

Study on Oral Epidermoid Carcinoma From Biopsy Cases in Taiwan

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SUMMARY

Two hundred and forty-five biopsy cases of oral epidermoid carcinoma were histologically and statistically studied. Epidermoid carcinoma was about 90% of 272 cases of oral primary malignant tumors. The male patients were predominant with 2.5:1 of male to female ratio. The tongue was the most common site of involvement. The site of next greatest frequency was the buccal mucosa in contrast with some other reports. The average age of the patients was 59 years with 80% of the individuals over 50 years of age. Ulceration was the prevalent sign of the tumor. The average delay between the onset of symptom to first visit was 6.9 months. Two systems have been applied for histological grading in addition to description of morphological details. As the result presented, it seemed that there was no stright correlation between the histological grading of carcinoma and the anatomical sites except verrucous carcinoma which was predominant in lips. Therefore, it was suggested that histological grade of the tumor is of limited important for the correlation between the oral primary tumor sites and the prognosis in most portion.

Although, there are so many different kinds of malignant neoplasm occuring in oral region, it is well known that epidermoid carcinoma is the most majority of the malignant tumors. However, due to the materials collected from different geographic areas, some clinical events such as age distribution and incidence in different intraoral anatomical sites were diverse in the reported studies^(1,2,3,4). Besides, there are still some other controversy on the factors influencing prognosis of the carcinoma and the criteria regarded as the bases for choice for treatment^(2,5,6,7,8,9). Even though, it is generally accepted that the histological grade of malig-

nancy of epidermoid carcinoma, as well as that of the other malignant tumors will relate to prognosis in some locations more or less^(10,11,12,13,14). In order to understand some clinical and histological aspects of oral epidermoid carcinoma affecting Chinese in Taiwan and also in the attempt to find whether or not the relationship existed between the distribution of different histological grade and the anatomical sites, the study was performed by use of all of the biopsy specimens and available clinical informations of 245 cases of oral epidermoid carcinoma obtained at the department of pathology of Taipei Medical College for

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epidermiologic analysis and histopathologic study.

MATERIALS AND METHODS

The material for this study was 245 biopsy cases of oral epidermoid carcinoma histologically diagnosed at the department of pathology of Taipei Medical College during the 12 years from January 1965 through December 1976. All of the cases were the biopsy specimens sent by local clinics and hospitals in Taiwan. The patients were all Chinese. The specimens were fixed in formalin or formalin-alcohol with exception of a few cases which were fixed in alcohol. After fixation and ordinarily embedded in paraffin, the specimens were cut into 2 to 5 μ in thickness and then stained with Hematoxylin-Eosin. Special stains such as Meyer's Mucicarmine, Masson's trichrome, PAS, Silver impregnation were

also done, if necessary. All of the available clinical data were reviewed and analyzed. All cases were carefully examined again under light microscope without any clinical informations. The carcinoma was histologically classified into well-differentiated epidermoid carcinoma, moderately differentiated epidermoid carcinoma, and anaplastic epidermoid carcinoma by Broders' criteria, namely depended on the cellular differentiation and mitosis⁽¹⁰⁾ Moreover, the carcinoma was also evaluated by a recently developed multifactorial grading system based on the tumor cell population (e.g. the cytoplasmic differentiation, the unclear pleomorphism and mitosis) and the tumor-host relationship (e.g. mode of invasion, stage of invasion and cellular response of plasmolymphocytic infiltration)^(11,12). In this system, there are six parameters (Table 1), each of which is graded from 1 to 4 points. The malignancy is determined on the

Table 1. Parameters for Histological Grading of Malignancy

Point Scale	Tumor cell population			Tumor-host relation		
	Cytoplasmic differentiation	Nuclear polymorphsim	Mitosis under HPF	Mode of invasion	Stages of invasion	Cellular response
1	highly keratini-zation	minimal	single	well-defined borderline	suspect	marked
2	moderately keratini-zation	moderate	a few	cord. less marked borderline	small and few cords invasion	moderate
3	minimal keratini-zation	highly	great	groups of cells, no distinct borderline	nodular into submucosa	slight
4	poorly keratini-zation	ana-plastic immature	numerous	diffuse growth	deep portion invasion	almost none

total points of six morphological parameters ranging from 6 to 24, the more total points the more malignant of the tumor. By use of these two grading systems, the 245 cases of oral epidermoid carcinoma were observed to find whether or not the relation exist between the different morphological grade and the anatomical site. Still, some histological details were also described.

