



A Retrospective Cohort Study of Major Salivary Gland Tuberculosis: Our 13 Year Experience

Poras Chaudhary¹ · Amrit K. Gupta¹ · Sam B. Padala¹ · Ashutosh Nagpal¹ · Romesh Lal¹

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Abstract The tuberculous infection of major salivary glands is rare because they are relatively resistant to tubercle bacilli. The aim of this study is to present our 13 year experience on major salivary gland tuberculosis. The clinical, histopathological, microbiological and imaging records of 9 cases of major salivary gland tuberculosis were reviewed retrospectively. The cases diagnosed with either microbiological culture and/or polymerase chain reaction assay and/or Histopathological examination were included in the study. Descriptive statistics were used to summarize the data. There were 9 cases with tuberculous involvement of major salivary glands; parotid (n = 5), submandibular (n = 3), sublingual (n = 1). The most common local symptom was painless swelling present in 8 cases and constitutional symptoms were present in all the cases. The previous history of TB was present in 5 out of 9 cases. Surgical intervention was done in 2 cases of parotid TB for diagnostic purpose and therapeutic intervention was required in 1 patient. Patients responded well to medical therapy. Two patients with disseminated disease died. The major salivary gland is rare in both immunocompetent and immunocompromised patients. Diagnosis is difficult and requires high degree of suspicion especially in isolated cases. Medical management yields satisfactory results.

Keywords Major salivary glands · Tuberculosis · Medical therapy · Good prognosis

Introduction

Tuberculosis (TB) is a worldwide health problem and a common endemic disease in India. Ninety five percent of TB cases are in developing nations [1]. The incidence of TB has not declined in developing nations and there is resurgence in TB cases in developed nations due to Human immunodeficiency virus (HIV) infection. Improved reporting because of advancement in diagnostic techniques and migration of population from endemic areas to developed nations are the major reasons for increase in incidence of extrapulmonary TB (EPTB) cases. EPTB accounts for approximately 15–20% of all TB cases in the world [2]. The incidence of major salivary gland involvement in reported studies on head and neck TB is 1.8% [3] and 3.9% [4].

The most common site of EPTB in head and neck region is cervical lymph nodes followed by larynx [4]. Major salivary glands involvement with TB is a rare occurrence because they are relatively resistant to infection by tubercle bacilli. This resistance is provided by antibacterial property of thiocyanate ions and proteolytic enzymes present in saliva [5]. Parotid gland is the most commonly affected gland with TB, constituting approximately 70% of total cases of salivary gland TB [6], followed by submandibular gland, while tuberculous involvement of sublingual gland is almost unknown. This is because of relatively better flow of saliva in submandibular gland [5]. EPTB at such rare sites is more common in patients with congenital or acquired immunosuppressive states.

Only a few case series and studies have been reported on major salivary gland TB. The aim of this study is to present our 13 year experience on major salivary gland TB.

✉ Poras Chaudhary
drporaschaudhary@yahoo.com

¹ General Surgery, Lady Hardinge Medical College,
New Delhi, India

Methods

Clinical, histopathology, microbiology and imaging records of patients of disseminated TB cases in which major salivary glands were found to be involved, also the records of patients in whom major salivary glands were found to be involved in isolation or with tuberculous involvement of other head and neck organs who underwent medical and/or surgical treatment in surgical unit 6 in our institute between January 2006 and December 2018 were reviewed retrospectively. Out of 18 cases of disseminated TB, microbiology, histopathology and imaging records were suggestive of involvement of major salivary gland with TB in 2 cases. Five cases of isolated TB and 2 cases of glandular involvement with other head and neck organs were identified. The cases diagnosed with either microbiological culture and/or polymerase chain reaction assay and/or Histopathological examination were included in the study.

Records of these 9 cases were reviewed in detail. The clinical and epidemiological parameters, various diagnostic methods, medical and surgical management, follow up and prognosis were evaluated. The protocol was approved by the ethical review board of the institute.

Statistical analysis: descriptive statistics were used to summarize the data.

Results

There were 9 cases with tuberculous involvement of major salivary glands; parotid ($n = 5$), submandibular ($n = 3$), sublingual ($n = 1$). There were 6 male and 3 female patients with a ratio of 2:1. Most of the patients were in the 4th decade of life (4/9). The youngest patient was 18 years old (parotid gland TB), while the oldest patient was 76 years old (parotid TB). The duration of symptoms ranged from 2 to 12 months.

In patients with parotid gland TB, the local symptom was painless swelling (5/5); in submandibular gland TB cases, of 3, 1 patient presented with painful swelling, while 2 had painless swelling. The constitutional symptoms were present in all the cases (100%). The most common constitutional symptoms were anorexia (9/9), fever (8/9) and weight loss (6/9). There was no case of bilateral glandular involvement or coexistence of tuberculosis with malignancy. The previous history of TB was present in 5 out of 9 cases (55.55%); the history of TB contact was seen in 4 out of 9 cases (44.44%). HIV positivity was seen in 55.55% of cases. In parotid gland, 2 out of 5, submandibular gland 2 out of 3 and 1 case of sublingual gland TB was HIV positive. PCR assay and FNAC were positive in 4 out of 9

cases (44.44%) each, and culture in 2 out of 9 cases (22.22%). Surgical intervention was done in 2 cases of parotid TB for diagnostic purpose (superficial parotidectomy), whereas therapeutic intervention was done in 1 case (incision and drainage for parotid abscess). The details of 9 cases of salivary gland TB are given in Table 1.

