

## Head and Neck Carcinomas in Patients under the Age of Forty Years

Mamoru Tsukuda, Kiminao Ooishi, Izumi Mochimatsu and Hirohisa Sato

Department of Otorhinolaryngology, Yokohama City University, School of Medicine, Fukuura 3-9, Kanazawa-ku, Yokohama, Kanagawa 236

From 1973 to 1988, 1,104 patients with head and neck carcinomas (excluding thyroid carcinoma) were admitted to the Yokohama City University Hospital, and among them, 48 (4.3%) were under the age of 40 years. We made a retrospective survey of these young patients. There were 36 males and 12 females. An increasing ratio of male to female was seen with increasing age. The primary site was most frequently the nasopharynx (29 cases), followed by the maxillary sinus (9 cases), and the tongue (4 cases). Squamous cell carcinoma in these young patients characteristically showed a low grade of differentiation.

Key words: Head and neck carcinoma — Young case — Retrospective survey

Among head and neck malignancies, rhabdomyosarcoma is reported to occur in pediatric patients,<sup>1)</sup> whereas carcinomas of the head and neck regions are much rarer in the young. Optimal diagnosis and therapies for this young population are urgently needed. Because of the preconception that carcinomas of the head and neck are diseases of the middle-aged and elderly, little attention has been paid so far to the development of carcinomas in the young. We therefore undertook a retrospective survey, the results of which are presented here.

### MATERIALS AND METHODS

Between 1973 and 1988, 1,104 patients (911 males and 193 females) with carcinomas of the head and neck (excluding thyroid carcinoma) were admitted to the Yokohama City University Hospital, and 48 (4.3%) of them were aged less than 40 at the time of initial diagnosis. All patients were characterized retrospectively by UICC classification (1987). Histopathological findings of nasopharyngeal carcinoma (NPC) were classified according to World Health Organization (WHO) criteria.<sup>2)</sup> Statistical analysis was performed by use of the chi-square test and Student's *t* test.

### RESULTS

There were 36 male and 12 female patients (Table I). The distribution by age showed that the number of patients increased with increasing age; four in the second decade, 10 in the third decade, and 34 in the fourth decade. The youngest patient was a 14-year-old boy with NPC. The male-to-female ratio was 3 to 1. This ratio is lower than that of the total cases (male to female=4.7 to 1). Interestingly, the male-to-female ratio was 1 to 1 for the second decade, 2.3 to 1 for the third decade, and 3.9 to 1 for the fourth decade, showing a steady increase with age.

The primary site was predominantly the nasopharynx (29 patients), followed by the maxillary sinus (9), tongue (4), salivary glands (3) (2 submandibular, 1 parotid gland), mesopharynx (1), hypopharynx (1), and external auditory canal (1) (Table II).

The analysis of histopathological findings from the primary site revealed that of the 29 cases of NPC, all were undifferentiated squamous cell carcinoma including lymphoepithelioma and anaplastic carcinoma (Table III). Of those in the maxillary sinus, the findings were 1 case of well differentiated squamous cell carcinoma, 1 of moderately and 3 of poorly differentiated squamous cell carcinoma, and 4 of anaplastic carcinoma. Carcinomas of the tongue included one well differentiated and 3 poorly differentiated squamous cell carcinoma. All of three carcinomas originating in the salivary glands were adenocarcinomas. Those of the mesopharynx and hypopharynx were both poorly differentiated squamous cell carcinoma. The one carcinoma in the external auditory canal was an adenocystic carcinoma.

Focusing on the relatively large number of cases of nasopharyngeal cancer and maxillary sinus cancer, clinical features were examined and compared with those in older patients (over 40 years old) who had been treated during the same period in our hospital. The numbers of cases over 40 years of age were 113 nasopharyngeal and 142 maxillary sinus carcinoma. The clinical stage of NPC was compared between the younger and older groups (Fig. 1). In terms of "T classification," T4 cases amounted to 17 (15% of the total) in the older group, and 11 (38%) in the younger. There was a statistically significant difference between these rates ( $P < 0.05$ ). In terms of "N classification," metastatic lymph nodes in the cervical region were positive in 27 of the 29 younger patients (93%), significantly higher than the 67% (41/113) in the older group ( $P < 0.05$ ). In the younger group, the percentage of N2 plus N3 was higher than that of the older group (66% vs. 36%). In terms of stage

classification as determined by TNM classification, 25 of the 29 patients (86%) had reached Stage III or Stage IV, indicating that NPC are likely to be found in a more advanced stage in the younger than in the older patients (80%).

