

**TUMORS OF SALIVARY GLANDS****Gaurav Solanki**

Jodhpur National University, Jhanwar Road, Narnadi, Jodhpur-324003, (Rajasthan) India

**Corresponding author\*:** [dr\\_gauravsolanki@yahoo.com](mailto:dr_gauravsolanki@yahoo.com)**Abstracts**

The glands are divided into major and minor salivary gland categories. The major salivary glands are the parotid, the submandibular, and the sublingual glands. The minor glands are dispersed throughout the upper aerodigestive submucosa. Salivary gland tumors are abnormal cells growing in the ducts that drain the salivary glands. Salivary glands tumors are uncommon and are subdivided into benign neoplasms, tumor-like conditions, and malignant neoplasms. They can be removed surgically or one can undergo radiation therapy for their cure. This article throws light on the types of salivary gland tumors, their signs and symptoms, treatment etc.

**Keywords:** Salivary gland, benign tumors, malignant tumors, signs and symptoms, treatment.

**1. Introduction**

The glands are divided into major and minor salivary gland categories. The major salivary glands are the parotid, the submandibular, and the sublingual glands. The minor glands are dispersed throughout the upper aero-digestive sub-mucosa (i.e. palate, lip, pharynx, nasopharynx, larynx, para-pharyngeal space)<sup>1-3</sup>.

Salivary gland tumors are abnormal cells growing in the ducts that drain the salivary glands. Salivary glands tumors are uncommon and represent 2-4% of head and neck neoplasms. They may be subdivided into benign neoplasms and malignant neoplasms. Most (70%) salivary gland tumors originate in the parotid gland. The remaining tumors arise in the submandibular gland (8%) and in the minor salivary glands (22%). 75% of parotid gland tumors are benign, slightly more than 50% of tumors of the submandibular gland and 60-80% of minor salivary gland tumors are found to be malignant<sup>4-6</sup>.

**2. Classification**<sup>7-11</sup>: Tumors arising from the salivary gland may arise from the salivary epithelium (the parenchyma) or the supportive stroma (mesenchymal). Salivary gland tumors may also arise from any cellular component including the basal cells ductal, striated intercalated ducts, acini and the myoepithelial cells. Salivary glands tumors can be broadly subdivided into two main types based on biological behavior - benign and malignant neoplasms.

**2.1 Benign Tumors:** Benign parenchymal tumors are known as Adenomas. These tumors are well circumscribed and generally not associated with pain of any kind. Such tumor cells do not metastasize and do resemble

parenteral cells in some manners. E.g. Pleomorphic Adenoma, Monomorphic Adenoma, etc.

**2.2 Malignant Tumors:** Malignant tumors are known as adenocarcinomas. These tumors are not well circumscribed and generally associated with pain. Such tumor cells do metastasize and don't resemble parenteral cells in any manner. E.g. Adenoid Cystic Carcinoma, Mucoepidermoid carcinoma, etc. these can be subdivided into low and high grade tumors.

**2.2.1 Low-grade**<sup>12-15</sup>:

- Acinic cell tumours: represent 1% of all salivary gland neoplasms. 95% arise in the parotid gland.
- Mucoepidermoid carcinoma (grades I or II).

**2.2.2 High-grade**<sup>16-18</sup>:

- Mucoepidermoid carcinoma (grade III): mucoepidermoid carcinoma is the most common malignancy of the **parotid gland** and is the second most common of the submandibular gland (after adenoid cystic carcinoma). It represents about 8% of all parotid tumours.
- Adenocarcinoma - poorly differentiated carcinoma and anaplastic carcinoma; represents 2-3% of salivary tumours.
- Squamous cell carcinoma.
- Malignant mixed tumours.
- Adenoid cystic carcinoma.

**3. Epidemiology**<sup>19-21</sup>:

- Tumours are most common in the 6th decade of life.
- Benign tumours are more common in women, but malignant tumours have an equal sex distribution.

