10.5005/jp-journals-10037-1065

CASE REPORT

The Coexistence of Tuberculous Lymphadenitis with Oral Squamous Cell Carcinoma: Review of Four Cases

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ABSTRACT

The coincident occurrence of tuberculous lymphadenitis, the form of extrapulmonary tuberculosis and oral squamous cell carcinoma (OSCC), is unusual. Tuberculous lymphadenitis is one of the common causes of lymphadenopathy. The diagnosis and treatment of OSCC in a patient with coexistent disease of tuberculous lymphadenitis assumes importance as it can prevent high mortality in patients with disease of OSCC. Regional lymph node enlargement in squamous cell carcinoma patient is not always caused by metastasis. We present here four case reports as an example of tuberculous lymphadenitis coexisting with squamous cell carcinoma of the oral cavity. Accurate diagnosis has helped in down-staging carcinoma of the oral cavity, and thereby helped in deciding the treatment planning. This also aids in identifying the curable disease.

Keywords: Metastasis, Squamous cell carcinoma, Tuberculous lymphadenitis.

How to cite this article: Agrawal A, Gadbail A, Hande A, Chaudhary M, Gawande M, Patil S, Tare K. The Coexistence of Tuberculous Lymphadenitis with Oral Squamous Cell Carcinoma: Review of Four Cases. Oral Maxillofac Pathol J 2016;7(1):676-678.

Source of support: Nil

Conflict of interest: None

INTRODUCTION

Despite increasing awareness and the availability of better imaging and other diagnostic tests, extrapulmonary tuberculosis remains a difficult diagnosis to make, due to its often nonspecific and protean manifestations. Extrapulmonary tuberculosis (TB) constitutes about 15 to 20% of all cases of TB with lymph nodes being the most common site of involvement.[1] Tuberculosis of the lymph node (tuberculous lymphadenitis) is the most common form of extrapulmonary tuberculosis.[2,3] In developed countries, tuberculous lymphadenopathy was observed in 1.6% of patients of TB.[4] However, in developing countries, almost two-third of the cases of lymphadenopathy are due to TB.[5] Tuberculosis should be strongly suspected in a young patient presenting with peripheral lymphadenopathy, with prolonged duration of illness, and involvement of cervical lymph nodes with multiple and matted appearance.[6] Coexisting TB with carcinoma has been previously reported in most organs, especially with lung cancer.[7] Munjal et al reported six cases of coexistence of carcinoma in breast and an ipsilateral enlargement of axillary lymph nodes caused by TB.[8] The synchronous occurrence of TB and oral squamous cell carcinoma (OSCC) is unusual and no single case has been reported in English language probably due to the declining incidence of TB in the West. The simultaneous occurrence of tuberculous lymphadenitis of cervical regional lymph nodes and OSCC can complicate the neoplastic disease, and thereby create problems in treatment decision. However, there is paucity of data in this regard. So, we have retrieved and analyzed the four cases of cervical tuberculous lymphadenopathy and OSCC.

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CASE REPORTS

The patients who had undergone radical neck dissection at tertiary care center of Sharad Pawar Dental College and Hospital, Sawangi, Wardha, Maharashtra, India, were considered in the study group. Out of all the cases reported in the center, 80 cases underwent radical neck dissection in time span of 12 months. Out of these, four cases showed simultaneous occurrence of tuberculous lymphadenitis and OSCC. The details of cases are summarized in Table 1.

Case 1

A 40-year-old female had underwent radical neck dissection after clinical and histopathological diagnosis of carcinoma of gingivobuccal sulcus. The investigations revealed the staging as T2N2. The lymph nodes were nontender, fixed to the underlying skin. The histopathological examination revealed the tumor size of approximately 2.5 × 3.5 × 3.5 cm showing features of well differentiated squamous cell carcinoma. From 12 lymph nodes palpable, lymph nodes at level Ia, Ib showed presence of caseation

Table 1: Details of all the four cases are summarized

Sl. no.	*Age/sex*	*Clinical stage*	*Surgery*	*Diagnosis*	*Tuberculous lymphadenitis*	*Habit history*
1	40/F	T2 N2	RND	WDSCC	Present at levels Ia and Ib	Positive
2	57/M	T1 N1	RND	WDSCC	Present at levels I and II	Positive
3	60/M	T2 N2	RND	MDSCC	Present at levels I to III	Positive
4	34/M	T1 N2	RND	WDSCC	Present at levels I	Positive

RND: Radical neck dissection; WDSCC: Well differentiated squamous cell carcinoma; MDSCC: Moderately differentiated squamous cell carcinoma

necrosis, epithelioid giant cells suggestive of tuberculous lymphadenitis with no evidence of metastasis.

Case 2

A 57-year-old male patient reported to Outpatient Department (OPD) of SPDC with nonhealing ulcer on buccal vestibule with few lymph nodes palpable. Preliminary investigations confirmed the diagnosis of carcinoma of buccal vestibule with clinical staging as T1N1. The patient underwent radical neck dissection at SPDC and histopathological examination revealed tumor size 2 × 2 × 1.5 cm approximately. Out of 12 lymph nodes palpable, lymph nodes at the levels I, II showed caseation necrosis and metastasis was observed at two levels.