Although maxillary sinus carcinoma was at the T4 stage in 25% (36/142) of the older group with this cancer, none of the 9 younger patients had T4 disease. Three were at T2 and the other 6 at T3. The staging of lymph node metastasis was N0 in all of these nine patients (data not shown).

The 1-year crude survival rate of NPC was better in the younger group than in the older (90% vs. 67%), although the survival rate in the longer term was low and

similar in both groups (38% vs. 33% 3-year and 21% vs. 23% 5-year survival rate, respectively).

On the other hand, the prognosis of maxillary sinus carcinomas was better in the younger group than in the

Table I. Characteristics of Patients

Age	No. of male	No. of female	Ratio of male to female
10-19	2	2	1.0:1
20-29	7	3	2.3:1
30-39	27	7	3.9:1
	36	12	3.0:1

Table II. Primary Site

Primary site	No. of patients
Nasopharynx	29
Maxillary sinus	9
Tongue	4
Salivary gland	3
Mesopharynx	1
Hypopharynx	1
External auditory canal	1
	48

Table III. Histology by Primry Site

Primary site	Histology	No. of patients
Nasopharynx	Undifferentiated squamous cell carcinoma	29
Maxillary sinus	Well diff. <sup>a)</sup> squamous cell carcinoma	1
	Moderately diff. squamous cell carcinoma	1
	Poorly diff. squamous cell carcinoma	3
	Anaplastic carcinoma	4
Tongue	Well diff. squamous cell carcinoma	1
	Poorly diff. squamous cell carcinoma	3
Salivary gland	Adenocarcinoma	3
Mesopharynx	Poorly diff. squamous cell carcinoma	1
Hypopharynx	Poorly diff. squamous cell carcinoma	1
External auditory canal	Adenoidcystic carcinoma	1

a) diff.: differentiated.

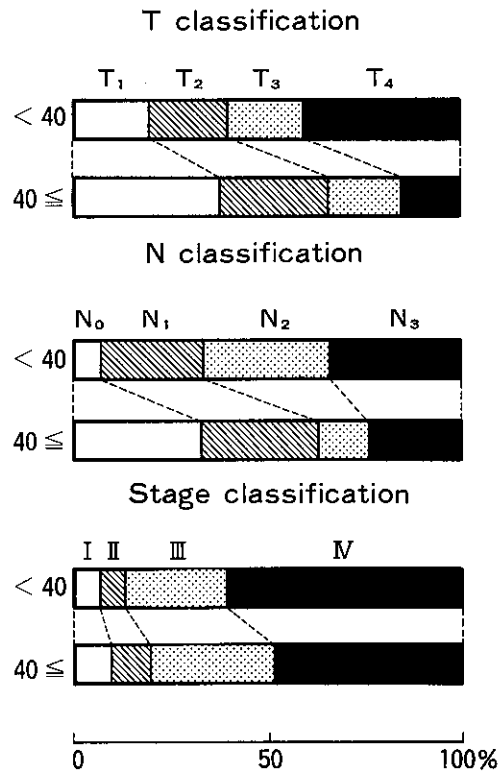


Fig. 1. Distribution of patients with nasopharyngeal carcinoma according to T, N and stage classification for the younger group (48 cases) and the older group (113 cases). Clinical staging was according to the UICC classification (1987), retrospectively.

older one. The respective survival rates in the younger group were 100% 1-year, 67% 3-year and 67% 5-year survival, compared to 81%, 46% and 37% in the older group.

In these 48 young patients, none of the 4 cases who were found in the second decade had a smoking habit. The smoking habit was found in 3 of 10 patients in the third decade and in 12 of 34 cases in the fourth decade. All of them were male. Three smokers in the third decade did not have a long-term history of smoking (2, 2 and 4 years, respectively). The maximum number of cigarettes smoked per day was 10. Only three cases of 12 smokers in the fourth decade had smoked for more than 10 years, and the number of cigarettes smoked daily was less than 10 in these cases.

There was no case with a drinking habit in the second or third decade. Two male cases in the fourth decade had a drinking habit of one glass or can of alcoholic beverage per day beyond the age of thirty. Neither smoking nor drinking habit was recorded for any female patient.

