Iranian Journal of Pathology (2013) 8 (3), 189- 193

Case Report

Malignant Pleomorphic Adenoma (Malignant Mixed Tumor) of the Minor Salivary Glands

Afsaneh Rajabiani[1], Fatemeh Kamrani Kanafi[1], Naser Kamalian[1], Saeed Shoar[2,3] ,Alireza Abdollahi[2], Sara Sheikhbahaei [2]

1. Dept. of Pathology, Dr. Shariati Hospital, Tehran University of Medical Sciences, Tehran, Iran
2. Dept. of Pathology, Imam Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
3. Development Association for Clinical Studies (DACS), School of Medicine, Tehran University of Medical Sciences, Tehran, Iran

ABSTRACT

Salivary gland tumors accounts for less than 1% of all tumors. Minor salivary gland tumors (MSGTs) are uncommon and make up about 10% of all salivary gland neoplasms. The clinical and histopathological distribution of these tumors vary geographically. A case of a 38 yr old man with a minor salivary gland mass at chin region is reported here. The tumor invaded into the anterior surface of the mandible bone and the surrounding soft tissues. The tumor was resected completely with a safe surgical margin of soft tissue and adjacent bone. Histologically, the tumor is characterized by a biphasic pattern, composed of admixture of epithelial and stromal components, associated with cytological atypia and prominent mitoses. The stromal elements are myxoid, chondroid, and osteoid. The chondroid component is more abundant and shows more atypical changes. Overall, the findings were interpreted as malignant pleomorphic adenoma of minor salivary glands of buccal mucosa.

Keywords: **Malignant Mixed Tumor, Minor Salivary Gland**

Received: 05 February 2012
Accepted: 02 October 2012
Address communications to: Dr Alireza Abdollahi, Dept. of Pathology, Imam Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran.
Email: dr_p_abdollahi@yahoo.com

Introduction

Salivary gland tumors accounts for less than 1% of all tumors, and approximately 6% of all head and neck tumors (1).

These tumors affect 3 major salivary glands, i.e. parotid, submandibular and sublingual glands, and hundreds of minor salivary glands lining throughout upper aerodigestive tract. Minor salivary gland tumors (MSGTs) are uncommon and make up about 10% of all salivary gland neoplasms with a higher tendency to palate involvement. Pleomorphic adenoma (PA) has been reported as the most common MSGT (2-7). PAs are composed of epithelial and myoepithelial cells in an abundant stroma which ranges from myxoid to hyaline and even chondroid to osteochondroid (8). Malignant mixed tumors are of three different subtypes: carcinoma ex pleomorphic adenoma (the most common form), carcinosarcoma, and metastasizing mixed tumor. The epithelial component becomes malignant and these tumors characteristically show high-grade biological behavior (9-11). The most common histological forms are poorly differentiated adenocarcinoma and undifferentiated carcinoma. Lung, skeleton, abdomen, and central nervous system are the most common sites of metastasis. Carcinosarcoma is a biphasic tumor with malignant degeneration of both stromal and epithelial components. The salivary gland carcinosarcoma may either arise from a preexisting PA (carcinosarcoma ex PA), or without any remnants of a benign PA (carcinosarcoma de novo) (11,12).

MSGTs represent a heterogeneous group of neoplasm with clinical and histopathological variation, under the influence of geographic and racial factors (5).

This study aimed at reporting a 38-year-old man with a minor salivary gland mass, diagnosed as malignant mixed tumor of the minor salivary gland, with the clinical and histopathological features. As a result, we should consider this kind of tumor when we face a minor salivary gland mass.

Case report

A 38-years old man was referred to the clinic of pathology in Dr Shariati Hospital affiliated to Tehran University of Medical Sciences in Tehran with the tumor of chin region and no relevant past medical history.

He had no history of other medical conditions including diabetes mellitus (DM), heart disease, hypertension, cigarette smoking or other medical disorders. Paraclinical data were totally normal.

Physical examination showed a mass in chin region, measuring 5.5 cm in the largest dimension, with variegated cut surfaces and deep invasion into the anterior surface of the mandible bone and the surrounding soft tissue (Fig. 1). No associated constitutional symptoms were noted.