RESULTS

Of the 272 cases of primary malignant tumors in oral cavity (not including the malignant tumors of tonsil), more than 90% were found to be epidermoid carcinoma (Table 2). The male patients were predominant. Of the 245 cases of primary oral epidermoid carcinoma, 175 cases (72%) were male and 70 cases (23%) were female, the male to female ratio was 2.5. The tongue was the most common site of involvement and about one-third of the carcinoma (79 cases) were located in the tongue in these materials. The buccal mucosa was the site of next greatest frequency and 52 cases (21.23%) were arising from this region. The distribution of the remaining 114 cases

was found to be as follows: 43 cases in the gingiva, 34 cases in the palate, 26 case in the lip, 7 cases in the mouth floor and 4 cases in the other sites (Table 3). Of the 79 cases involving the tongue, more than one half (43 cases) occurred in the tongue margin with slightly predominant in the left side, but it was rare in tongue tip (only 2 cases). Of the 52 cases of buccal mucosa carcinoma, 30 cases were located in the left side, the cause of left side prevalent was not know. The occurrence revealed no significant difference between the upper and the lower gingivae and between the soft and the hard palates, but there was so difference of the occurrence between the upper and lower lips. Of the 26 cases of lip carcinoma, there were only two cases in the upper lip and the remainders were located in the lower lip and mouth angle. The age of the patients with oral epidermoid carcinoma widely distributed. The youngest patient who was with tongue carcinoma was 27 years old and the oldest one was 84 years of age also with tongue carcinoma. About 80% (183) of the patients were over 50 years of age (Table 4). The average age of the 237 patients whose age has been recorded was 59 years, with 74% of the cases between the age of 40 and 69 years. But, there was a difference of 6 years in average age of the patients between the male and the female groups and it was 57.3 years for 169 male individuals and 63 years for the 68 female cases. As the result showed in Table 4, if it reviewed according the different intraoral anatomical sites, the patients with epidermoid carcinoma of the tongue and the mouth floor were somewhat younger than those with tumors in the buccal mucosa, the gingiva, the palate

Table 2. Classification of Primary Malignant Tumors in Oral Cavity of 272 Biopsy Cases

Classification	No. of Cases	Percentage
Epidermoid carcinoma	245	90.07
Adenoid cystic carcinoma	6	2.21
Basal cell carcinoma	6	2.21
Adenocarcinoma	4	1.47
Mucoepidermoid carcinoma	3	1.10
Fibrosarcoma	2	.74
Malignant melanoma	2	.74
Sarcoma, unclassified	2	.74
Lymphosarcoma	1	.37
Rhabdomyosarcoma	1	.37

Table 3. Distribution of 245 Cases of Oral Epidermoid Carcinoma

Location	No. of Cases	Total	%
Tongue		79 (23)*	32.24
Right margin	18		
Left margin	25		
Root	17		
Ventral surface	3		
Tip	2		
Not further specified	14		
Buccal mucosa		52 (20)	21.23
Right side	13		
Left side	30		
Not further specified	9		
Gingiva		43 (12)	17.55
Upper	15		
Lower	21		
Not further specified	7		
Palate		34 (5)	13.88
Soft palate	12		
Hard palate	19		
Not further specified	3		
Lip		26 (4)	10.61
Upper	2		
Lower	18		
Angle	6		
Floor of mouth		7 (3)	2.86
Other sites		4 (3)	1.63
Total	245	245 (70)	100.00

* Female case

and the lip. Regarding the whole group, the duration from symptoms onset to first visit was ranging from 1 week to 4 years, and the average duration was 6.9 months (Table 5). A patient with gingival lesion was found to be with the shortest period before seeking aid. For about 50% (36 cases) of the 77 recorded cases. The period was less than 3 months. However, the average duration was also widely different among patient groups divided by location, it was 6.9 months for the patients with tongue carcinoma (24 cases), 9.3 months for those with buccal mucosa carcinoma (17 cases), and 4.6 months, 5.3 months and 10.9 months for the patients with gingival lesion (13 cases), palatal lesion (8 cases) and lip lesion (9 cases),

respectively. Nevertheless, there was only 1.4 months of average duration for the 6 patients with carcinoma in the mouth floor and the other sites, and no one delayed more than 2 months before first examination.

