

## Cancers of the Upper Aerodigestive Tract in Korea

Cancers of the upper aerodigestive tract (UADT) constitute 3.5-4% of all malignancies. Since the majority of cases are squamous cell carcinomas which are related with epidemiologic factors, a different pattern of UADT cancer might be present between the Western and Asian populations. We performed a pathology-based statistical study on UADT cancers in Korean patients. Cases from Korea Cancer Center Hospital, from January 1, 1988 through December 31, 1998, were subjected to the study. Among 2,842 cases, epithelial malignancies accounted for 87.8%, with squamous cell carcinoma as the major type (76.5%). The larynx was the most commonly affected site (26%), followed by the oral cavity (25.1%), oropharynx (13%), nasopharynx (9%), hypopharynx (8.4%), paranasal sinuses (6.4%), nasal cavity (6%) and salivary glands (6.1%). The percentage of squamous cell carcinoma was highest (98.7%) at the hypopharynx, and lowest at the nasal cavity (42.3%), which showed the most diverse tumor entities. Korean patients with UADT cancers presented with a higher incidence of non-epidermoid malignancy including sarcoma (1.5%) and malignant melanoma (1.4%), and a higher frequency of involvement of the sinonasal tract, compared with the Western patients.

**Key Words :** Head and Neck Neoplasms; Incidence; Carcinoma, Squamous Cell; Sarcoma; Larynx; Hypopharynx; Oropharynx; Mouth Mucosa; Nasopharynx; Nasal Mucosa

Kyung-Ja Cho\*, Shin-Kwang Khang\*,  
Seung-Sook Lee<sup>†</sup>, Jae-Soo Koh<sup>†</sup>,  
Jin-Haeng Chung<sup>†</sup>, Yong-Sik Lee,  
Yoon-Sang Shim

Department of Diagnostic Pathology\*, Asan Medical  
Center, University of Ulsan College of Medicine;  
Departments of <sup>†</sup>Anatomic Pathology and  
Otolaryngology, Korea Cancer Center Hospital, Seoul,  
Korea

Received : 3 September 2001

Accepted : 19 October 2001

### Address for correspondence

Kyung-Ja Cho, M.D.  
Department of Diagnostic Pathology, Asan Medical  
Center, University of Ulsan College of Medicine, 388-1  
Pungnap-dong, Songpa-gu, Seoul 138-736, Korea  
Tel : +82-2-3010-4545, Fax : +82-2-472-7898  
E-mail : kjc@med.ulsan.ac.kr

## INTRODUCTION

Cancers of the upper aerodigestive tract (UADT) mostly consist of carcinomas of the mucosal epithelium or secretory gland origin. The major histologic type worldwide is squamous cell carcinoma (SCC), which comprised 95% of 42,990 UADT cancers in the recent Surveillance, Epidemiology, and End Results (SEER) registries in U.S.A. (1). SCC of the UADT has a strong epidemiologic background, including racial difference and environmental factors, such as alcohol and tobacco consumption, diet, and viral infection. Therefore, a different pattern of UADT cancer is expected between the Western and Asian population. Since standardized multi-institutional studies on UADT cancers have not been activated, only limited statistical data on this category have been available in Korea (2). We report a pathology-based statistics on cancers of the UADT, from a single institute in Korea.

## MATERIALS AND METHODS

All patients who had been diagnosed with a head and neck tumor at Korea Cancer Center Hospital, from January 1, 1988 through December 31, 1998, were retrieved from

the pathology report file of the hospital. Tumors of the head and neck lymph node, skin, eyelids, eye, teeth, ear, and central nervous system were excluded. Metastatic or recurrent tumors in the same patients were not counted separately. Minor salivary gland tumors from the oral or oropharyngeal region were classified as salivary gland tumors. A total of 2,842 cases of malignancies of the larynx, hypopharynx, oropharynx, oral cavity, nasopharynx, nasal cavity, paranasal sinuses (PNS), and salivary glands were subjected to the study. Their hematoxylin-and-eosin-stained pathologic slides were reviewed by one of the authors (KJC). In cases with ambiguous original diagnoses, reclassifications were performed after peer review and ancillary studies.