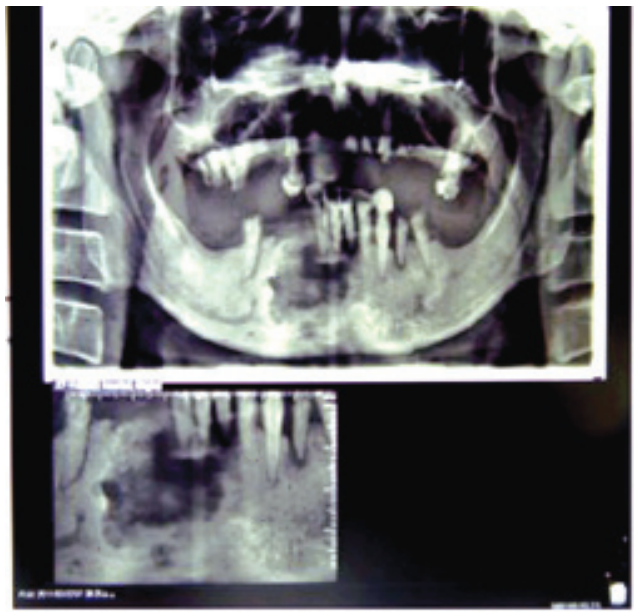

Fig. 1 - Perineurial invasion of tumor (Panorex radiography)

The surgical specimen consisted of an ill-defined tumor mass with irregular outer surface and attachment to a bony fragment that is the anterior portion of mandible bone.

Microscopic examination on Hematoxylin-eosin-stained slides showed a biphasic composition, including epithelial and stromal elements. The

epithelial element is predominantly composed of atypical cells, in the form of solid sheets and nests, including prominent mitotic figures. These findings could be representative of undifferentiated carcinoma. These epithelial cells are set against abundant stroma with myxoid, hyalinized, cartilaginous, and even osteoid features. The stroma is mainly composed of well-developed chondroid areas, showing hypercellularity and cellular atypia as well as many mitotic features

The tumor cells had infiltrated into the surrounding soft tissue and bony trabeculae showing evidence of perineurial invasion (Fig. 2). According to these findings, the tumor is a true malignant pleomorphic adenoma (carcinosarcoma) of the minor salivary gland.

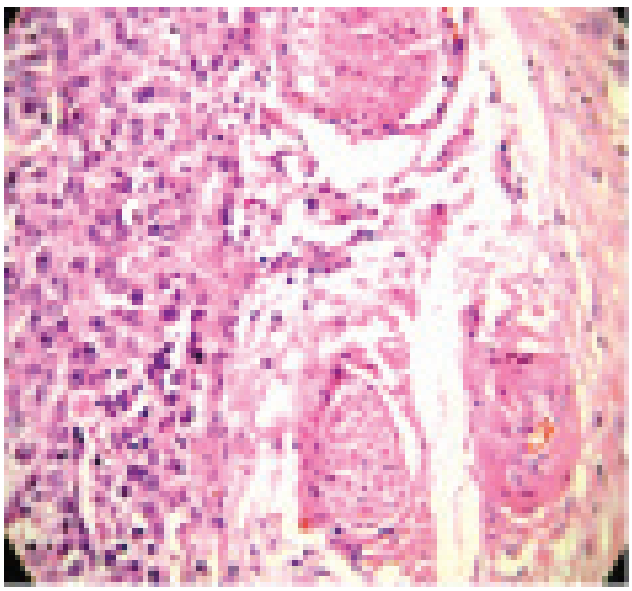

Fig. 2: Infiltrative tumor with invasion into the mandible bone (×400)

Various areas of tumor stroma show positive immunoreactions for the following markers: Vimentin, S-100 protein (either in chondrocytes or in stromal cells), smooth muscle actin and Glial Fibrillary Acidic Protein. The proliferative index is high in both epithelial and stromal elements (Ki67 positive in 80-90% of tumor cells)

Because the epithelial component is undifferentiated, the epithelial membrane antigen (EMA) and cytokeratin did not yield prominent and specific positive immunoreactions.