Imaging studies such as X-ray chest, ultrasonography (USG) and contrast enhanced computed tomography (CECT) of head and neck were done in all the cases. CECT abdomen and chest were done in 2 cases with parotid gland TB with disseminated disease. Laryngoscopy and biopsy was done in 1 patient with oral cavity and vocal cord involvement. Plain chest radiograph showed tuberculous infection in 5 patients, of which 2 patients had evidence of active TB, whereas 3 patients had sequelae of old infection in the form of apical calcific foci. USG examination showed diffuse parotid gland enlargement in 4 patients, focal lesion in 1. Collection was seen in 1 patient. Enlarged periglandular lymph node showed hypoechoic center, enlarged cervical lymph node of size 2.4 cm was seen in 1 patient. Submandibular gland showed diffuse enlargement in all the cases with multiple small collections in 2 patients. CECT confirmed the findings of USG. CT features were in the form of nodular enlargement with homogenous enhancement, multiple, round solid nodule with rim enhancement with central lucency within the lesion.

Overall, the prognosis was good. The mortality in the present study is 22.22%. Two patients with disseminated disease with parotid gland involvement died during the course of medical therapy. Rest of the 7 patients recovered with antituberculous therapy (ATT) and antiretroviral therapy (ART) was also continued in HIV positive patients. ATT was given for 9 months in HIV negative primary glandular involvement. Twelve months ATT was given to those who had associated head and neck involvement and to those who were HIV positive with primary involvement.

Discussion

The true incidence of major salivary gland TB is unknown. The causative organism for major salivary gland TB is *Mycobacterium tubercle bacilli*; though, with the recent surge in TB patients associated with HIV, the atypical mycobacterial cases have also increased [6]. EPTB due to atypical mycobacterial is still not seen in salivary gland lesions. The tubercle bacilli usually reach the gland through haematogenous or lymphatic dissemination and less commonly via duct [7]. The lesions can be diffuse or nodular. The nodular form is more common and results from involvement of intraglandular or periglandular lymph nodes and may result in cold abscess formation within the gland [5, 7]. In diffuse form, there are multiple areas of

Table 1 Data of nine cases of major salivary gland tuberculosis; TB tuberculosis, HIV human immunodeficiency virus, CXR X-ray chest, USG ultrasonography, CECT contrast enhanced computed tomography, PCR polymerase chain reaction, FNAC fine needle aspiration cytology, ATT antituberculous therapy, ART antiretroviral therapy

Gland	Cases	Age/sex/duration of symptoms	Clinical features and HIV status	Comorbidity	Primary/secondary TB	History of TB/contact	Culture/PCR/FNAC	Imaging studies (CXR, USG, CECT)	Surgical intervention for diagnosis/treatment	Prognosis and follow up
Parotid	Case 1	18/M/7 months	Painless swelling, fever, anorexia, weight loss HIV-negative	No	Primary, no head and neck TB	Yes/yes	Culture, PCR and FNAC negative	CXR, USG neck and CECT head and neck	Superficial parotidectomy done, biopsy positive	Received ATT for 9 months, recovered, alive
	Case 2	45/F/4 months	Painless swelling, fever, anorexia HIV- negative	No	Primary, no head and neck TB	No/yes	Culture, PCR and FNAC negative	CXR, USG neck and CECT head and neck	Superficial parotidectomy done, biopsy positive	Received ATT for 9 months, recovered, alive
	Case 3	76/M/4 months	Painless swelling, cervical lymphadenopathy, fever, anorexia, weight loss HIV- negative	Hypertension, diabetes mellitus, COPD	Primary with tuberculous cervical lymphadenopathy	No/No	Culture, PCR negative and FNAC inconclusive	CXR, USG neck and CECT head and neck	Cervical lymph node biopsy and excisional biopsy from gland positive for TB	Received ATT for 12 months, recovered, alive
	Case 4	46/M/9 months	Anorexia weight loss, fever, breathlessness, painless swelling, loose motion HIV- positive	No	Disseminated TB	Yes/No	Culture negative, PCR and FNAC positive	CXR, USG neck and CECT head and neck, chest and abdomen done	None	ATT started, patient died within 12 days due to septicemia
	Case 5	42/F/10 months	Fever, weight loss, anorexia, painless swelling, pain abdomen, vomiting, malena HIV- positive	No	Disseminated TB	Yes/No	Culture, PCR and FNAC positive	CXR, USG neck and CECT head and neck, chest and abdomen	Incision and drainage done for parotid abscess	ATT started, developed drug induced hepatitis and dies of multiorgan failure
Submandibular	Case 1	39/M/2 months	Painful swelling, fever, anorexia, weight loss HIV positive	No	Primary, no head and neck TB	Yes/Yes	PCR positive, culture negative, FNAC positive	CXR, USG neck and CECT head and neck	None	Received ATT for 12 months, recovered, alive
	Case 2	46/M/8 months	Painless swelling, fever, anorexia HIV positive	No	Primary, no head and neck TB	No/yes	Culture and PCR positive, FNAC positive	CXR, USG neck and CECT head and neck	None	Received ATT for 12 months, recovered, alive
	Case 3	45/F/1 year	Painless swelling, anorexia HIV negative	hypothyroidism	Primary, no head and neck TB	No/No	Culture and PCR negative, FNAC negative	CXR, USG neck and CECT head and neck	Diagnostic excision of gland done, biopsy positive	Received ATT for 9 months, recovered, alive
Sublingual	Case 1	41/M/3 months	Fever, anorexia, weight loss, cervical lymphadenopathy, aphthous ulcer, recent change of voice HIV- positive	No	Primary with tuberculous cervical lymphadenitis and vocal cord and oral cavity TB	Yes/No	Culture and PCR negative, FNAC from cervical lymph node positive	CXR, USG neck and CECT head and neck	None	Received ATT for 12 months, recovered, alive

