Adenolymphoma: A probing entity: Case report and review

Anand Pratap Singh, Ankita Tandon[1], Aman Chowdhary[1], Sheetal Mujoo

Department of Oral Medicine and Radiology, Rungta College of Dental Sciences and Research, Bhilai-Durg, Chhattisgarh, [1]Department of Oral Pathology and Microbiology, JamiaMilliaIslamia, New Delhi, India

Address for correspondence:
Dr. Anand Pratap Singh, Department of Oral Medicine and Radiology, Rungta College of Dental Sciences and Research, Bhilai-Durg, Chhattisgarh, India. E-mail: anandsingh001@gmail.com

Abstract

Warthin's tumor undoubtedly is the most frequent monomorphic adenoma of the major salivary glands. Clinically, it appears as a slow-growing tumor often fluctuant on palpation due to its cystic nature. The treatment of choice is complete excision with wide tumor-free margins. This article highlights a case of Warthin's tumor of the parotid gland in an elderly male patient along with a review of the literature on the aforementioned pathology.

Key words: *Papillary cyst adenoma, parotid gland, Warthin's tumor*

INTRODUCTION

Benign neoplasms of the salivary glands are frequently encountered in dental practice. These account for 3% of the tumors involving the head and neck. The majority of them occur in the parotid gland, and 80% of them are benign. Of these benign neoplasms, 50-80% are pleomorphic adenomas and 5-20% are Warthin's tumors (WT).[1,2] However, Warthin's tumor is the most frequent monomorphic adenoma of the major salivary glands.[3]

This is a curious benign neoplasm with its intimidating histological name, Papillary Cyst Adenoma Lymphomatosum. It was first reported in 1895 by Hildebrand. Albrecht and Artz in 1910 termed this salivary gland tumor as papillary cyst adenoma. However, the eponym WT has been extensively used ever since Aldred Warthin reported two cases of this tumor in 1929.[4,5] Earlier in the literature this was also referred to as adeno-lymphoma, papillary cyst adenoma, cystadeno-lymphoma, and epitheliolymphoid cyst.

WT is generally a disease of elderly men, with the highest incidence in the sixth and seventh decades and the male:female ratio is 4.6:1.[6] The typical features on cytology

of WT include oncocytic cells in cohesive, monolayered sheets; background lymphocytes; and amorphous, cystic debris.[7] Histopathologically, it has a cystic appearance with a double layer of oncocytes surrounding a lymphoid stroma. There are two main cellular components: Epithelial and lymphoid. Treatment consists primarily of tumor removal with superficial parotidectomy and conservative follow-up.[6]

The following case presentation deals with WT of the left parotid gland and highlights its clinicopathologic concepts along with its therapeutic management.

CASE REPORT

A 65-year-old male patient visited the Department of Oral Medicine, with the chief complaint of swelling below the left ear lobe since six years. Swelling was insidious in onset and gradually increasing up to its present size. Medical and family history was non-contributory. Patient was a known smoker since the past 25 years and there was no history of alcohol consumption.

On examination, the lesion extended from the left ear lobule to the lower border of the ramus of the mandible superoinferiorly and also extended behind the left ear [Figure 1]. It was approximately 5 cm in greatest dimensions; smooth contoured, was firm in consistency and had well-defined borders. There were no surface markings and the temperature of the swelling was not elevated. It was midly tender on palpation.

