Second Primaries after Major Salivary Gland Cancer

Uchechukwu C. Megwalu, MD; Edward J. Shin, MD
Department of Otolaryngology-Head and Neck Surgery, The New York Eye and Ear Infirmary, New York, NY, USA

ABSTRACT

Study Objective: to evaluate the risk of second primary cancers in patients with major salivary gland cancer using a large population database, and to examine the effects of sex, salivary gland cancer histology, and radiation therapy on the risk of second primaries.
Design: retrospective population-based study using the Surveillance, Epidemiology, and End Result (SEER) cancer database.
Setting: N/A
Patients or Participants: 15,572 men and women ages 15 and above, diagnosed with cancer of the major salivary glands from 1973 to 2006.
Interventions: N/A
Measurements and Results: There was an increased risk of oral cavity, salivary, lung and bronchus, kidney, and thyroid cancers. Men had an increased risk of developing kidney cancer, compared with women. Patients with mucoepidermoid carcinoma had an increased risk of a second salivary gland cancer, and thyroid cancer. Patients with adenoid cystic carcinoma had an increased risk of oral cavity and nasopharyngeal cancers. Patients with acinar cell had an increased risk of salivary, kidney, and thyroid cancers. Patients who received radiation therapy had a higher incidence of lung and bronchus, laryngeal, and thyroid cancers compared with patients who did not receive radiation therapy. Patients had an increased risk of developing second primaries, even 10 years after diagnosis of primary salivary gland cancer.
Conclusions: Patients with major salivary gland cancers at a risk for certain second primary cancers. This highlights the need for long-term surveillance in these patients, not only for recurrence, but also for second primary cancers.

CONTACT

Uchechukwu C. Megwalu, MD
The New York Eye and Ear Infirmary
Email: megwaluu@yahoo.com
Phone: (212) 979-4545
Website: www.nyee.edu

INTRODUCTION

Salivary gland cancers are relatively rare, with an annual age-adjusted incidence of 0.9 in 100,000.[1] They account for approximately 6% of head and neck malignancies, and 0.3% of all cancers.[2] It is thought that several factors, such as exposure to ionizing radiation, dental x-rays, and silica dust may play a role in the development of salivary gland cancer.[3] However, the etiology of salivary gland cancer is not completely understood.

Surveillance after treatment of salivary gland cancer generally focuses on monitoring of locoregional and distant recurrence. There is evidence that monitoring for second primary cancers should also be considered. Several studies have examined the incidence of second primary cancers in salivary gland cancer patients with varied, sometimes conflicting, results.[4,5] Unfortunately, most of these studies had small sample sizes, and none included cases diagnosed after 1992. The purpose of our study was to evaluate the risk of second primary cancers in patients with major salivary gland cancer using a large population database, and to examine the effects of sex, salivary gland cancer histology, and radiation therapy on the risk of second primaries.

METHODS AND MATERIALS

Data was obtained from the Surveillance, Epidemiology, and End Result (SEER) program of the National Cancer Institute, which includes data from 9 population-based registries: 5 states (Connecticut, Hawaii, Iowa, New Mexico, and Utah), and 4 standard metropolitan areas (Atlanta, Georgia; Detroit, Michigan; San Francisco-Oakland, California; and Seattle-Puget Sound, Washington). The study cohort consisted of men and women ages 15 and above, diagnosed with cancer of the major salivary glands from 1973 to 2006. The International Classification of Diseases for Oncology (ICD-O) site codes used for major salivary gland cancer were C07.9 (parotid gland), C08.0 (Submandibular gland), C08.1 (sublingual gland), C08.8 (overlapping lesion of major salivary glands, C08.9 (major salivary gland, NOS). The ICD-O histology/behavior codes were grouped into several categories: mucoepidermoid (8430/3), adenoid cystic (8200/3), adenocarcinoma (8255/3), acinar carcinoma (8430/3). SEER files also contain information on the initial type of therapy within broad categories, but do not record subsequent therapies. Radiation therapy is recorded as: none; beam radiation; radioactive implants; radioisotopes; combination of beam with implants or isotopes; Radiation, NOS; other radiation; refused; recommended, unknown if administered; and unknown. For the purposes of our study, these were grouped into 2 broad categories: radiation, and no radiation. The latency exclusion period for second primaries was 6 months. The SEER computer software (SEER*Stat 6.5.2) was used for statistical analysis. Standardized incidence ratios (SIR) were calculated to evaluate the risk of second primaries for each site.