The clinical signs of oral epidermoid carcinoma were mainly including ulceration, induration and fungating or elevated growing mass, although bleeding, abscess, swelling, fistula, cystic appearance, nasal obstruction, and rupture were described in a few cases. Of 169 cases in which signs and symptoms have been indicated, 154 cases (91%) revealed one or more of the above mentioned three main findings. Of 113 cases grossly manifested as ulceration (of which, 13 cases also superimposed with induration or growing mass), 42 cases were located in the tongue, 25 cases in the buccal mucosa, 16 cases in the palate, 14 cases in the gingiva, 12 cases in the lip and 4 cases in the mouth floor and the other sites. Of the 25 cases presented growing mass, 7 cases were located in tongue, 5 cases in buccal mucosa, 4 cases in lip and 3 cases in each of the rest locations. There was no cases with nerve paralysis. During the first examination, patients with regional lymph node enlargement clinically suspected to be lymph node metastasis were found to be 21 cases in total (there were 11 cases of tongue lesion, 7 of buccal mucosa lesion, 2 of palate lesion and 1 of gingiva lesion). Of the 11 cases of tongue carcinoma with enlargement of cervical lymph nodes, 7 were arising from the tongue base and the another one case involving right tongue margin showed bilateral cervical node enlargement. Still, one case of buccal mucosa carcinoma with enlarged submaxillary

Table 4. Age Distribution in 237 Cases of Oral Epidermoid Carcinoma

Location	*Under 40 yr.	40-49 yr.	50-59 yr.	60-69 yr.	Over 69 yr.	Average (yr.)
Oral cavity as a whole	11 (4.6%)	43 (18.2%)	65 (27.4%)	68 (28.7%)	50 (21.1%)	59
Tongue	5	16	23	19	13	57
Buccal mucosa	2	6	13	14	16	62
Gingiva	3	7	10	13	9	59.5
Palate		5	13	9	6	59.5
Lip	1	4	3	12	4	59.5
Mouth floor		2	3	1	1	57
Other sites		2		1	1	55

*The youngest one was 27 years old.

Table 5. Duration from Occurrence to First Visit (77 cases)

Location	Under months	3-6 months	6-12 months	Over 12 months	Average (month)
Oral cavity as a whole	36 (47%)	17 (22%)	18 (23%)	6 (8%)	6.9
Tongue	11	6	6	1	6.9
Buccal mucosa	4	2	9	2	9.3
Gingiva	9	2	1	1	4.6
Palate	1	6	1		5.3
Lip	5	1	1	2	11
Mouth floor and other sites	6				1.4

nodes revealed histologically infiltrating to the ipsilateral parotid gland after 2 years later. However, all of the enlarged lymph nodes were not examined microscopically and the details were still unknown. Different diagnosis has clinically been made for 218 cases. Of 218 cases, 103 cases were suspected as carcinoma, 37 cases as malignant tumor and 34 cases as rule-out carcinoma or malignant lesion. There were only 10 individuals on whose records a definite

statement of chewing betel nut has been noted. History of leukoplakia was mentioned in 7 cases (3 in tongue and 4 in buccal mucosa), there was a patient who was with leukoplakia in buccal mucosa for 13 years before carcinoma developed. The size of the lesion were not stated during biopsy except that of 12 cases of tongue lesion, the mean size of those 12 cases was 3 cm. in diameter with the largest one measuring 6 cm. in diameter.