- Neoplasms of salivary glands have an incidence of about 1 to 2 per 100,000 per annum in England.
- They are fewer than 1% of all cancers and 3-6% of all tumours of the head and neck.
- Malignancy typically presents after age 60, whilst benign lesions usually occur after age 40.
- Certain ethnic groups, e.g. Inuit populations, have a higher rate of salivary gland tumours which is maintained even after migration to a low incidence area. The responsible environmental or genetic factors are unknown.

#### 4. Signs and Symptoms<sup>22-24</sup>:

- A firm, usually painless swelling in one of the salivary glands (in front of the ears, under the chin, or on the floor of the mouth).
- The size of the swelling gradually increases.
- Difficulty moving one side of the face, known as facial nerve palsy
- Pain while eating or chewing
- Presence of a lump in the mouth, under the jaw, or in the neck that does not go away in 2 - 3 weeks.
- Parotid neoplasms most commonly occur in the tail of the gland as a discrete mass in an otherwise normal gland.
- Submandibular neoplasms often appear with diffuse enlargement of the gland.
- Sublingual tumours produce a palpable fullness in the floor of the mouth.
- Minor salivary gland tumours vary according on the site of origin - painless masses on the palate or floor of the mouth are the most common form but laryngeal salivary gland tumours can produce airway obstruction, dysphagia, or hoarseness. In the nasal cavity or paranasal sinus they cause nasal obstruction or sinusitis.
- Facial palsy with a salivary gland mass indicates malignancy.
- Hardness, Fixation, Tenderness, Infiltration of surrounding structures, e.g. facial nerve, local lymph nodes, Overlying skin ulceration, etc can also be noticed.
- Cranial nerve palsy.

**5. Exams and Tests<sup>25</sup>:** An examination by a health care provider or dentist shows a larger-than-normal salivary gland, usually one of the parotid glands. Tests may include X-rays of the salivary gland (called a ptyalogram or

sialogram) to look for a tumor, CT scan or MRI to confirm that there is a growth, and to see if the cancer has spread to lymph nodes in the neck and Salivary gland biopsy or fine needle aspiration to determine whether the tumor is benign or malignant.

**6. Prognosis<sup>26</sup>:** Most salivary gland tumors are noncancerous and slow growing. Removing the tumor with surgery usually cures the condition. In rare cases, the tumor is cancerous and further treatment is needed.

**7. Treatment<sup>27</sup>:** The recommended treatment is usually surgery to remove the affected salivary gland. If the tumor is benign, no other treatment is usually needed. Radiation therapy or extensive surgery may be needed if the tumor is cancerous. Chemotherapy is sometimes used in patients who are considered high risk, or when the disease has spread beyond the salivary glands.

#### 8. Complications<sup>28-30</sup>:

- Cancerous tumors may cause further complications, including spread to other organs (metastasis).
- Rarely, surgery to remove the tumor can injure the nerve that controls movement of the face.
- Damage to the facial nerve may occur as a result of parotid tumour infiltration or surgery. Risk of damage is higher with repeat operations. Perioperative facial nerve monitoring may reduce this risk.
- Recurrence of benign or malignant tumours. Pleomorphic adenomas must be completely removed at primary surgery as recurrent tumours are often multifocal and can occur 10-15 years later with much reduced cure rates (<25%).
- Malignant change - pleomorphic adenomas can undergo malignant change and are called carcinoma ex-pleomorphic adenoma. They represent about 2-4% of salivary gland malignancies. Sudden rapid growth of a previously stable mass is typical. They are aggressive and have a poor prognosis.
- Frey's syndrome (redness and sweating on the cheek, which can appear when eating, seeing or thinking about certain kinds of food which produce strong salivation) can occur after parotid surgery. The autonomic nerves reform inappropriately

(parasympathetic impulses going to sympathetic nerves) so that a stimulus to salivation will make the face sweat.