Intraoral examination revealed normal mucosa and orifices

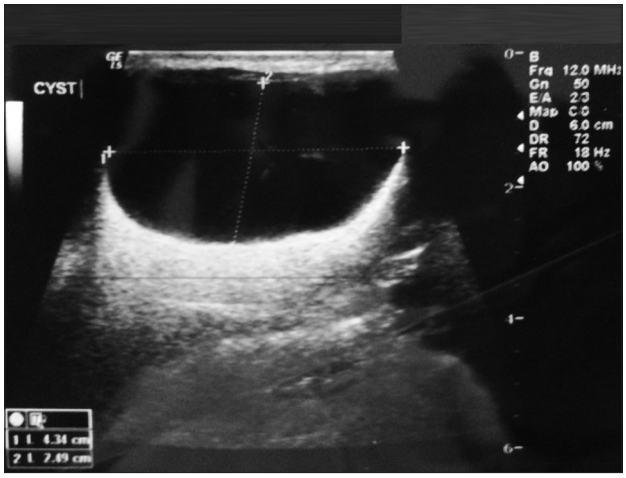

Figure 2: Ultrasonograph showing well-defined hypoechoic mass

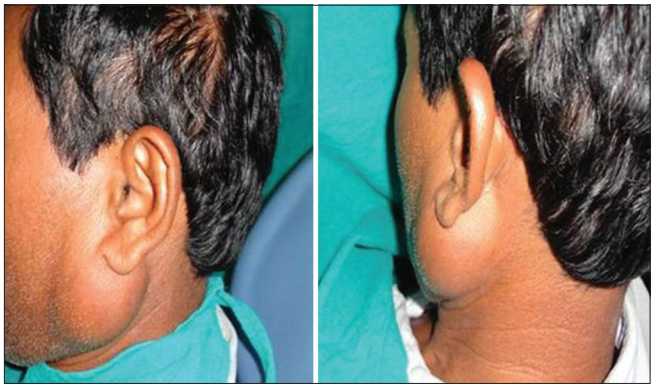

Figure 1: Clinical picture

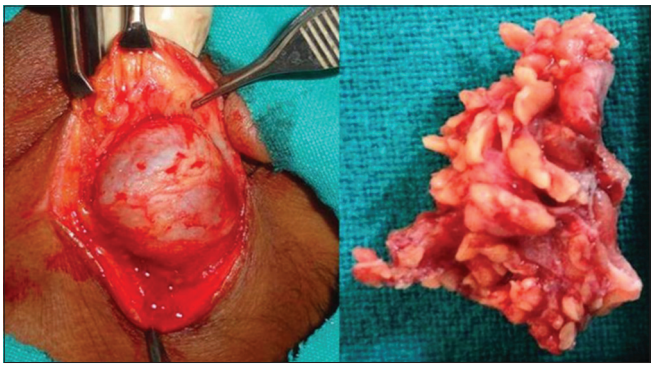

Figure 4: Tumor after superficial parotidectomy

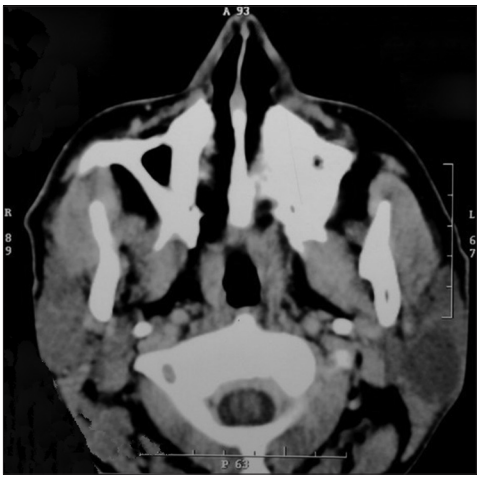

Figure 3: Computed tomography examination showing the lesion

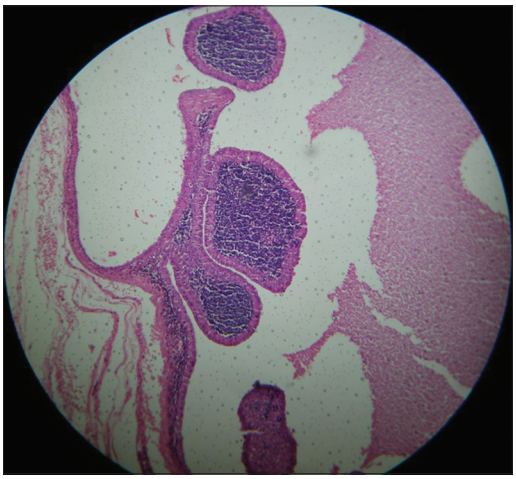

Figure 5: Microscopic picture (×10)

of the parotid gland. Stimulation of the parotid glands yielded normal salivary flow with normal consistency, quantity and color. Other intraoral findings were non-contributory. On aspiration, a clear fluid, light brown in color but viscous in consistency was obtained.

Based on the history and clinical examination, a provisional diagnosis of Warthin's tumor was given. A differential diagnosis of pleomorphic adenoma, a low-grade parotid malignancy, lipoma and neurofibroma arising in the salivary gland were included. The investigatory workup included complete hemogram, extra-oral radiograph, ultrasonography, computed tomography and excisional biopsy of the lesion.

Routine hematological investigation values were found to be within normal limits. The orthopantomogram revealed no abnormalities. Ultrasonographic finding showed a well-defined hypoechoic mass in the lower pole of the left parotid gland. The mass measured about 4.34 × 2.49 × 3.39 cm [Figure 2]. The rest of the parotid gland parenchyma was normal and there was no evidence of ductal dilatation. Computed tomography examination revealed a rounded and well-defined cystic lesion involving the superficial lobe of the left parotid gland [Figure 3].

Later, excisional biopsy of the lesion was planned using partial parotidectomy as the technique of choice [Figure 4]. The tissue obtained was fixed in 10% of neutral buffered formalin, and processed routinely. The sections stained with Hematoxylin and Eosin revealed cystic spaces lined by a papillary epithelial proliferation which was bilayered. The cells of the epithelial lining appeared intensely eosinophilic. At the core of papillary projections a variable amount of lymphoid tissue with mature lymphocytes was observed [Figure 5].

