and cloxacillin. An orthopantomograph (figure 6) showed that the root stumps of 73 and 33 were impacted.

Case 2 intraoral periapical radiograph (figure 7) of 36 showed coronal radiolucency involving enamel, dentin and

Figure 6 Orthopantomograph showing a horizontally impacted canine but no signs of odontogenic infection.

Figure 7 Intra oral periapical radiograph of 36 showing well-defined periapical radiolucency with a radioopaque margin with furcation involvement.

pulp. There was radiolucency involving furcation area, extending periapically. Chest radiograph (figure 8) revealed no pathology. Pus culture and sensitivity tests showed that microorganisms were sensitive to ciprofloxacin, gentamycin, amikacin, cefotaxime, piperacillin, ceftriaxone, ceftazidime and polymyxin B.

Acid-fast bacilli test for sputum was negative for all six cases. Fine needle aspiration cytology (FNAC) of the lymph nodes was done in all the six cases. The cytospin revealed many epithelioid granulomas and area of caseous necrosis in the background of foamy macrophages and lymphocytes which were suggestive of TB lymphadenitis for all cases (figure 9).

DIFFERENTIAL DIAGNOSIS

For case 1 differential diagnoses of chronic periapical abscess, submandibular space infection and chronic osteomyelitis were given.

Figure 8 Chest Radiograph showing no abnormality.

Figure 9 Photomicrograph of fine needle aspiration cytology smear showing both caseous necrosis and epithelioid cell granuloma (H&E, ×1000).

For case 2 differential diagnoses of chronic periapical abscess, submandibular space infection and non-Hodgkin's lymphoma were given.

For Cases 3–6 benign lymphoid hyperplasia, adenoma, lipoma sebaceous cyst and mucoepidermoid carcinoma were given as differential diagnoses.

TREATMENT

All the patients were given directly observed treatment, short-course (DOTS) for 6 months where the standardised treatment regimen was directly observed by a healthcare worker. For the first 2 months they were given pyrazinamide, isoniazid and rifampicin thrice daily. For the next 4 months they were given isoniazid and rifampicin thrice daily.

OUTCOME AND FOLLOW-UP

All these patients were followed up for a period of 6 months and there was complete regression of the swelling without any other complications.

DISCUSSION

In India, tubercular lymphadenitis is one of the most common forms of extrapulmonary tuberculosis (EPTB).¹ Among communicable diseases worldwide, TB is the second leading cause of death after HIV/AIDS. TB kills nearly two million people per year, most of whom live in the lowest-income countries.² Head and neck involvement represents 12% of patients with EPTB.³

The most frequent site of EPTB in children aged 15 years and lesser was the lymph nodes, accounting for the majority (52.9%) of cases in children.² Tuberculous lymphadenitis is the common form of EPTB occurring in close to 10% of children presenting with TB in endemic areas.⁴

In the neck the 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. They are initially non-fluctuant: lymph node suppuration and spontaneous drainage may occur after caseation and necrosis development. Fever, weight loss, fatigue and malaise are usually absent or minimal. Lymph node involvement typically occurs between 6 and 9 months following the initial infection.⁵

The clinical manifestations of tuberculous lymphadenitis are thought to be a local manifestation of a systemic disease.⁶ Apart

from the bacterial factors, the clinical features are influenced by host factors such as age, sex, nutrition, genetics, family history of contact and the immune competence of the patient. This leads to varied clinical and morphological presentations. Various studies have shown that more women than men have tuberculous lymphadenitis.⁷⁻⁹ Constitutional symptoms are more common in men than in women. Although these symptoms are similar to those described in pulmonary TB,¹⁰ the pattern of symptoms is different, and as expected, the traditional markers of TB, such as cough or cough with expectoration, are rare in tuberculous lymphadenitis.¹¹⁻¹² Women usually have a quiescent presentation or report multiple, vague and atypical constitutional symptoms. These observations reflect biological, hormonal, social, environmental or behavioural differences between men and women. Biologically there is a fundamental difference in the immune systems of men and women.¹³ Ramanathan *et al*¹⁴ 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 socio-economic and nutritional status, which can affect the immune response to the disease.¹¹⁻¹⁴⁻¹⁵ 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.¹⁰⁻¹²⁻¹⁶ There are also differences between men and women with regard to the clinical signs of the disease. Men more frequently have enlarged posterior cervical, submandibular, bilateral and matted lymph nodes, while women usually have an enlarged unilateral, single supraclavicular node. Dvorski¹⁷ noted similar findings in his study.¹⁷ The group of nodes affected in peripheral lymphadenitis depends on the location of the initial focus of infection, as it is considered part of the primary complex and a manifestation of early postprimary TB.¹⁸ The triad of multiplicity, matting and caseation helps in reaching a diagnosis of tuberculous lymphadenitis in many cases, but it is not the most common presentation in women.

