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Case Report

Tuberculous Lymphadenitis in Maxillofacial Area – a Case Report

Bistra Blagova[1]*, Lina Malinova[2] and Vesela Ivanova[3]

[1]*Maxillofacial Surgery Division, University Multiprofile Hospital for Active Treatment and Emergency Medicine, Bulgaria*

[2]*Department of Anatomy, Histology and Embryology, Medical University of Sofia, Bulgaria*

[3]*Department of General and Clinical Pathology, Medical University of Sofia, Bulgaria*

***Corresponding author:** *Bistra Blagova, DDS, DMD, Maxillofacial Surgery Division, University Multiprofile Hospital for Active Treatment and Emergency Medicine NI Pirogov, Gen Totleben Blvd 21, 1606 Sofia, Bulgaria*

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Abstract

Introduction: Tuberculosis (TBC) is usually a chronic pulmonary disease with a high prevalence in developing countries, which carries a significant mortality rate. Lymph node involvement remains the most common extrapulmonary involvement of *Mycobacterium tuberculosis*. However, the clinical picture of TBC in the head and neck area can be varied and often misleading.

Case report: We present a 13-year-old female with diffuse hard painful submandibular swelling with intact skin that develops gradually over a week. She presented with misdiagnosis and poor initial dental treatment. The patient was diagnosed with right submandibular TBC lymphadenitis based on histopathological report and confirmed by a positive QuantiFERON TB test.

Conclusion: TBC of the head and neck is not such a rare disease. Although it has harmful local and systemic effects and is devoid of characteristic clinical and radiographic features, it is a diagnostic challenge. As early diagnosis with timely treatment can thwart complications, it is therefore important that clinicians are aware of the condition and take it into account in their differential diagnosis.

Keywords: Bacille Calmette Guerin (BCG); lymphadenitis; *Mycobacterium tuberculosis*; QuantiFERON TBC Test; tuberculosis (TBC)

Introduction

Tuberculosis (TBC) is reported to be one of the most common systemic bacterial infectious diseases [1]. It is expected to spread to approximately 8 million individuals each year; 3 million people die from complications related to the disease [2] and is a major cause of child morbidity and mortality in developing countries [3]. Tuberculous (TBC) lymphadenopathy is a common cause of peripheral adenopathy in children [4], and lymphadenopathy is a common clinical symptom of extrapulmonary TBC in the pediatric age group responsible for up to 50% of all extra thoracic TBC [5]. In endemic areas, TBC is the most common cause (22 – 48%) of persistent cervical lymphadenopathy [6]. TBC lymphadenitis was defined as a painless firm or soft swelling in a group of superficial lymph nodes [7]. It is a chronic granulomatous infection principally caused by *Mycobacterium tuberculosis* and less frequently by ingestion of *Mycobacterium bovis* infected unpasteurized cow's milk or by other atypical mycobacteria [8]. Tuberculosis can affect every organ in the body except nails, hair and teeth [9]. TBC chiefly affects the pulmonary system besides involving extrapulmonary locations comprising head and neck region. Extrapulmonary TBC is rare occurring in 0.05 – 5 % of patients with TBC [8]. In this way,

this disease rarely features in the differential diagnosis of head and neck lesions. So, the aim of our report is to call clinicians' attention to this pathology by presenting a case of a child patient diagnosed with submandibular TBC lymphadenitis.