Caseation or abscesses involving the entire gland parenchyma [5, 7].

It has been reported that parotid gland gets affected more commonly in localized spread while submandibular gland involvement is seen more commonly with systemic disease [8]. In the present study, there were two cases of disseminated TB and in both of them parotid gland was found to be involved. In this study, patients with TB involving other areas of head and neck region, parotid glands was found to be affected in one patient with associated tuberculous cervical lymphadenopathy and sublingual gland was involved in one patient with TB of oral cavity and vocal cords, whereas a study has reported that the incidence of coexistent site of tuberculous involvement is 20% [4].

The most common clinical features were painless swelling (100%) and presence of associated constitutional symptoms (100%) such as fever, anorexia, and weight loss. The other study has reported that constitutional symptoms are associated in only 26% of cases [4]. The bilateral glandular involvement was not seen in our study. The previous history of TB was present in 55.55% of cases. It has been reported that pulmonary involvement is seen in up to 25% of cases [3].

The best way to diagnose TB is demonstration of bacilli by Histopathological examination. FNAC is an easy and convenient way of demonstrating the organism. In our study, FNAC was positive in 44.44% of cases. The inability of FNAC to diagnose the case is probably because of presence of necrosis. Studies have reported that the sensitivity and specificity of FNAC is 80% and 93% respectively [9, 10]. PCR assay is an effective method of diagnosing TB in cases where FNAC fails to demonstrate the organism. The false positivity of PCR assay is high. The aspirate, saliva and tissue can be used for PCR assay. PCR assay was also positive in 44.44%; while culture was positive in only 22.22% of cases. The sensitivity of acid-fast bacilli (AFB) staining and culture is 28.6% [11]. FNAC, culture and PCR assay were performed in all the cases in our study. Excisional biopsy was done in 2 cases.

Though, the cases of coexistent malignancy with TB have also been reported [3, 12, 13] but in the present study there was no case of coexistence of TB and malignancy of salivary glands. Coexisting HIV infection was present in 55.55% of cases in this study while the literature reports that the incidence of HIV infection is up to 30% in head and neck TB cases [3].

There are no specific diagnostic findings of salivary gland TB on imaging studies. X-ray chest, USG of the involved gland and neck and CECT head and Neck were done in all the cases. X-ray chest was done to document any associated chest lesion. Ultrasound features were in the form of diffuse glandular enlargement and focal

hypoechoic or anechoic areas within the gland. CECT confirmed USG findings and showed round, thick walled rim enhancing lesion within the gland with central lucency.

The disease is medically curable; therefore, it is crucial to diagnose TB cases without surgical intervention so as to avoid the trauma of anaesthesia and major surgery. Pre-operative diagnosis of salivary gland tuberculosis is difficult because of lack of specific clinical features and imaging findings. FNAC is the study of choice to diagnose this pathology. The saliva, aspirate and tissue obtained through trucut biopsy can be used for AFB staining, culture and PCR assay. Incisional biopsy is contraindicated. Excisional biopsy is indicated in presence of suspicious clinical, epidemiological, imaging features and laboratory parameters such as raised ESR, positive Montoux test.

Patients were treated standard antituberculous drugs; four drug combination for 2–4 months followed by two drug combination for 6–12 months. The prognosis was good and all the patients recovered well medical therapy. Two patients with disseminated disease died due to multiorgan failure and septicemia. Surgical intervention is indicated only for medical treatment failure and complications [5]. Medical therapy should be continued after surgical intervention.

In conclusion, this study shows that major salivary gland is rare in both immunocompetent and immunocompromised patients. In disseminated disease also, salivary glands rarely gets affected. Diagnosis is difficult and requires high degree of suspicion especially in isolated cases. Medical management yields satisfactory results.

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Compliance with Ethical Standards

Conflict of interest The author(s) declare that they have no competing interests.

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