Discussion

Tumors of salivary gland represent less than 1% of all tumors; minor salivary gland tumors are infrequent, accounting for 10-15% of all salivary gland tumors. The frequency and distribution of these tumors varies geographically (5, 13).

Approximately about one half of the tumors that arise in these glands are malignant. A study conducted on Iranian patients with MSGTs showed the predominance of benign MSGTs (53.7% of cases) over the malignant ones (13). This finding corresponds well with other studies such as Eveson JW *et al*. (54%), Yih *et al*. (56%), Pires *et al*. (55.9%), Waldron *et al*. (57.5%), Toida *et al*. (67%) , and Buchner *et al*. (59%). (3, 4, 6, 13-16). However, Dan Wang *et al*. found that malignant MSGTs were slightly more frequent than benign ones (53.9%) in Chinese population (17). Similar figures are reported by Jansisyanont *et al*. (76.3%) (18).

Pleomorphic adenoma is the most frequent type of benign MSGTs with the prevalence rate of 33-78%. The second most frequent benign MSGT is Cystadenoma. Mucoepidermoid Carcinoma (MEC) is considered to be the most commonly encountered malignant variety of MSGTs (4, 6, 13, 14, 18).

According to many studies, the most common site for MSGTs was the palate. The buccal mucosa and the lip were other major sites (3-6, 13-17).

A study on 82 Iranian patients with intra-oral MSGTs reported the tongue and jaw as the next most frequent sites after the palate and buccal mucosa (13).

The usual clinical presentation of MSGTs is a single, smooth, and nodular mass, but malignant MSGTs grow faster and become ulcerated and over infected, showing adhesion and invasion

into the surrounding tissues (5).

Three entities of malignant pleomorphic adenoma are recognized: carcinoma ex pleomorphic adenoma, carcinosarcoma, and metastasizing pleomorphic adenoma. The metastasizing pleomorphic adenoma is histologically indistinguishable from benign PA but it metastasizes widely to distant sites and can cause mortality (19).

Accurate diagnosis is confirmed mainly by histopathology in paraffin blocks, sometimes demanding additional immunohistochemical studies. Carcinosarcoma is a biphasic tumor. The epithelial component is usually an undifferentiated carcinoma or poorly differentiated adenocarcinoma. The sarcomatous component is usually a chondrosarcoma, or a combination of sarcoma and a malignant proliferation of myoepithelial cells. Histological criteria include cellular dysplasia, vascular, lymphatic, or perineurial invasion, as well as perineurial, lymphatic, or vascular invasion, associated with infiltrative tumoral growth, necrosis or calcification. The presence of one or two of these criteria is sufficient for the diagnosis of malignancy. If the carcinomatous component is undifferentiated, the immunoreacrion for EMA and CK could be weak or non- specific, like other poorly differentiated tumors of the head and neck. The sarcomatous component shows positive reactivity for vimentin, chondrosarcoma for S-100 protein, muscular component for actin, and glial components for GFAP (10).

Carcinosarcoma of the salivary glands arise mainly from the parotid gland (65% of all the cases), but any of the minor salivary glands could be involved (10). Malignant pleomorphic adenomas have also been reported in the trachea and nasal cavity (20, 21). The prognosis is unfavorable (56% 5-year survival and 31% 10-year survival). There is a strong correlation between the local extension and stage of the tumor and patient prognosis. Tumor grading of malignancy and facial nerve palsy are important prognostic factors (10).

Carcinomas of the salivary glands arise mainly from the parotid gland, but any minor salivary gland could be involved and we should consider these kinds of tumors.

Acknowledgement

The authors declare that there is no conflict of interest.

References

1. Stenner M, Klussmann JP. Current update on established and novel biomarkers in salivary gland carcinoma pathology and the molecular pathways involved. Eur Arch Otorhinolaryngol 2009;266(3):333-41.