Case 3

A 60-year-old male reported to OPD of SPDC with complaint of painless growth over the maxillary posterior region of the jaw. Preliminary investigations confirmed the diagnosis of carcinoma of maxilla with lymph nodes palpable and the disease was staged as T2N2. The patient had undergone radical neck dissection at SPDC and histopathological examination revealed tumor size of 3.4 × 2 × 3 cm approximately. Out of 12 lymph nodes palpable, lymph nodes at levels I, II, III show caseation necrosis and metastasis was observed only at one level.

Case 4

A 34-year-old male was diagnosed as the carcinoma of gingivobuccal sulcus had underwent radical neck dissection. Preliminary investigations confirmed the diagnosis and clinical staging was T1N2 and size of the lesion 2 × 2.5 × 3 cm approximately. Out of 12 lymph nodes palpable, tuberculous lymphadenitis was seen at level I with no evidence of metastasis.

All the cases showed no signs of pulmonary tuberculosis and have received radiotherapy which is on regular follow-up with no evidence of further disease progression.

DISCUSSION

Tuberculosis is worldwide in distribution, but is particularly more prevalent in Asia and Africa. According to 2008 World Health Organization (WHO) report, 9.2 million cases were detected and 1.7 million people lost their lives due to TB worldwide. India, China, Indonesia, South Africa and Nigeria rank first to fifth respectively in terms of absolute numbers of cases.[9] India has the highest TB burden accounting for one-fifth of the global incidence. The relationship between tuberculous lymphadenitis and malignancy is obsolete. Leukemias and lymphomas are commonly associated with mycobacterial reinfections. The association of TB with carcinoma was initially described 200 years ago by Bayle who considered 'cavitation cancereuse' as one of the various types of TB.[10]

In general, chronic inflammatory conditions have been thought to create the appropriate microenvironment for malignancy development through a number of mechanisms, i.e. the higher rate of cell turnover, is thought to increase the risk for genetic errors. Mycobacterial infections may escape the host's cellular response and killing and establish chronic and persistent inflammation.[11] There is ample experimental evidence that *Mycobacterium tuberculosis* is capable of inducing DNA damage.[12] Specifically, various mycobacterial cell wall components may induce production of nitric oxide and reactive oxygen species.[13] It should be noted at this point that nitrative DNA damage as well as oxidative DNA damage have been implicated in inflammation-related carcinogenesis. Recent data reveal that *M. tuberculosis* may also enhance synthesis of BCL-2 and this could lead to increased anti-apoptotic activity. The combination of direct DNA damage, apoptosis inhibition and perpetuation of chronic inflammation may enhance mutagenesis of progeny cells, and these effects coupled with enhanced angiogenesis, may lead to a microenvironment that is highly conducive to tumorigenesis. Nevertheless, smoking has been found as a risk factor as either tuberculous acquisition or progression of the disease.[14] The risk of TB increases with the dose of cigarettes and duration of smoking. Impairment of the clearance of secretions on the tracheobronchial mucosal surface as well as reduced phagocytic ability of the pulmonary alveolar macrophages and lower level of secreted proinflammatory cytokines might be the possible mechanisms of *M. tuberculosis*' escape from the first line of host defenses, which explain how exposure

to tobacco smoke may predispose to TB.[15] The synthesis of the available evidence enabled us to establish three different types of association between malignancy and tuberculosis:

- The development of cancer on the background of a previous tuberculous/infection.
- The concurrent existence of TB and malignancy in the same patient(s) or clinical specimen(s).
- The diagnostic challenges arising from the multifaceted presentations of these two disorders.[15]

The association of tuberculosis and cancer has been recorded in most of the organs and has been described and explained by many authors in many diverse ways.[8] Kaplan et al reviewed 58,245 patients with cancer and identified 201 cases of coexisting tuberculosis. Highest prevalence was seen in patients with Hodgkin's disease followed by lung cancer, lymphosarcoma, reticulum cell sarcoma and breast cancer. Recently, Munjal et al reported six cases of coexistence of carcinoma in breast and an ipsilateral enlargement of axillary lymph nodes caused by tuberculosis.[8] In this study, four cases of OSCC with coexistence of tuberculous lymphadenitis.

All four cases underwent radical neck dissection and showed no metastatic spread to regional cervical lymph node. While performing histopathological examination of resected enlarged lymph node revealed the tuberculous lymphadenitis. Coexistence of two diseases in one organ is always a diagnostic and therapeutic challenge.[16] This can create a dilemma in diagnosis and treatment as there are no pathognomonic symptoms or signs to distinguish both diseases.[8] Most decisions in the management of OSCC are taken based on TNM staging of the tumors. While both OSCC and undiagnosed tuberculos lymphadenitis are likely to occur in developing countries, their coexistence is rare which can lead to over staging of nodes. In all the reported patients, the synchronous presence of OSCC and tuberculous lymphadenitis to clinical overstating of malignancy based on which the management decisions were taken. However, treatment compliance remains an enigmatic problem in these cases.

CONCLUSION

Clinicians need to be aware of the myriad manifestations of TB and resist the temptation of premature diagnostic closure. The diagnosis of a tuberculous infection remains challenging and requires a high index of suspicion, especially when it complicates the clinical presentation of cancer patients. Accurate diagnosis may help us in downstaging the disease and also identifying curable disease which helped in modifying the treatment protocol. The diagnosis and treatment of tuberculosis in a patient with cancer assumes importance as it can prevent high morbidity in patients with coexistent disease. Also, further research is warranted to determine if a tuberculous infection, similar to other chronic infections and inflammatory conditions, may facilitate carcinogenesis.

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