## RESULTS

Table 1 shows the frequency percentages and categories of cancers of previously mentioned sites of the UADT. The larynx was the most commonly affected site, comprising 26% of total cases, followed by the oral cavity (25.1%), oropharynx (13%), nasopharynx (9%), hypopharynx (8.4%), PNS (6.4%), nasal cavity (6%), and salivary glands (6.1%). On pathologic categorization, the majority of the tumors were carcinomas (87.8%), and the remaining non-

**Table 1.** Distribution & histologic categories of upper aerodigestive tract cancers

| Categories \ Sites | Lx          | Hpx        | Opx         | OC          | Npx        | NC         | PNS        | SG         | Total         |
|--------------------|-------------|------------|-------------|-------------|------------|------------|------------|------------|---------------|
| Carcinoma          | 734         | 237        | 246         | 640         | 223        | 110        | 148        | 157        | 2,495 (87.8%) |
| Sarcoma            | 2           | -          | 2           | 16          | 1          | 4          | 14         | 4          | 43 (1.5%)     |
| Melanoma           | 1           | 1          | -           | 15          | -          | 13         | 10         | -          | 40 (1.4%)     |
| Lymphoma           | 2           | 2          | 120         | 43          | 32         | 39         | 16         | 11         | 255 (9.0%)    |
| Others             | -           | -          | 1           | -           | 1          | 4          | 3          | -          | 9 (0.3%)      |
| Total              | 739 (26.0%) | 240 (8.4%) | 369 (13.0%) | 714 (25.1%) | 257 (9.0%) | 170 (6.0%) | 181 (6.4%) | 172 (6.1%) | 2,842 (100%)  |

Lx, larynx; Hpx, hypopharynx; Opx, oropharynx; OC, oral cavity; Npx, nasopharynx; NC, nasal cavity; PNS, paranasal sinuses; SG, salivary glands.

**Table 2.** Distribution & histologic types of epithelial malignancies of upper aerodigestive tract

| Categories \ Sites                    | Lx          | Hpx         | Opx         | OC          | Npx        | NC         | PNS        | SG         | Total        |
|---------------------------------------|-------------|-------------|-------------|-------------|------------|------------|------------|------------|--------------|
| Squamous cell carcinoma               | 727 (33.4%) | 237 (10.9%) | 222 (10.2%) | 637 (29.3%) | 144 (6.6%) | 72 (3.3%)  | 112 (5.1%) | 24 (1.1%)  | 2,175 (100%) |
| Variants                              | 10          | 1           | 3           | 14          | 16         | 12         | 5          | -          | 61           |
| Undifferentiated carcinoma            | -           | -           | 24          | -           | 79         | 12         | 2          | 4          | 121          |
| Neuroendocrine carcinoma              | 4           | -           | -           | 3           | -          | 3          | 3          | -          | 13           |
| Adenocarcinoma                        | 3           | -           | -           | -           | -          | 23         | 31         | 129        | 186          |
| Adenocarcinoma, NOS                   | 3           | -           | -           | -           | -          | 8          | 9          | 11         | 31           |
| Adenoid cystic carcinoma              | -           | -           | -           | -           | -          | 13         | 20         | 50         | 83           |
| Mucoepidermoid carcinoma              | -           | -           | -           | -           | -          | 1          | 2          | 33         | 36           |
| Malignant mixed tumor                 | -           | -           | -           | -           | -          | 1          | -          | 13         | 14           |
| Polymorphous low grade adenocarcinoma | -           | -           | -           | -           | -          | -          | -          | 10         | 10           |
| Others                                | -           | -           | -           | -           | -          | -          | -          | 12         | 12           |
| Total                                 | 734 (29.4%) | 237 (9.5%)  | 246 (9.9%)  | 640 (25.7%) | 223 (8.9%) | 110 (4.4%) | 148 (5.9%) | 157 (6.3%) | 2,495 (100%) |

Lx, larynx; Hpx, hypopharynx; Opx, oropharynx; Npx, nasopharynx; OC, oral cavity; NC, nasal cavity; PNS, paranasal sinuses; SG, salivary glands; NOS, not otherwise specified.

epithelial malignancies included malignant lymphomas (9%), sarcomas (1.5%), malignant melanomas (1.4%) and miscellaneous types (0.3%).

Histologic types of the carcinomas according to each site are shown in Table 2. SCC and its variants (basaloid, sarcomatoid, and verrucous) occupied 76.5% of total cases and 87.2% of all carcinomas, followed by adenocarcinomas (including salivary types) (6.5%), undifferentiated carcinomas (4.3%), and neuroendocrine carcinomas (0.5%).

Table 3 shows the types and distribution of non-epithelial malignancies. Malignant lymphomas, most commonly from the oropharynx, comprised 73.5% of 347 non-epithelial malignancies. The number of cases of sarcoma and that of malignant melanoma were similar. Sarcomas most commonly developed at the oral cavity and PNS. The most frequent types were osteosarcoma and rhabdomyosarcoma. Mucosal melanomas, comprising 1.4% of UADT cancers, occurred mainly at the nasal cavity, PNS, and oral cavity. Characteristics for each primary site are as follows.