The patient did not present with any post-surgical complications. The patient is under regular follow-up to check recurrences, if any.

DISCUSSION

The most accepted hypothesis about the origin of WT is that it develops from salivary duct inclusions in the lymph nodes, after the embryonic development of the parotid gland. This hypothesis is further supported by the frequent detection of salivary gland tissue in the peri- and intraparotidal lymph nodes. In the parotid region, lymph nodes are occasionally noted to have oncocytic and papillary changes. On the other hand, the tumors presenting epithelial differentiations similar to those observed in WT develop outside lymph nodes and have no lymphoid stromal component[8].

Benign tumors have only rarely been associated with cigarette smoking, which focuses attention on the nature of the underlying neoplastic process and how it may differ from other benign tumors. Although generally believed to be an adenoma, WT, as suggested by Allegra, may be a delayed hypersensitivity reaction.[9]

An interesting fact that caught the attention of the pathologists is that a decline in the incidence in men and a concurrent increased incidence in women has been observed in recent years. The change is probably due to decline in the smoking habit in men and a reverse trend in women.[10] The increased frequency of adenolymphoma has been ascribed to the association of adenolymphoma with smoking and the proportional increase in female smokers.[11] Studies conducted among atomic bomb survivors suggest that radiation may also be implicated in the tumorigenesis. An earlier claim of a strong association with Epstein–Barr virus (EBV), because of the EBV–DNA found in tumor cells in some studies has not been substantiated.[5]

Clinically, WT occurs almost exclusively in the parotid glands, in its superficial lobe and rarely in the deeper lobe (10%).[5] The other preferred locations include the buccal mucosa, submaxillary gland, lip and palate.[12] The patients can be asymptomatic or can have facial pain, rarely, facial nerve palsy may be seen in tumors associated with inflammation and fibrosis, which can be mistaken for malignant tumor. Ipsilateral earache, tinnitus and deafness are uncommon ear symptoms that might be seen in some patients.[5] The size is variable, from a few millimeters to centimeters, averaging 2 to 4 cm in diameter, with a preferred location in the lower pole of the gland (in the jaw angle).[12] Similar findings were observed in our case.

It has been reported predominantly in whites, less frequently in Orientals, and rarely in blacks. The incidence rate is higher than that of salivary gland cancer but is lower than that of benign mixed tumors (pleomorphic adenoma). Malignant transformation is rare.[9]

Macroscopically WT presents as a spherical or ovoid mass, with a dense fibrous capsule and displaying multiple cystic compartments filled with a viscous yellow or dull brown material. However, Eveson and Cawson found 77% cases with an incomplete capsule, a full capsule in 8% and 16% tumors in which there was no evidence of capsule.[12]

The cytological smears in our case showed variable amounts of cellularity, ranging from barely optimum cellularity to occasional hypercellularity. There was an admixture of epithelial fragments, occasional single epithelial cells, and abundant lymphocytes noted in a granular cystic

background. The epithelial cells were oncocytic in appearance with large nuclei, prominent nucleoli, and moderately abundant granular cytoplasm.

Since WT can be multifocal, a preoperative diagnosis by means of Fine Needle Aspiration Biopsy is mandatory and complete bilateral screening of the gland by MRI is needed to program surgery.[3] Tumors originating in the major salivary glands are accessible to biopsy by fine needle aspiration. An experienced cytopathologist can reliably distinguish malignant salivary pathologies from benign, but a histological classification based on only aspiration is an unrealistic goal. Computerized tomography and magnetic resonance imaging enable accurate assessment of tumor extension, compression or infiltration of adjacent structures, presence of nodal metastases and better planning of the therapeutic approach. The definitive diagnosis is done through a histopathological study.[13] Dynamic dual-phase scinti-scanning with technetium-99, a recognized method of identifying adenolymphoma, could be used more frequently in these selected patient groups.[11] Lesion vascularity on initial power Doppler examination is often relatively sparse, but WT that did contain areas of vascularity on initial examination showed a reduction in this vascularity as the tumor size reduced.[14]

With regard to luminal cells of the tumor lining the lymphoid stroma the cells reveal a similar aspect to the striated ducts of the normal salivary glands and have numerous mitochondria. These cells, called oxifile or oncocytic cells are swollen epithelial cells, with abundant eosinophilic granular cytoplasm, rich in mitochondria and enzymes. An increased number of oncocytic cells are also observed in the normal salivary glands once the person gets older. The diffuse proliferation of the oncocytes without other changes has no pathologic significance and is called oncocytosis or oncocytic metaplasia.[5,8]