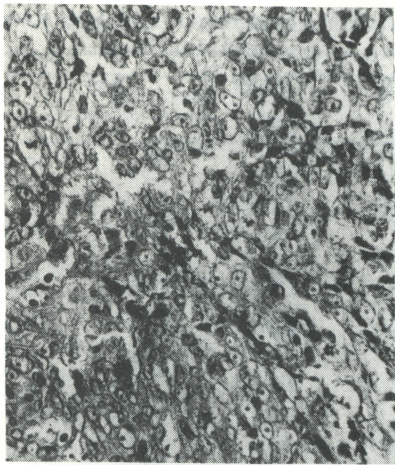


Fig. 1. Anaplastic epidermoid carcinoma composed of tumor cells resembling transitional cells with numerous mitotic figures. (TPMC 75-712, upper gingiva, 400X)

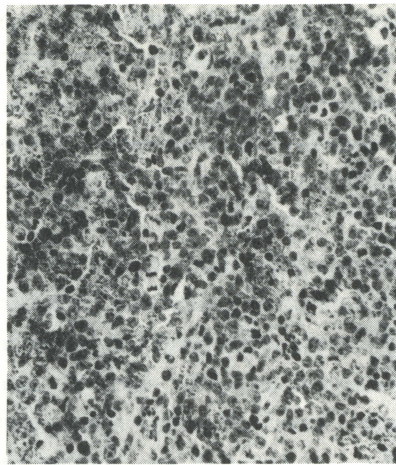


Fig. 2. Anaplastic epidermoid carcinoma composed of tumor cells resembling parabasal cells with numerous mitotic figures. (TPMC 70-2764, hard palate, 400X)

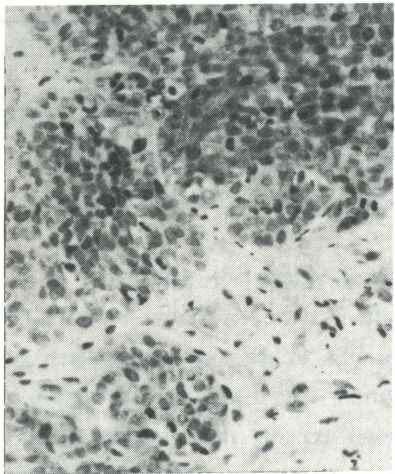


Fig. 3. Anaplastic epidermoid carcinoma composed of tumor cells resembling intermediate epithelial cells with minimal plasmolymphocytic infiltration. (TPMC 72-3097, hard palate, 400X)

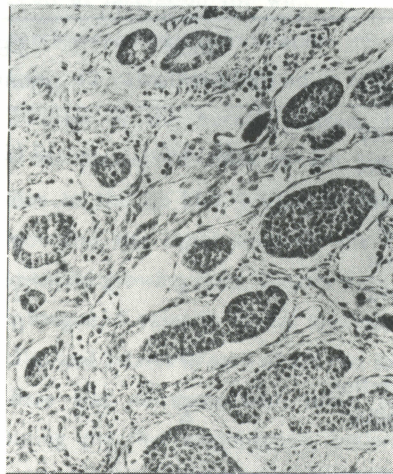


Fig. 4. Anaplastic epidermoid carcinoma showing remarkable lymphatic invasion. (TPMC 68-878, buccal mucosa, 200X)

Microscopically, there were 24 cases to be morphologically classified as anaplastic epidermoid carcinoma (8 cases in the tongue, 7 cases in the palate, 6 cases in the gingiva and 3 cases in the buccal mucosa). The majority of the oral anaplastic epidermoid

carcinoma were mainly composed of the tumor cells resembling parabasal cells, intermediate epithelial cells and/or transitional cells in sheet-like or cord like arrangement (Fig. 1,2,3). Keratinization was poor or even absent. There was no evidence of epi-

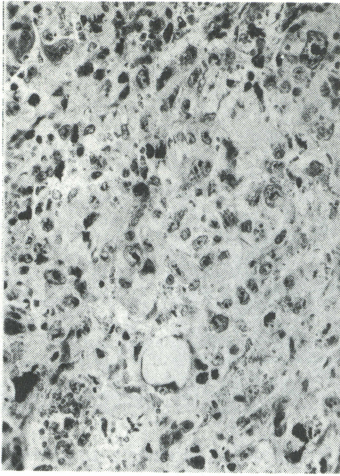


Fig. 5. Anaplastic epidermoid carcinoma composed of tumor giant cells with tripolar mitotic figures. (TPMC 70-3629, lower gingiva, 400X)