## DISCUSSION

The incidence of head and neck carcinoma in the young is relatively low. We retrospectively investigated young patients with head and neck carcinoma in the present study in order to clarify the characteristics of cancers developing in the younger population. In our institute, head and neck carcinoma patients aged less than 40 represented 4.3% of the total number of 1,104 patients who were treated during the same period.

Carniol *et al.*<sup>3)</sup> restricted their study to head and neck carcinomas excluding thyroid cancer, in the same age group as ours and reported that such patients accounted for 1.3% of their 2,700 patients with head and neck carcinomas in all age groups. This ratio is much smaller than ours. On the other hand, Clark *et al.*<sup>4)</sup> reported that 2.7% of 10,232 patients with head and neck malignant tumors, including thyroid cancer, were younger than 30 years old. If the line is drawn at the age of 30, the percentage of young patients becomes 1.3% (14/1104) in our study.

The patient distribution by age was 4 in the second, 10 in the third and 34 in the fourth decade, showing a rapid increase with age after 30. The male-to-female ratio was 3 in favor of the males. However, as the male-to-female ratio in the total cases treated during the same period was 4.7, the number of female patients was relatively higher in the younger group. The sex ratio increased from 1.0 to 2.3 and then to 3.9 at successive decades of age, increasing rapidly, particularly as age exceeded 30.

Analysis by primary site showed that there were 29 cases of nasopharyngeal and 9 of maxillary sinus carcinomas. The two accounted for 80% of the total cases with

carcinoma. In Carniol's study,<sup>3)</sup> the number of patients under 40 years of age with carcinomas was almost the same for the nasopharynx (11), mesopharynx (12), and larynx (11). None of these had malignant tumors in the maxillary sinus. According to an analysis of head and neck malignancies by Clark *et al.*,<sup>4)</sup> with the exception of thyroid malignancy, the nasopharynx, followed by the oral cavity and mesopharynx were the most common sites of involvement. The percentage of carcinomas in the maxillary sinus was less than 10% in young patients. These results may be related to the fact that even in older people, the incidence of maxillary sinus cancer is low in Europe and the U.S.<sup>5)</sup> As pointed out by Muir and Nectoux,<sup>6)</sup> the incidence of this cancer is higher in Japan than in other countries. However, the number of patients with maxillary sinus carcinoma has rapidly decreased in Japan, recently.<sup>7)</sup> Sakai *et al.*<sup>7)</sup> have reported that of 773 Japanese patients with maxillary sinus carcinoma, 77 cases (10%) were younger than 40 years old and the incidence of this cancer showed a rapid increase after 40 years of age. A similar tendency was also observed in our study. In the total of 151 patients with maxillary sinus cancer seen during the study period, the percentage of those younger than 40 was 6% (9/151). Aging seems to be an important associated factor in the development of this cancer.

In other countries, many cases of laryngeal cancer in young people have been reported.<sup>3,4,8,9)</sup> In our study, there were no patients with laryngeal cancer. Such racial differences with respect to the development of laryngeal cancer in the young are noteworthy. The problem of whether they are related to differences in life habits such as smoking, environmental factors (such as air pollution) or unknown intrinsic factors remains to be elucidated.

The trend for NPC to be more common in young people is identical in Japan and Caucasian countries,<sup>3,4,10)</sup> both of which have a low incidence of this cancer. This cancer is one of the most common carcinomas of the head and neck in China and South East Asia. In these high-incidence areas, NPC presents most frequently in the 5th decade,<sup>11)</sup> whereas in low-incidence areas, this cancer usually presents most frequently in the seventh decade. This tendency emerges from the results of a nation-wide epidemiological study in Japan.<sup>12)</sup>

Histopathological analysis revealed that all 29 cases of NPC were undifferentiated squamous cell carcinoma (WHO Type 3). It has been reported that most cases of this type of cancer in the young are of an undifferentiated type<sup>10,11)</sup> and such a tendency was confirmed in our study.

Of 9 cases of maxillary sinus carcinoma, 3 cases were a poorly differentiated type of squamous cell carcinoma, and 4 were anaplastic cell carcinoma. Of 142 cases of maxillary sinus cancer in older patients aged over 40 in this period, only eight cases (6%) were of poorly differ-

entiated squamous cell or anaplastic carcinoma type. A similar tendency holds for tongue cancer. Despite the small number of patients, all cases of the mesopharynx and hypopharynx were of a poorly differentiated squamous cell carcinoma type. These histopathological results indicate that low-grade differentiation types are common in squamous cell carcinomas of the young.