WT has an epithelial component and a lymphoid stroma. The epithelial cells, the oncocytes, are disposed on two layers, a luminal layer of oncocytic columnar cells, supported by a discontinuous layer of oncocytic basal cells. The nuclei of the luminal cells appear uniform and display palisading towards the free surface. The basal cells possess round to oval nuclei, centrally located, small, with conspicuous nucleoli. The cytoplasm of oncocytes is granular and eosinophilic due to accumulation of mitochondria. The lumen of the cysts contains thick proteinaceous secretions, cellular debris, cholesterol crystals, and sometimes, laminated bodies that resemble corpora amylacea.[5]

Seifert observed a variable quantitative rapport between the stromal and epithelial component. The relative proportions of epithelial and lymphoid components in WT vary. Seifert recognizes four subtypes: Subtype 1 (classic WT) is 50% epithelial (77% of all WT); Subtype 2 (stroma-poor) is 70-80% epithelial (14% cases); Subtype 3 (stroma-rich) is only 20-30% epithelial (2%); and Subtype 4 is characterized by extensive squamous metaplasia.[15]

WT histologically is very peculiar and causes fewer problems in differential diagnosis. However, presence of cellular atypia and a pseudoinfiltrative appearance of the metaplastic squamous epithelium in the residual tumor often can be mistaken for squamous cell or mucoepidermoid carcinoma. Squamous metaplasia of WT usually lacks keratinization, which is seen in most squamous cell carcinoma. In contrast to low-grade mucoepidermoid carcinoma, there is no definite infiltrative growth and the tumor cells appear more frankly squamous. A differential diagnosis must be made also with a variant of papillary thyroid carcinoma recently reported as "Warthin-like". The microscopic characteristic is a prominent lymphoid stroma and oncocytic metaplasia of the epithelium, but the nuclei have chromatin clearing, inclusion and groove-formation and the epithelial cells show immunohistochemical expression of thyroglobulin.[5]

The differential diagnosis of this malignancy should be performed preferably with pleomorphic adenoma and cystoadenoma. The anatomico-pathological diagnosis is generally easy, but it also should be distinguished from canalicular adenoma, sialadenoma as well as from branchial cyst when involving the parotid gland.[12]

Sunardhi-Widyaputra and Van Darmne in 1993 immunohistochemically studied the presence of tenacin, a molecule in the mesenchyme of salivary glands believed to play a role in the embryogenesis and development of tumors, in Papillary Cystadenoma Lymphomatosum and in oncocytoma. They found the protein to be abundant in Papillary Cystadenoma Lymphomatosum, prominent in the proximity of the basement membrane, beneath the oncocytic epithelial components. Tenacin staining in oncocytoma was focal although oncocytes are the actively proliferating cells in this tumor. The presence of oncocytic myoepithelial cells both in Papillary Cystadenoma Lymphomatosum and in oncocytoma surrounded by tenacin suggested that both tumors may arise from stem cells that are capable of differentiating into aberrant epithelial cells (oncocytes), myoepithelial cells in variable proportion or both.[4]

Recent molecular studies have shown that the epithelial component is polyclonal and does not exhibit clonal allelic losses, suggesting that this tumor is not a true neoplasm.[16] Recent studies have also reported the presence of B-cells (CD20), NK (CD56) and T (CD3), including helper subtypes (CD4) and suppressor (CD8) in the tumor's

stroma, something similar to that of normal or reactive lymph nodes. Also, it was found that CD20-positive B-lymphocytes were located in the germ centers and peripheral B-area while CD3-positive T-lymphocytes are located interfollicularly.[17]

Surgeons are traditionalists, and the early experience of our peers has colored current surgical opinion and slowed the introduction of conservative surgery for the benign parotid lump. This situation is now changing, and centers with experience of treating parotid tumors increasingly recognize that benign tumors can be removed safely by techniques much less invasive than a formal parotidectomy.[16] This surgical modality is based on meticulous dissection immediately outside the tumor capsule with preservation of the facial nerves.[18]

In view of the possible association of WT with extra-salivary neoplasms, extensive workup of the patients harboring multiple WT is, therefore, indicated and long-term follow-up is mandatory, due to the possible occurrence of metachronous salivary and extra-salivary tumors even after prolonged time intervals.[3]

Rarely, either the epithelial or lymphoid component of WT can undergo malignant transformation with an estimated incidence of less than 0.1%. In order of frequency, the commonest carcinomas are squamous cell carcinoma, oncocytic carcinoma, adenocarcinoma, undifferentiated carcinoma, mucoepidermoid carcinoma and Merkel cell carcinoma.[5]

Complications must be unusual and of low frequency for the surgical resection of a WT, including some complications considered of minor importance, such as paresis of the ear lobe resulting from manipulation and/or section of the auricularis magnus branch of the superficial cervical plexus. The auricularis magnus nerve, in its path toward the ear lobe, may pass through the tumor, hampering the dissection. Another complication of lesser importance is the change of facial contour due to resection of a large portion of the parotid gland.[19] None of the complications, however, seemed to appear in our case.

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