### Larynx

Cancers of the larynx accounted for 26% of total cases, and mostly were SCC and its variants (98.3%). Variants

were basaloid and sarcomatoid SCC. Rare cases of neuroendocrine carcinoma and adenocarcinoma also occurred. Non-epithelial malignancies comprised only 0.5%.

### Hypopharynx

Almost all (98.8%) cases were SCC. Only 3 cases of non-epithelial neoplasm affected this site.

### Oropharynx

Two thirds of the cases were carcinomas, which were classified as squamous cell (60.1%) and undifferentiated types (6.5%). The remaining one third were mostly malignant lymphomas (32.5%), except for a few cases of other types. The palatine tonsils were the most prevalent subsite for malignant lymphoma, of which 80% were of a B cell type.

### Oral cavity

Being the second most common site for the UADT cancers, the oral cavity also had SCC as its major type (89.6%). However, sarcomas (2.2%), melanomas (2.1%), and lymphomas (6.0%) were more frequent at the oral cavity than

**Table 3.** Distribution & histologic types of non-epithelial malignancies of upper aerodigestive tract

| Categories                     | Sites | Lx       | Hpx      | Opx         | OC        | Npx        | NC         | PNS       | SG        | Total      |
|--------------------------------|-------|----------|----------|-------------|-----------|------------|------------|-----------|-----------|------------|
| Sarcoma                        |       | 2        | -        | 2           | 16        | 1          | 4          | 14        | 4         | 43         |
| Osteosarcoma                   |       | -        | -        | -           | 5         | -          | -          | 2         | 1         | 8          |
| Rhabdomyosarcoma               |       | -        | -        | -           | 4         | -          | 1          | 2         | 1         | 8          |
| Hemangiopericytoma             |       | -        | -        | -           | 1         | -          | 1          | 3         | -         | 5          |
| Hemangioendothelioma           |       | -        | -        | -           | 1         | -          | -          | 1         | -         | 2          |
| Kaposi's sarcoma               |       | -        | -        | -           | 1         | -          | -          | -         | -         | 1          |
| Malignant fibrous histiocytoma |       | -        | -        | -           | 1         | -          | -          | 4         | -         | 5          |
| Synovial sarcoma               |       | -        | -        | -           | -         | -          | -          | 2         | 1         | 3          |
| Fibrosarcoma                   |       | -        | -        | -           | 2         | -          | -          | -         | -         | 2          |
| Leiomyosarcoma                 |       | 1        | -        | -           | -         | 1          | -          | -         | -         | 2          |
| Unclassified                   |       | 1        | -        | 2           | 1         | -          | -          | -         | 1         | 5          |
| Malignant melanoma             |       | 1        | 1        | -           | 15        | -          | 13         | 10        | -         | 40         |
| Malignant lymphoma             |       | 2        | 2        | 120         | 43        | 32         | 39         | 6         | 11        | 255        |
| Others                         |       | -        | -        | -           | -         | -          | -          | -         | -         | 9          |
| Esthesioneuroblastoma          |       | -        | -        | -           | -         | 1          | 4          | -         | -         | 5          |
| Paraganglioma                  |       | -        | -        | 1           | -         | -          | -          | -         | -         | 1          |
| Meningioma                     |       | -        | -        | -           | -         | -          | -          | 3         | -         | 3          |
| Total                          |       | 5 (1.4%) | 3 (0.9%) | 123 (35.4%) | 34 (9.8%) | 60 (17.3%) | 60 (17.3%) | 33 (9.5%) | 15 (4.3%) | 347 (100%) |

Lx, larynx; Hpx, hypopharynx; Opx, oropharynx; Npx, nasopharynx; OC, oral cavity; NC, nasal cavity; PNS, paranasal sinuses; SG, salivary glands.

in the previously mentioned sites.

#### Nasopharynx

Undifferentiated carcinomas accounted for 30.7%, although SCC were more common (56.2%). Malignant lymphoma, being the third commonest type of cancer (12.5%) at this site, equally consisted of B cell and T cell types.

#### Nasal cavity

The nasal cavity was the least common site for head and neck malignancy (6%), and revealed the lowest relative incidence of SCC (42.2%). Adenocarcinoma including salivary types was the second most common type of carcinoma, comprising 13.5% of nasal cavity cancers. Malignant lymphoma was also a major cancer (23%) at this location, and 75% of them were of an angiocentric T/NK cell type. Sarcomas and melanomas accounted for 10% of the cases. Four cases of olfactory neuroblastoma, which is a unique cancer of the olfactory mucosa, were identified. The nasal cavity proved to be the origin of diverse types of malignancy.