No difference was observed in the prognosis of NPC between the younger and the older patients. Some authors<sup>13,14)</sup> have suggested that the prognosis of this cancer is generally more favorable in the younger population. As described in our results, the T and N stagings of NPC are more advanced in the younger population than in the older.<sup>11)</sup> This implies greater difficulty in early diagnosis in the younger group, indicating a poor prognosis for this cancer. It should be pointed out that most patients, especially the young, are likely to delay seeking treatment, since the difficulty in identifying the early appearance of pathognomonic signs makes patients doubtful as to whether they are suffering from NPC.<sup>15)</sup>

Young patients with maxillary sinus cancer, which is more often diagnosed in the early stage, had a better prognosis in the younger group in comparison to those over 40 years old.

Several studies have been reported on tongue cancer in the young.<sup>4,16-19)</sup> Byers<sup>16)</sup> studied 11 patients younger than 30 years old. In his report, undifferentiated squamous cell carcinoma was found at a high rate, i.e., in 5 of the 11 patients. He pointed out that cases with this histological type, whose primary lesions had advanced to T3 or T4, had a poor prognosis whether radiation therapy, surgery, or any other therapeutic approach was employed. Newman *et al.*<sup>17)</sup> studied 13 young cases with tongue cancer and suggested that early diagnosis was able to improve the prognosis. The 4 patients with tongue cancer whom we treated achieved successful results with combined therapy of radiation and surgical treatment, which can be explained by the fact that they were all in the T1 or T2 stage and had no lymph node metastasis (N0).

With the exclusion of the nasopharynx, most of the carcinomas in this study were diagnosed early and

resulted in favorable outcomes. Based on these results, we would like to suggest that if aggressive therapeutic approaches can be employed on the basis of early diagnosis, it should be possible to treat younger patients with head and neck carcinomas and achieve successful outcomes.

Etiologic factors in early life such as smoking and drinking are often regarded as being contributing factors to the development of head and neck cancers.<sup>17, 18, 20-22)</sup> In the present study of 48 young patients, 15 of 36 male cases had smoking and/or drinking habits, while neither smoking nor drinking habit was recorded for any female patient. Head and neck cancers nevertheless did develop in female patients. Etiologic factors cited as important cancer-promoting factors in tongue cancer include mismatch of braces, dental caries, poor quality of oral hygiene, and so on.<sup>18)</sup> However, no such factors were found in the four patients with tongue cancer in the present study, suggesting the presence of other etiologic factors in the development of head and neck cancers in younger patients as well. We also evaluated other etiologic factors such as the presence of multiple anomalies, genetic and chromosomal disposition, medication and viral infection during pregnancy, past history of radiation therapy, and previous use of one or more immunosuppressive drugs. Especially in younger cases of the first and second decades, none of our cases showed involvement of any such factors.

Chemotherapy and radiation therapy, which are often used for treatment of head and neck carcinomas, are also prone to impair the immunocompetence of treated patients. There is a possibility that the development of second independent malignancies might be promoted by this immunological impairment in patients with primary head and neck cancers.<sup>3, 4, 23, 24)</sup> Carniol *et al.*<sup>3)</sup> reported the development of a second cancer in a new site different from the primary lesion in three of 36 patients. In our study, none of the patients developed a second cancer, possibly because the observation period was short. However, long-term follow-up will be necessary to determine such outcomes in young patients with carcinomas.

(Received February 26, 1993/Accepted April 17, 1993)

## REFERENCES

- 1) Anderson, G. J., Tom, L. W. C., Womer, R. B., Handler, S. D., Wetmore, R. F. and Postic, W. P. Rhabdomyosarcoma of the head and neck in children. *Arch. Otolaryngol. Head Neck Surg.*, **116**, 428-431 (1991).
- 2) Shanmugaratnam, K. and Sobin, L. H. Histological typing of upper respiratory tract tumours. In "International Histological Classification of Tumours, No. 19." pp. 32-33 (1978). World Health Organization, Geneva.
- 3) Carniol, P. J. and Fried, M. P. Head and neck carcinoma in patients under 40 years of age. *Ann. Otol.*, **91**, 152-155 (1982).
- 4) Clark, R. M., Bosen, I. B. and Laperriere, N. J. Malignant tumors of the head and neck in a young population. *Am. J. Surg.*, **144**, 459-462 (1982).
- 5) Levertu, P., Roberts, J. K., Kraus, D. H., Levine, H. L., Wood, B. G., Medendorp, S. V. and Tucker, H. M.