RESULTS

From 1973 through 2006, the SEER system received 15,572 reports of major salivary gland cancer on patients ages 15 and above. There were 8,480 men and 7,092 women. Mucoepidermoid was the most common histology (20%), followed by adenoid cystic carcinoma (11%), and acinar cell (9%). There were only 6 cases of adenocarcinoma.

There was an increased risk of oral cavity, salivary, lung and bronchus, kidney, and thyroid cancers overall (Table 1). Men had an increased risk of developing kidney cancer, while women did not.

Patients with mucoepidermoid carcinoma had an increased risk of a second salivary gland cancer, and thyroid cancer. Patients with adenoid cystic carcinoma had an increased risk of oral cavity and nasopharyngeal cancers. Patients with acinar cell carcinoma had an increased risk of salivary, kidney, and thyroid cancers. (Table 2).

RESULTS

Patients who received radiation therapy had an increased incidence of lung and bronchus, laryngeal, and thyroid. Patients who did not receive radiation therapy had an increased incidence of kidney cancer (Table 3). Both groups had an increased risk of developing salivary gland and oral cavity second primaries.

Patients with salivary gland cancer have an increased risk of developing oral cavity, salivary gland, and lung and bronchus second primaries, even 10 years after diagnosis of primary salivary gland cancer (Table not shown).

Table 1. Risk of second primary cancers by site

	Male and female O/E	Male O/E	Female O/E
All sites	1.24*	1.27*	1.20*
Oral cavity	3.48*	3.72*	2.97*
Salivary Gland	9.97*	6.25*	16.51*
Oropharynx	1.62	1.62	1.61
Nasopharynx	2.5	1.82	4.01
Esophagus	0.89	0.58	1.88
Stomach	0.71	0.71	0.69
Small Intestine	0.68	0.6	0.78
Colon	1.14	1.09	1.2
Larynx	1.66	1.53	2.31
Lung and Bronchus	1.60*	1.77*	1.32*
Melanoma of the Skin	1.17	1.37	0.81
Female Breast	0.96	0	0.96
Cervix	1.28	0	1.28
Uterus	0.71	0	0.71
Ovary	1.2	0	1.2
Prostate	1.08	1.08	0
Kidney	1.68*	1.70*	1.64
Brain	0.86	1.06	0.59
Thyroid	2.66*	3.26*	2.38*

* p<0.05

Table 2. Risk of second primary cancers by site and primary histology

	Muco-epidermoid O/E	Adenoid cystic O/E	Acinar cell O/E
Oral cavity	1.53	3.76*	1.57
Salivary Gland	8.97*	7.61	31.36*
Nasopharynx	0	16.88*	0
Esophagus	0.51	0	1.1
Larynx	1.11	0	1.3
Lung and Bronchus	1.25	1.14	1.48
Melanoma of the Skin	0.36	1.26	0.34
Bones and Joints	5.68	8.94	0
Female Breast	0.95	1	1.11
Cervix	2.5	2.04	0
Uterus	0.84	0.99	0.31
Ovary	1.15	1.37	0.57
Prostate	1.1	1.17	1.23
Kidney	1.24	2.12	2.98*
Brain	1.09	0	0
Thyroid	3.97*	2.61	3.85*