2. Speight PM, Barrett AW. Salivary gland tumours. Oral Dis 2002;8(5):229-40.

3. Waldron CA, el-Mofty SK, Gnepp DR.Tumors of the intraoral minor salivary glands: a demographic and histologic study of 426 cases. Oral Surg Oral Med Oral Pathol 1988;66(3):323-33.

Pires FR, Pringle GA, de Almeida OP, Chen SY. Intraoral minor salivary gland tumors: a clinicopathological study of 546 cases. Oral Oncol 2007;43(5):463-70.

5. Pons Vicente O, Almendros Marqués N, Berini Aytés L, Gay Escoda C. Minor salivary gland tumors: A clinicopathological study of 18 cases. Med Oral Patol Oral Cir Bucal 2008;13(9):E582-8.

6. Buchner A, Merrell PW, Carpenter WM. Relative frequency of intra-oral minor salivary gland tumors: a study of 380 cases from northern California and comparison to reports from other parts of the world. J Oral Pathol Med 2007;36(4):207-14.

7. Shishegar M, Ashraf MJ, Azarpira N, Khademi B, Hashemi B, Ashrafi A.Salivary gland tumors in maxillofacial region: a retrospective study of 130 cases in a southern Iranian population. Patholog Res Int. 2011;2011:934350.

8. Dabbs DJ. Diagnostic Immunohistochemistry. 3rd ed. New York:Saunders Elsevier;2010.

9. Chimona TS, Koutsopoulos AV, Malliotakis P, Nikolidakis A, Skoulakis C, Bizakis JG. Malignant

mixed tumor of the nasal cavity. Auris Nasus Larynx 2006;33(1):63-6.

10. Mag A, Cotulbea S, Marin Horea A, Lupescu S, Drăgănescu V, Doroş C, *et al*. True Malignant Mixed Tumor (Carcinosarcoma) Of The Parotid Gland – Case Report. TMJ 2010;60(4):338-42.

11. Akan H, Yildiz L, Unal R. Carcinoma ex pleomorphic adenoma of the minor salivary gland with pulmonary metastasis. Diagn Interv Radiol 2008;14(1):3-5.

12. M Sherif S. Pleomorphic Adenoma, Immunohistochemistry. Available in: http://emedicine.medscape.com/article/1630933-overview 2009;14, 2009.

13. Jaafari-Ashkavandi Z, Ashraf MJ, Afandak N. A clinico-pathologic study of 82 intraoral minor salivary gland tumors. Iran Red Crescent Med J 2011;13(9):674-7.

14. Yih WY, Kratochvil FJ, Stewart JC. Intraoral minor salivary gland neoplasms: review of 213 cases. J Oral Maxillofac Surg 2005;63(6):805-10.

15. Eveson JW, Cawson RA. Tumors of the minor (oropharyngeal) salivary glands: a demographic study of 336 cases. Oral Pathol 1985;14:500-9.

16. Toida M, Shimokawa K, Makita H, Kato K, Kobayashi A, Kusunoki Y, *et al*. Intraoral minor salivary gland tumors: a clinicopathological study of 82 cases. Int J Oral Maxillofac Surg 2005;34(5):528-32.

17. Wang D, Li Y, He H, Liu L, Wu L, He Z. Intraoral minor salivary gland tumors in a Chinese population: a retrospective study on 737 cases. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2007;104(1):94-100.

18. Jansisyanont P, Blanchaert RH Jr, Ord RA. Intraoral minor salivary gland neoplasm: a single institution experience of 80 cases. Int J Oral Maxillofac Surg 2002;31(3):257-61.

19. Seifert G. Update on salivary gland tumors. Rev Esp Patol 1999;32(3):431-5.

20. Demirag F, Topcu S, Kurul C, Memis L, Altinok T. Malignant pleomorphic adenoma (malignant mixed tumor) of the trachea: a case report and review of the literature. Eur Arch Otorhinolaryngol 2003;260(2):96-9.

21. Hemmi A, Hiraoka H, Mori Y, Wataya T, Sato H, Jinnai M, *et al*. Malignant pleomorphic adenoma (malignant mixed tumor) of the trachea. Report of a case. Acta Pathol Jpn 1988;38(9):1215-26.