- Squamous cell carcinoma of the paranasal sinuses: The Cleveland Clinic experience 1977–1986. *Laryngoscope*, **99**, 1130–1136 (1989).
- 6) Muir, C. S. and Nectoux, J. Descriptive epidemiology of malignant neoplasms of nose, nasal cavities, middle ear and accessory sinuses. *Clin. Otolaryngol.*, **5**, 195–211 (1980).
  - 7) Sakai, S., Hohki, A., Fuchihata, H. and Tanaka, Y. Multidisciplinary treatment of maxillary sinus carcinoma. *Cancer*, **52**, 1360–1364 (1983).
  - 8) Lipkin, A., Miller, R. H. and Woodson, G. E. Squamous cell carcinoma of the oral cavity, pharynx, and larynx in young adults. *Laryngoscope*, **96**, 790–793 (1985).
  - 9) Singh, W. and Kaur, A. Laryngeal carcinoma in a six year old with a review of the literature. *J. Laryngol. Otol.*, **101**, 957–958 (1987).
  - 10) Singh, W. Nasopharyngeal carcinoma in Caucasian children, a 25-year study. *J. Laryngol. Otol.*, **101**, 1248–1253 (1987).
  - 11) Jonathan, S. T. S., Poon, Y. F., Wei, W. I. and Choy, D. Nasopharyngeal carcinoma in young patients. *Cancer*, **65**, 2606–2610 (1990).
  - 12) Sawaki, S., Hirayama, T. and Sugano, H. Studies on nasopharyngeal carcinoma in Japan. *Gann Monogr. Cancer Res.*, **18**, 63–74 (1976).
  - 13) Baker, S. R. and Wolfe, R. A. Prognostic factors of nasopharyngeal malignancy. *Cancer*, **49**, 163–169 (1982).
  - 14) Qin, D., Hu, Y., Yan, J., Xu, G., Cai, W., Wu, X., Cao, D. and Gu, X. Analysis of 1379 patients with nasopharyngeal carcinoma treated by radiation. *Cancer*, **61**, 1117–1124 (1988).
  - 15) Hasselt, C. A. V. and Tsao, S. Y. Nasopharyngeal carcinoma: modes of presentation. *Ann. Otol. Rhinol. Laryngol.*, **100**, 544–550 (1991).
  - 16) Byers, R. M. Squamous cell carcinoma of the oral tongue in patients less than thirty years of age. *Am. J. Surg.*, **130**, 475–478 (1975).
  - 17) Newman, A. N., Rice, D. H., Ossoff, R. H. and Sisson, G. A. Carcinoma of the tongue in persons younger than 30 years of age. *Arch. Otolaryngol.*, **109**, 302–304 (1983).
  - 18) Usenius, T., Karja, J. and Collon, Y. Squamous cell carcinoma of the tongue in children. *Cancer*, **60**, 236–239 (1987).
  - 19) Amichetti, M. Squamous cell carcinoma of the oral tongue in patients less than fifteen years of age. *J. Cranio-Max.-Fac. Surg.*, **17**, 75–77 (1989).
  - 20) Chen, J., Katz, R. V. and Krutchkoff, D. J. Epidemiology of oral cancer in Connecticut, 1935 to 1985. *Cancer*, **66**, 2796–2802 (1990).
  - 21) Mabuchi, K., Bross, D. S. and Kessler, I. I. Cigarette smoking and nasopharyngeal carcinoma. *Cancer*, **55**, 2874–2876 (1985).
  - 22) Link, M. J. O., Kaugars, G. E. and Burns, J. C. Comparison of oral carcinomas in smokeless tobacco users and nonusers. *J. Oral Maxillofac. Surg.*, **50**, 452–455 (1992).
  - 23) Li, F. P., Cassady, R. and Jaffe, N. Risk of second tumors in survivors of childhood cancer. *Cancer*, **35**, 1230–1235 (1975).
  - 24) Cooper, J. S., Scott, C., Marcial, V., Griffin, T., Fazekas, J., Laramore, G. and Hoffmann, A. The relationship of nasopharyngeal carcinomas and second independent malignancies based on the radiation therapy oncology group experience. *Cancer*, **67**, 1673–1677 (1991).