* p<0.05

Table 3. Effect of radiation therapy on risk of second primary cancer

	Radiation O/E	No Radiation O/E
All sites	1.37*	1.14*
Oral cavity	3.64*	3.47*
Salivary Gland	12.36*	8.35*
Oropharynx	2.7	0.76
Nasopharynx	2.76	2.37
Esophagus	1.23	0.64
Larynx	3.08*	0.48
Lung and Bronchus	2.11*	1.18
Melanoma of the Skin	1.38	0.86
Bones and Joints	6.07	0
Female Breast	0.91	1.02
Cervix	1.66	1.07
Uterus	0.48	0.88
Ovary	1.54	1.01
Prostate	1.03	1.16
Urinary Bladder	1	0.79
Kidney	1.48	1.90*
Brain	0.84	0.91
Thyroid	2.95*	2.39

* p<0.05

DISCUSSION

The results of our studies show that patients diagnosed with major salivary gland cancer are at increased risk for developing second primary cancers, especially in the salivary gland, oral cavity, thyroid, lungs, and kidneys.

The risk of second primaries remains high even 10 years after diagnosis of the initial primary cancer, especially for cancers of oral cavity, salivary gland, and lung/bronchus. This emphasizes the importance of long-term surveillance for patients after treatment of major salivary gland cancer. The sites of second primary cancers were similar between the sexes, except for kidney cancer, which showed increased risk in men, compared with women.

The sites of second primary cancers varied according to the histology of the primary salivary gland cancer. Radiation therapy increased the risk of developing cancers of the thyroid, laryngeal, and lung/bronchus. However, there was an increased risk of developing oral cancer, or a second salivary gland cancer regardless of radiation status.

The increased risk of thyroid cancer may be due to the fact that ionizing radiation exposure is a significant risk factor for both thyroid and salivary gland cancer.[3,6] This is supported by the increased risk of thyroid cancer seen in patients who received radiation therapy. A study on second primaries after thyroid cancer also found an increased risk of salivary gland cancer in thyroid cancer patients. [9] The increased risk of oral cavity, lung, and kidney cancers cannot be explained by any currently known common etiology.

CONCLUSIONS

Our study highlights the importance of surveillance in patients with major salivary gland malignancy, not only for locoregional and distant recurrences, but also for second primary cancers. Our results show that the risk of second primary cancers persists even 10 years after diagnosis of the initial cancer. This suggests the need for long-term surveillance, probably throughout the patient's lifetime.

REFERENCES

1. Pinkston JA, Cole P. Incidence rates of salivary gland tumors: results from a population-based study. Otolaryngology - Head & Neck Surgery 1999; 120(6):834-40.
2. Ries LAG, Hankey BF, Miller BA *et al.*, Cancer statistics review 1973-88, National Cancer Institute, Bethesda (MD) (1991) NIH Publication No 91-2789.
3. Spitz MR, Fueger JJ, Goepfert H, Newell GR. Salivary gland cancer. A case-control investigation of risk factors. Archives of Otolaryngology -- Head & Neck Surgery. 1990; 116(10):1163-6.
4. Biggar RJ, Curtis RE, Hoffman DA, Flannery JT. Second primary malignancies following salivary gland cancers. British Journal of Cancer. 1983; 47(3):383-6.
5. Sun EC, Curtis R, Melbye M, Goedert JJ. Salivary gland cancer in the United States. Cancer Epidemiology, Biomarkers & Prevention. 1999; 8: 1095-1100.
6. Becker FO, Economou SG, Southwick HW, Eisenstein R. Adult thyroid cancer after head and neck irradiation in infancy and childhood. Annals of Internal Medicine. 1975; 83(3):347-51.
7. Brown AP, Chen J, Hitchcock YJ, Szabo A, Shrieve DC, Tward JD. The risk of second primary malignancies up to three decades after the treatment of differentiated thyroid cancer. Journal of Clinical Endocrinology & metabolism. 2008; 93(2): 504-515.