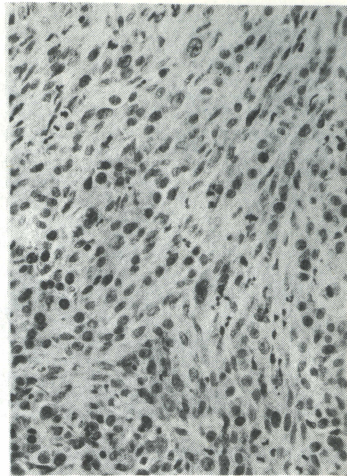


Fig. 6. Anaplastic epidermoid carcinoma composed of spindle shaped tumor cells with sarcomatous appearance. (TPMC 74-6744, lower gingiva, 200X)



Fig. 7. Well-differentiated epidermoid carcinoma with slight plasmolymphocytic infiltration. (TPMC 74-1338, mouth floor, 200X)

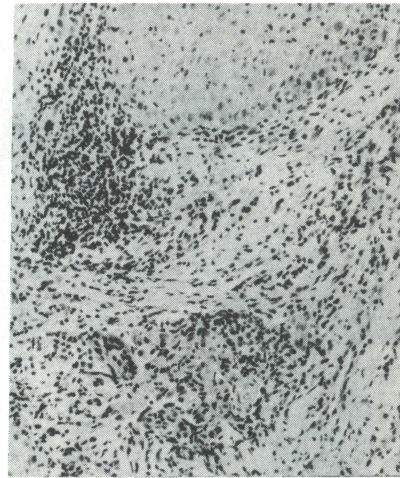


Fig. 8. Well-differentiated epidermoid carcinoma showing a few cords of tumor cells invasion into submucosa. (TPMC 74-1338, mouth floor, 200X)

thelial pearl formation to be seen, the intercellular bridge was obscured and always difficult to be detected. But, the mitotic figure was quite remarkable, and small foci of necrosis were not uncommon. There were 9 cases of anaplastic epidermoid carcinoma microscopically composed of cells resembling

transitional cell or parabasal cells as the main histological picture (Fig. 1,2). Of the 9 cases, 7 were found arising from the posterior portion of the oral cavity (6 cases in tongue base and 1 case in soft palate). The main histologic picture showing the tumor cells resembling intermediate epithelial cells was



Fig. 9. Well-differentiated epidermoid carcinoma involving into the underlying connective tissue by papillomatous nodules. (TPMC 75-11024, buccal mucosa, 100X)



Fig. 10. Verrucous carcinoma containing a thick keratin layer on the papillary tumor surface with marked plasmolymphocytic infiltration. (TPMC 74-7361, lower lip, 40X)

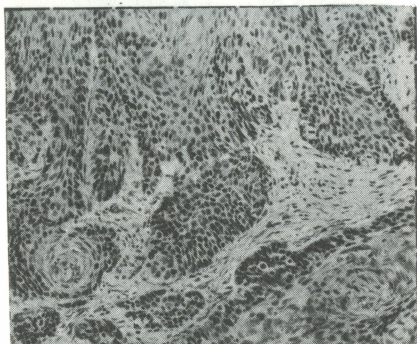


Fig. 11. Moderately differentiated epidermoid carcinoma revealing numerous mitotic figure with almost no plasmolymphocytic infiltration. (TPMC 70-7145, tongue, 200X)



Fig. 12. Moderately differentiated epidermoid carcinoma with marked plasmolymphocytic infiltration. (TPMC 76-4706, tongue, 100X)

found in 8 cases (Fig. 3,4). Giant tumor cells could be seen in some cases, but there were rare lesions composed of giant tumor cells as the main histologic picture, and only 6 of such cases were present in this material. The giant cell usually contains one irregularly enlarged and hyperchromic nucleus with abundant cytoplasm (Fig. 5), they were generally polygonal in shape, but bizarre

giant cells were also disclosed. The intercellular bridge might or might not be detected among giant cells but definitely no epithelial pearl formation. There was not only numerous mitotic figure but also not difficult to find multipolar mitosis in the lesion mainly composed of giant cells (Fig. 5). A case of anaplastic epidermoid carcinoma almost composed of spindle-shaped tumor