- Xerostomia and oral mucositis may occur following radiotherapy.

## 9. Some Patents on Salivary Gland Tumors:

**9.1 Detection of MECT1-MAML2 fusion products<sup>31</sup>:** The present invention provides methods and compositions for the diagnosis and treatment of cancer, including cancers involving the NOTCH pathway. In particular, the present invention provides methods and compositions for the diagnosis of Mucoepidermoid carcinoma, the most common malignant salivary gland tumor. The present invention provides methods and compositions for the diagnosis of other tumors associated with translocation.

**9.2 Multiple-Tumor Aberrant Growth Genes<sup>32</sup>:** The invention relates to the multi-tumor aberrant growth gene having the nucleotide sequence of any one of the strands of any one of the members of the High Mobility Group protein genes or LIM protein genes, including modified versions and derivatives thereof. The gene and its derivatives may be used in various diagnostics and therapeutic applications.

**9.3 Plag Gene Family and Tumorigenesis<sup>33</sup>:** The present invention relates to a novel gene family identified as T-genes and being implicated in tumorigenesis having nucleotide sequence of any one of the strands of any one of the members of the PLAG and CTNNB1 gene families. The genes and their derivatives may be used in various diagnostic and therapeutic applications.

**9.4 Imatinib Combinations for Head and Neck Cancers<sup>34</sup>:** The inventor Timothy Ward suggested in this patent that 4-(4-methylpiperazin-1-ylmethyl)-N-{-4-methyl-3-(-4-pyridin-3-yl) -pyrimidin-2-ylamino)-phenyl]-benzamide or a pharmaceutically acceptable salt thereof can be used in the treatment of head and neck cancers.

**9.5 Methods of Treating Cell Proliferative Disorders<sup>35</sup>:** The present disclosure provides methods for the treatment of cell proliferative disorders by administration of a Syk kinase or Syk/Flt-3 kinase inhibitor. Cell proliferative disorders treatable by the methods for hematopoietic neoplasms and virally associated tumors. The compounds are also

directed to therapeutic or prophylactic inhibition of tumor metastasis.

## References:

1. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology: Head and Neck Cancers. National Comprehensive Cancer Network: 2009.
2. Posner M. Head and neck cancer. In: Goldman L, Ausiello D, eds. *Cecil Medicine*. 23rd ed. Philadelphia, Pa: Saunders Elsevier; 2007: chap 200.
3. Lee SC et al; Salivary Gland Neoplasms, Medscape, Dec 2009.
4. Hatch RL, Shah S; Warthin Tumor: A Common, Benign Tumor Presenting as a Highly Suspicious Mass.; *JABFP* Vol. 18 No. 4. 320-322. July-August, 2005.
5. Roh JL, Huh J, Suh C; Primary non-Hodgkin's lymphomas of the major salivary glands. *J Surg Oncol.*; 97 (1): 35-9. Jan 1, 2008.
6. Oral Health Resources - Cancer Fact Sheet. Hosted on the Centers for Disease Control and Prevention website. Page accessed August 13, 2006.
7. Schuller DE, McCabe BF; Salivary gland neoplasms in children. *Otolaryngol Clin North Am. Otolaryngol Clin North Am.*; 10 (2): 399-412. Jun, 1977.
8. Improving outcomes in head and neck cancers, NICE; 2004.
9. Boysen T, Friberg J, Andersen A, et al; the Inuit cancer pattern--the influence of migration. *Int J Cancer*. 122 (11): 2568-72; Jun 1, 2008.
10. <http://www.worldwidewounds.com/1997/july/Thomas-Guide/Dress-Select.html>.
11. Schneider AB, Sarne DH; Long-term risks for thyroid cancer and other neoplasms after exposure to radiation. *Nat Clin Pract Endocrinol Metab. Nat Clin Pract Endocrinol Metab* (2): 82-91; 2005, Dec.
12. Sadetzki S, Oberman B, Mandelzweig L, et al; Smoking and risk of parotid gland tumors: a nationwide case-control study. *Cancer*. 112(9):1974-82; May 1, 2008.
13. Sadetzki S, Chetrit A, Jarus-Hakak A, et al; Cellular phone use and risk of benign and malignant parotid gland tumors--a nationwide case-control study. *Am J Epidemiol*. 2008 Feb 15; 167(4):457-67. Epub; Dec 6, 2007.