Historically, lymph node tuberculosis (LNTB) has been called the 'King's evil' referring to the divine benediction which was presumed to be the treatment for it. It was also referred to as 'scrofula' meaning 'glandular swelling' (Latin) and 'full-necked sow' (French).¹⁹ Peripheral lymph nodes are most often affected and cervical involvement is the highest.¹²⁻²⁰ In India and other developing countries LNTB continues to be the most common form of EPTB and lymphadenitis because non-tuberculous mycobacteria (NTM) is seldom seen.²¹⁻²³ On the other hand, NTM are the most common cause of lymphadenopathy in the developed world.²⁴⁻²⁵ In patients with mycobacterial lymphadenitis in the USA, *Mycobacterium tuberculosis* has been the most common pathogen among adults whereas NTM were the most common pathogens among children.²⁶ LNTB often affects children and young adults. Female predilection has been reported in some studies. In HIV-negative patients, isolated cervical lymphadenopathy is most often seen in about two-thirds of the patients.²⁷ Bem *et al.*²⁸ observed that among HIV-negative as well as HIV-positive patients, cervical lymph nodes were most commonly affected followed by axillary and inguinal lymph nodes. Multifocal involvement was observed in 39% and 90% among HIV-negative and HIV-positive patients, respectively. Patients with mediastinal lymphadenopathy may present with cough and dysphagia.²⁷ With a wider availability of (CT) scan, it is expected that more cases of intrathoracic and intra-abdominal lymphadenopathy and other associated lesions may be reported. Peripheral TB lymphadenopathy has been classified into five stages.²⁹ These include: (i) stage 1, enlarged, firm mobile discrete nodes showing non-specific reactive hyperplasia;

(ii) stage 2, large rubbery nodes fixed to the surrounding tissue owing to periadenitis; (iii) stage 3, central softening because of abscess formation; (iv) stage 4, collar-stud abscess formation; and (v) stage 5, sinus tract formation. Physical findings depend upon the stage of the disease. When EPTB is suspected as a possible diagnosis, every attempt should be made to procure tissue/relevant body fluid for diagnostic testing. Most accessible tissue should be procured for histopathological, cytopathological and microbiological diagnoses. For example, when working up a patient with suspected LNTB, the most easily accessible representative peripheral lymph node should be excised and subjected to diagnostic testing. Similarly, cerebrospinal and ascitic fluids' examinations provide most valuable diagnostic clues in patients with neurological and peritoneal TB, respectively. With the advent of ultrasound scan and subsequently CT scan and the (MRI), and widespread availability of upper gastrointestinal endoscopy, colonoscopy, laparoscopy, cystoscopy and biopsy under visual guidance and other invasive investigations such as hysterosalpingography and colposcopy, tremendous progress has been achieved in precise anatomical localisation of the lesions of EPTB antemortem. If no accessible tissue/fluid is available for analysis, radiologically guided FNAC or biopsy may be required to secure tissue for diagnosis. In countries like India where TB is highly endemic, tuberculin skin test result alone is not sufficient evidence to diagnose EPTB in adult patients. In patients with LNTB, FNAC, excision biopsy of the most accessible peripheral lymph node confirms the diagnosis most of the times. CT scan is helpful in localising intrathoracic and intra-abdominal lymphadenopathy and radiologically guided FNAC and biopsy. When available, video-assisted thoracoscopic surgery (VATS) can be a valuable minimally invasive procedure to procure tissue for diagnostic testing in patients with intrathoracic lymphadenopathy and pleural disease. Laparoscopy facilitates visual inspection of the lesions and facilitate procurement of tissue for histopathological confirmation of the diagnosis.²⁷

According to WHO estimates, 9.27 million new active disease cases corresponding to an estimated incidence of 139/100 000 population occurred throughout the world in 2007. Only 5.5 million of 9.27 million cases of TB (new cases and relapse cases) were notified to national TB programmes of various countries, while the rest were based on assessments of effectiveness of surveillance systems. The highest number of TB cases occurred in Asia (55%) followed by Africa (31%). The highest incidence rate (363 /100 000 population) was recorded for the African region, mainly because of high-prevalence of HIV infection. The six most populous countries of Asia (China, India, Indonesia, Pakistan, Bangladesh and Philippines) accounted for >50% of all TB cases worldwide. An estimated 1.37 million (15%) of incident TB cases in 2007 were coinfecting with HIV. Nearly 80% of the HIV-infected TB patients were living in the African region.³⁰⁻³¹

Learning points

- ▶ The condition should be considered as entity in the differential diagnosis of cervicofacial lymphadenopathy.
- ▶ Diagnosis should be made with histopathological investigations.
- ▶ Appropriate diagnosis and prompt treatment can improve the overall health of the patient and can prevent him/her from developing any systemic complications of tuberculosis in future.

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