Case Report

A 13-year-old female sought firstly management by her dentist because of swelling within her right submandibular region. A root canal treatment of her lower right first molar was initiated by reason of large carious lesion. Later, as the symptoms progressed, she was referred to the maxillofacial surgery unit. On examination, there was a slightly tender firm right-sided submandibular swelling nearly 4 cm × 5 cm. The superimposing skin was intact with blueish colour compared to the surrounding skin. No palpable pathologically enlarged regional lymph nodes were evident (Figure 1). There was no dysphagia or odynophagia. The patient denied recent fever, upper respiratory infection, B-symptoms or constitutional symptoms. Additionally, she had no recent sick contact, travelling and or any pets or animal contact. The patient had normal mouth opening and showed no neurological deficit. Intraorally, the oral mucosa was intact without clinical signs of inflammation. Her lower right first molar was with cotemporary obturation, without any pain on palpation and percussion. The panoramic radiograph revealed periapical changes around that tooth (Figure 2). The routine blood investigations were done for the patient. They were unremarkable except that erythrocyte sedimentation rate was elevated (35 mm/h). Her chest X-ray gave a normal impression (Figure 3). Empirically antibiotic treatment was initiated via intravenous amoxicillin combined with clavulinic acid 875 mg twice daily. Within 24 hours following the hospitalization the swelling got fluctuant and the patient was posted for incision and drainage under general anesthesia. Excised specimen was submitted for histopathological and microbiological examination. The microbiological culture of the tissue was positive only for Staphilococcus Coa (-) MSS and Staphilococcus aureus. However, the histopathological examination of the biopsied example showed a dense chronically inflamed fibrous tissue with evidence of ill-defined infiltrated by coalescent epithelioid histiocytic granuloma with areas of central caseous necrosis (Figure 4). The report gave feeling as "TBC lymphadenitis" [10]. On addition history taking, patient's elder sister gave a history of extrapulmonary TBC at the age of 6. She had inderwent anti-TBC treatment and had not had any symptoms for the past 7 years. So, a clinical diagnosis of a right submandibular TBC lymphadenitis was pondered and confirmed by positive QuantiFERON TBC Test. The operative field healed uneventful. The patient was referred to the respiratory department for a full TBC workup and anti-TBC therapy was commenced.

Figure 1: A diffuse swelling in left submandibular region.

Figure 2: Preoperative orthopantomography.

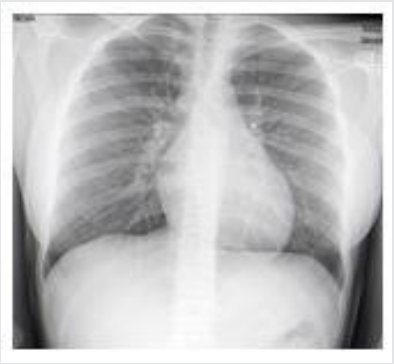

Figure 3: The chest X-ray revealed no pathology.

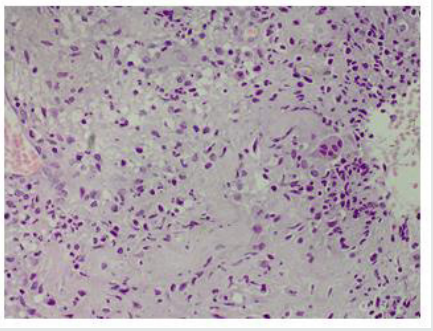

Figure 4: Low power view showing a granuloma composed of epithelioid histiocytes with abundant eosinophilic cytoplasm and multinucleated giant cell formation, consistent with a tuberculous etiology (hematoxylin-eosin stain, x 40).

Discussion

Tuberculosis (TBC) is a chronic granulomatous disease caused by different strains of mycobacteria, usually *Mycobacterium tuberculosis* in humans [11]. Robert Koch, a German physician, discovered the Tuberculosis bacillus in 1882 [12]. The history of TBC dates back to about 15,000 to 20,000 years ago. Hippocrates describes scrofula in ancient Greece [13]. It has been found in relics from ancient Egypt, China and India. Archaeologists have discovered spinal tuberculosis as Pott's disease in Egyptian mummies [14]. In medieval Europe, scrofula was known as the "King's Evil" because some monarchs touched patients to "cure" the disease [13]. In the 18th century, it peaked in 900 deaths per 100,000 and was called the "white plague." This was considered a stigma in society and even compared to a "devouring dragon" in some parts of Europe. After Robert Koch demonstrated the causative agents of mycobacteria in lymph nodes in 1882, scrofula was finally recognized as a consequence of tuberculosis [13]. In 1884, Edward Livingston Trudeau began the concept of isolating these patients from society, treating them with rest and nutrition [14]. Later, in 1908, Bacillus Calmette Guerin was invented by Albert Calmette and Camille Guerin in Lille, France. But it was first used in humans in 1921.