#### Paranasal sinuses

SCC was also the most common type (62%) at this location, but the incidences of adenocarcinomas (17.1%), sarcomas (7.7%), and melanomas (5.5%) were relatively high.

#### Salivary gland

Eighty-six percent of major and minor salivary gland can-

cers were non-epidermoid, dominated by adenoid cystic carcinomas (29.1%), mucoepidermoid carcinomas (19.2%), and malignant mixed tumors (8.3%).

## DISCUSSION

Cancers of the UADT are relatively common forms of malignancy in the socioeconomic situation with high risk factors, such as tobacco and alcohol abuse, poor oral hygiene, and nutritional deficiency. The incidences of head and neck malignancies tend to be underestimated, because UADT is anatomically composed of a number of small sites and sub-sites. According to the recent Annual Report of the Central Cancer Registry in Korea (2), cancer of the larynx was the 11th common form of malignancy in males. When numbers of cancers arising from the oral cavity, pharynx, salivary gland, sinonasal tract, and larynx were taken together, they accounted for 3.6% of total (82,320) malignancies and 4.9% of 46,908 male patients, representing the 5th place next to the stomach, liver, lung, and colon cancers. It is interesting that this proportion is very similar to that in the previous SEER statistics by National Cancer Institute, U.S.A., in which cancers of the UADT represented 3.5% of all malignancies (3). Since the UADT cancer incidence among black males in the U.S.A. was twice of that recorded among white males, it can be assumed that the Korean male population shows racial predisposition for UADT cancer at the intermediate level between black and white males.

The pathologic aspects of UADT cancers tend to be overlooked, because most of them are squamous cell carcinomas, which are not much attractive to both pathologists and

clinicians. However, the head and neck is the location with the most diverse pathologic manifestations, as it is anatomically composed not only of squamous or columnar epithelium, of either ectodermal or endodermal origin, but also of various types of mesenchymal and neural tissues.

In this study, squamous cell carcinomas and its variants accounted for 76.5% of all UADT cancers, and this proportion was smaller than those reported in the U.S.A./Canadian statistics (1, 3). If we exclude malignant lymphoma to render the data to be comparable with them, SCC represented 84.1% of total, still lower than 88.6%, 94.1%, or 94.6% of U.S.A./Canadian statistics. Anatomic distribution of SCC was similar to that of the Western population, with the larynx and oral cavity involved in approximately two thirds of cases. However, the relative frequencies of involvement of the nasopharynx (6.6%), nasal cavity (3.3%), and PNS (5.1%) were higher among Korean patients than those from the U.S.A./Canadian statistics (nasopharynx, 4.4-5.1%; nasal cavity, 1.3-2.0%; sinuses, 1.8%) (1). Incidences of nasopharyngeal undifferentiated carcinoma and sinonasal adenocarcinoma also appeared to be higher among Koreans. Besides the conventional SCC, some distinct variants of SCC occurred in the head and neck. Among them, basaloid squamous carcinoma (4) most often involved the supraglottic larynx and hypopharynx, while sarcomatoid carcinoma (5) was prevalent at the sinonasal tract.

True sarcomas are rare in the head and neck. In this study, they accounted for 1.5% of UADT cancers, and this proportion was higher than those reported in the Western countries (0.5-1.24%) (1, 3, 6). Prevalent sites for sarcoma were the PNS (including maxilla) and oral cavity (including mandible), and the most common histologic types were osteosarcoma and rhabdomyosarcoma. The latter tumor frequently involved children and adolescents, but also adults. Differential diagnosis between rhabdomyosarcoma and non-rhabdomyosarcomatous sarcoma is important in terms of therapeutic and prognostic implications, and is not difficult if immunohistochemistry is applied (7). The etiology of sarcomas of the head and neck is not well known. Risk factors for carcinomas do not appear to be involved in sarcoma development (8). A well recognized etiologic factor for head and neck sarcoma is the ionizing radiation, as documented in patients with carcinoma or retinoblastoma after radiotherapy (9, 10). Our series included one case of osteosarcoma, which developed 9 yr after radiation treatment for tongue cancer.

Mucosal melanomas of the UADT account for about 1% of all malignant melanomas (11, 12). They represented 1.4% of UADT cancers in our series, while the recent U.S.A./Canadian statistics showed only 0.4% of melanoma cases (1). Mucosa of the sinonasal tract was the most frequently affected site, as previously described (11, 13). Oral cavity malignant melanomas in our series appeared to be more common than in previous reports (13, 14). Diagnosis of the head and neck mucosal melanoma requires a high

index of suspicion, because not only of its rarity, but also of its histologic diversity. They are commonly amelanotic, and can show small round cell, epithelioid, spindle cell, pleomorphic, or myxoid pattern, mimicking many other types of malignancy (11, 14). Once suspected, immunohistochemical study can almost confirm the diagnosis.