14. Epidemiology of Dental Disease, hosted on the University of Illinois at Chicago website. Page accessed January 9, 2007.
15. Schuz J, Jacobsen R, Olsen JH, et al; Cellular telephone use and cancer risk: update of a nationwide Danish cohort. *J Natl Cancer Inst.* 98(23):1707-13; Dec 6, 2006.
16. Referral for suspected cancer, NICE Clinical Guideline, 2005.
17. Lee YY, Wong KT, King AD, et al; Imaging of salivary gland tumours. *Eur J Radiol.* Mar 11, 2008.
18. <http://www.cancer.com>
19. Jeannon JP, Calman F, Gleeson M, et al; Management of advanced parotid cancer. A systematic review. *Eur J Surg Oncol.* Nov 20, 2008.
20. Milano A, Longo F, Basile M, et al; Recent advances in the treatment of salivary gland cancers: emphasis on molecular targeted therapy. Epub. Mar 9, 2007.
21. Oral Health Topics: Anesthesia Frequently Asked Questions, hosted on the American Dental Association website. Page accessed August 16, 2006
22. American Society of Dental Surgeons. American Journal of Dental Science. Harvard University. p. 270.
23. Ganly I, Patel SG, Coleman M, et al; Malignant minor salivary gland tumors of the larynx. *Arch Otolaryngol Head Neck Surg.* *Arch Otolaryngol Head Neck Surg.* 2006
24. Nitzan D, Kronenberg J, Horowitz Z, et al; Quality of life following parotidectomy for malignant and benign disease. *Plast Reconstr Surg.* Oct, 2004.
25. Laurie SA, Licitra L; Systemic therapy in the palliative management of advanced salivary gland cancers. *J Clin Oncol.* 2006 Jun 10; 24 (17): 2673-8.
26. Agulnik M, Siu LL; An update on the systemic therapy of malignant salivary gland cancers: role of chemotherapy and molecular targeted agents. *Curr Med Chem Anticancer Agents.* 4(6):543-51; Nov 4, 2004.
27. Strick MJ, Kelly C, Soames JV, et al; Malignant tumours of the minor salivary glands--a 20 year review. *Br J Plast Surg.* 57(7):624-31; Oct, 2004.
28. Human Health, hosted on the British Nutrition Foundation website; 2004. Page accessed August 13, 2006.
29. Ellies M, Schaffranietz F, Arglebe C, et al; Tumors of the salivary glands in childhood and adolescence. *J Oral Maxillofac Surg.* 64 (7):1049-58; Jul, 2006.
30. Chahin F et al; Salivary Gland Tumors, Minor, Benign, Medscape, Nov 2008
31. K. Frederic in-ventor. Detection of MECT1-MAML2 fusion products. US patent: 7,214,488; 2007 May 8.
32. Bullerdiek Jorn in-ventor. Multiple-Tumor Aberrant Growth Genes. US patent: 10,352,615; 2003 Jan 28.
33. Van De Ven Willem in-ventor. Plag Gene Family and Tumorigenesis. US patent: 6,234,657; 1999 Jun 25.
34. Ward Timothy in-ventor. Imatinib Combinations for Head and Neck Cancers. US patent: 7,587,324; 2004 Mar 17.
35. Masuda Esteban in-ventor. Methods of Treating Cell Proliferative Disorders. Rigel Pharmaceuticals, Inc., South San Francisco, CA. US patent: 7,951,375; 2006 Apr 18.