In spite of dramatic improvement in public health care measures in the last four to five decades, TBC still remains a dreaded disease of today's world. It is estimated that about 32 % of the world's population are infected with TBC [15]. Each year 3 million people worldwide die from TBC [16]. The World Health Organization estimates approximately 20 million active cases of tuberculosis, 80% of which belong to the developing countries [17]. The diagnosis of extrapulmonary TBC is often overlooked because it has no specific pathognomonic signs [18]. Cervical TBC remains the most common form of head and neck tuberculosis, as has been found in various studies with figure ranging from 60 % to 90 % [19]. Primary orofacial TBC is observed more widely in children and young adults/adolescents [20]. A new classification system of orofacial TBC in different forms and locations is presented [18] (Table 1). The most common form of extrapulmonary TBC is TBC lymphadenitis or scrofula, especially in the cervical region [21] and accounts up to 5 % of the cervical lymphadenopathy [22]. It often affects children and young adults in age range of 30 – 40 years and shows female predilection [23], as in our case. This condition is commonly caused by *Mycobacterium tuberculosis* although atypical mycobacterium such as Mycobacterium avium and Mycobacterium kansasii, has been reported in the literature, especially involving children. Interestingly, five stages involving the progression of TBC lymphadenitis has been described by Jones and Campbell [24] (Table 2). So, according to the new proposed classification of TBC patients our case can be classified as type IV stage 3, where there was abscess formation.

Table 1: Andrade's classification for orofacial tuberculosis [18].

Type I	Lumpy jaw: patient presents with extraoral swelling without any intraoral or extraoral draining sinuses; the focus of infection involves the mandible or maxilla; in general, the patient's oral hygiene is good.
Type II	Patients report a history of extraction and present with nonhealing extraction sockets with/without intraoral or extraoral draining sinus/sinuses.
Type III	Patients report no history of extraction and present with intraoral or extraoral draining sinus/sinuses in the orofacial region and an osteomyelitic bony lesion.
Type IV	Tuberculous lymphadenitis of the head face neck region without any features of type I, II, III, or V.
Type V	Lesion of other sites in and around the oral cavity, eg, maxillary antrum, salivary glands, orofacial muscles gingiva, tongue, etc.

Table 2: Stages of progression of tuberculous lymphadenitis – Jones and Campbell classification [24].

Stage 1:	enlarged, firm, mobile, discrete nodes showing non-specific reactive hyperplasia;
Stage 2:	large rubbery nodes fixed to surrounding tissue owing to periadenitis;
Stage 3:	central softening due to abscess formation;
Stage 4:	collar-stud abscess formation;
Stage 5:	sinus tract formation.

Most patients with cervical TBC lymphadenitis do not present with systemic symptoms [25] similar to presented patient. The definition of cases with this pathology is according to following criteria: painless, enlarged lymph nodes > 2 cm in one or more sites, with or without periadenitis, with or without constitutional symptoms such as fever, night sweat, weight loss etc., with or without evidence of TBC elsewhere, or presence of an abscess with or without discharging sinus [19]. However, in extrapulmonary disease, the clinical and radiographic signs could be more nonspecific [23]. The early manifestation of head and neck TBC is often similar to neoplasms or inflammation and because the systemic symptoms of TBC may not be obvious, clinical consideration of TBC usually occurs only after an ineffective anti-inflammatory treatment, biopsy or even surgical resection [21]. Neoplasms, lymphoma, other granulomatous and inflammatory processes [26], nodal metastases (local or distant), hyperplastic nodes, Castleman's disease and sarcoidosis [27] are among the differential diagnoses. So, it could be assumed, that the diagnosis generally needs a histological examination of tissue and demonstration of the infective organisms in the specimen [23]. Fine needle aspiration cytology is a simple and costeffective investigative tool for the diagnosis of TBC lymphadenitis, with a reported specificity of 93 % and a sensitivity of 77 % [28]. The histological picture of TBC is characterized by the presence of caseous and non-caseous granulomas with multinucleated giant Langhans cells [23]. However, this does not necessarily lead to positive results [29]. In our case, it can be concluded that the presence or absence of constitutional symptoms or contact history cannot be relied upon as a reliable diagnostic evidence in cases of extrapulmonary tuberculosis of the head and neck [19]. Initially, the diagnosis was delayed due to the suspicion of odontogenic infection, nonspecific clinical features and a negative chest X-ray. Finally, the diagnosis of TBC was suggested by the biopsy result and confirmed with a positive QuantiFERON TBC test. However, the World Health Organization currently recommends that such serological tests not be used to diagnose TBC, as they provide inconsistent assessments of susceptibility and specificity [30]. Other tests, such as a tuberculin skin test and interferon-gamma release tests, may help make the diagnosis; however, false negative results have been reported [21]. However, no test can distinguish latent TBC from active TBC [31]. Cultivation of *Mycobacterium tuberculosis* remains the gold standard, but a period of 8 to 10 weeks is required, and sensitivity varies with host and sample preparation [32].