The prognosis of malignant melanoma is known to be the worst among UADT cancers, showing 17-45% of 5-yr survival rates (11-14), as compared with 50-59% of carcinoma (1, 3) and 60-66% of sarcoma (7, 15, 16). It is regrettable that our data could not supply an adequate survival analysis.

Although SCC was the most common type of cancer at any location of the UADT (except salivary glands), its proportion was different among the sites. The nasal cavity, which is composed of ectoderm-derived columnar epithelial mucosa with numerous secretory glands, neuron-derived olfactory epithelium, and soft and bony mesenchymal tissue with abundant vasculature, revealed the most diverse types of malignant tumors. SCC accounted for only 42.3% of nasal cavity cancers. Both pathologists and clinicians always should have a high index of suspicion on the variety of cancers that affect such sites, since many of them are distinct in terms of treatment modality and prognosis.

It was an unexpected finding that a relatively higher incidence of non-epidermoid malignancy was noted among head and neck cancer patients in Korea, than in the Western countries. A standardized multi-center study would be required to prove significance in the difference. Furthermore, pathogenetic studies on non-epidermoid malignancy of the UADT should be encouraged.

## REFERENCES

1. Skarsgard DP, Groome PA, Mackillop WJ, Zhou S, Rothwell D, Dixon PF, O'Sullivan B, Hall SF, Holowaty EJ. *Cancers of the upper aerodigestive tract in Ontario, Canada, and the United States. Cancer* 2000; 88: 1728-38.
2. Annual report of the central cancer registry in Korea. *Central Cancer Registry Center in Korea, Ministry of Health and Welfare, Republic of Korea, April, 2001.*
3. Muir C, Weiland L. *Upper aerodigestive tract cancers. Cancer* 1995; 75: 147-53.
4. Kim JY, Cho KJ, Lee SS, Khang SK, Shim YS. *Clinicopathologic study of basaloid squamous carcinoma of the upper aerodigestive tract. J Korean Med Sci* 1998; 13: 269-74.
5. Berthelet E, Shenouda G, Black MJ, Picariello M, Rochon L. *Sarcomatoid carcinoma of the head and neck. Am J Surg* 1994; 168: 455-8.
6. Gorsky M, Epstein JB. *Head and neck and intra-oral soft tissue sarcomas. Oral Oncol* 1998; 34: 292-6.
7. Lyos AT, Goepfert H, Luna MA, Jaffe N, Malpica A. *Soft tissue sarcoma of the head and neck in children and adolescents. Cancer* 1996; 77: 193-200.

8. Odell PF. *Head and neck sarcomas: a review. J Otolaryngol* 1996; 25: 7-13.
9. Patel SG, See AC, Williamson PA, Archer DJ, Evans PH. *Radiation induced sarcoma of the head and neck. Head Neck* 1999; 21: 346-54.
10. Draper GJ, Sanders BM, Kingston JE. *Second primary neoplasms in patients with retinoblastoma. Br J Cancer* 1986; 53: 661-71.
11. Kingdom TT, Kaplan MJ. *Mucosal melanoma of the nasal cavity and paranasal sinuses. Head Neck* 1995; 17: 184-9.
12. DeMatos P, Tyler DS, Seigler HF. *Malignant melanoma of the mucous membranes: a review of 119 cases. Ann Surg Oncol* 1998; 5: 733-42.
13. Nandapalan V, Roland NJ, Helliwell TR, Williams EM, Hamilton JW, Jones AS. *Mucosal melanoma of the head and neck. Clin Otolaryngol* 1998; 23: 107-16.
14. Gorsky M, Epstein JB. *Melanoma arising from the mucosal surfaces of the head and neck. Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1998; 86: 715-9.
15. Le QT, Fu KK, Kroll S, Fitts L, Massullo V, Ferrell L, Kaplan MJ, Phillips TL. *Prognostic factors in adult soft-tissue sarcomas of the head and neck. Int J Radiat Oncol Biol Phys* 1997; 37: 975-84.
16. Dijkstra MD, Balm AJ, Coevorden FV, Gregor RT, Hart AA, Hilgers FJ, Keus RB, Loftus BM. *Survival of adult patients with head and neck soft tissue sarcomas. Clin Otolaryngol* 1996; 21: 66-71.