The treatment of TBC has undergone a vast change in the past century. The Infectious Disease Society of America (IDSA) recommends 6 months of the following treatment for lymphadenitis caused by drug-susceptible organisms [33]: isoniazid, rifampin, pyrazinamide and ethambutol for 2 months, followed by isoniazid and rifampin for another 4 months. The 6-month recommendation is supported by studies that showed no difference between 6 and 9 months of treatment in cure rates (89 % – 94 %) [34] or relapse rates (3 %) [35]. The benefit of routine corticosteroid therapy for peripheral TBC lymphadenitis is unknown and IDSA guidelines do not recommend the use of steroids in the treatment of TBC lymphadenitis [33]. Adjuvant immunotherapy with anti–tumor necrosis factor agents has been studied in small numbers of patients for routine treatment of all forms of TBC, but available data are insufficient to make a recommendation [36]. IDSA guidelines recommend surgical excision only in unusual circumstances, and these circumstances are not defined explicitly [33]. Although surgical excision combined with antibiotic therapy has produced favorable outcomes, we are not aware of controlled studies that have compared excision plus antibiotic therapy with antibiotic therapy alone. A unique and disturbing feature of successful treatment of drug susceptible TBC lymphadenitis is the frequency with which patients experience worsening of symptoms during treatment (i. e.,

paradoxical upgrading reaction - PUR). Manifestations of PUR have included enlarging lymph nodes [37], new nodes, pain and draining sinuses [37,38]. The occurred fluctuation of the swelling resulting in incision and drainage in our patient could be determined as a PUR. Namely surgery has been recommended for PUR and for treatment failure in cases of TBC lymphadenitis and for patients who have discomfort from tense, fluctuant lymph nodes [38]. In a retrospective review, aspiration, incision and drainage or excision were associated with a trend toward a shorter duration of PUR [37]. Surgical excision is the recommended therapy for cervical lymphadenitis due to nontuberculous mycobacteria in children and has been associated with better outcomes than 3 months of 2-drug antibiotic therapy [39].

Conclusion

Tuberculosis (TBC) is on the rise, particularly its extrapulmonary manifestations. The twenty-first century is likely to see a 'new' TBC, with isolated extrapulmonary manifestations. TBC of the head and neck region though not very redundant, still remains an imperative clinical subsistence, which should be always kept in mind. At instances like the current case, where there is the absence of systemic signs and symptoms, swift identification of TBC can become challenging. Awareness by the clinician of such atypical presentations would make identification of this pathology uncomplicated. Although the disease may exhibit ambiguous presentation and associated with high morbidity, the targeted investigations and the efficient collaboration between the medical personnel, prompt toward the correct diagnosis and curative treatment. Initial diagnosis of the ailment would be beneficial not only to provide early treatment to the patients with increasing their morbidity and mortality, but also averting the spread of the disease to others.

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