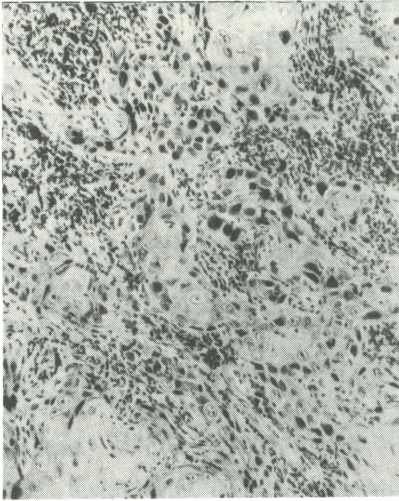


Fig. 13. Moderately differentiated epidermoid carcinoma with great number of irregularly enlarged nuclei. (TPMC 75-6561, tongue, 200X)

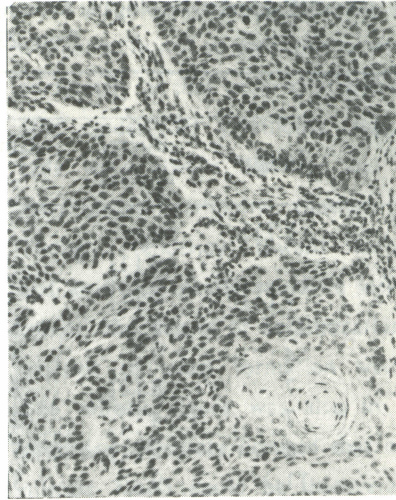


Fig. 14. Moderately differentiated epidermoid carcinoma with numerous mitotic figures and moderate plasmolymphocytic infiltration. (TPMC 70-6467, buccal mucosa, 200X)

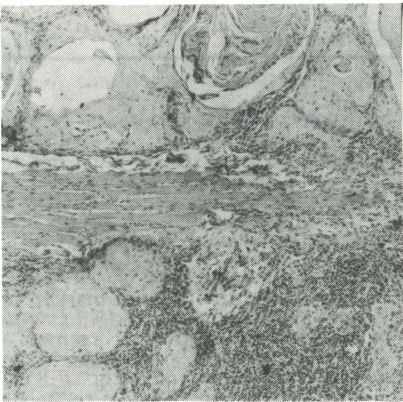


Fig. 15. Moderately differentiated epidermoid carcinoma invasion to muscle layer. (TPMC 66-137, tongue, 100X)

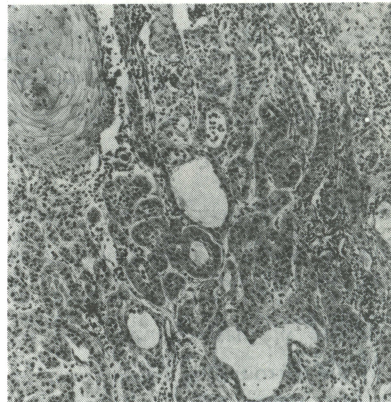


Fig. 16. Moderately differentiated epidermoid carcinoma with pseudo-adenoid structures. (TPMC 68-1427, lower lip, 100X)

cells was found involving the gingiva, the tumor cells of this lesion arranged in sarcomatous fashion with rather remarkable mitosis (Fig. 6). Almost all of the anaplastic epidermoid carcinoma appeared to have numerous tumor cells containing irregular elongated or immature nuclei, and the

lesion certainly revealed massive and diffuse invasive growing into the underlying connective tissue without few exceptions. The border between the lesion and the adjacent normal tissue was rather ill-defined and obscured. Lymphatics invasion was noted (Fig. 4), (In all of the 245 cases, there were

Table 6. Histological Grading of Oral Epidermoid Carcinoma from 229 Biopsy Specimens

Total malignancy point	Number of Case						
	Tongue	Buccal mucosa	Gingiva	Palate	Lip	Mouth floor	Other sites
7	1 [1]						
8		3 [1]		2 [2]	2 [2]		
9	2 [1]	2 [1]				1 [1]	
10	1	1	1	2 [1]	2 [2]		
11	4	3	2		3 [2]	1	
12	7	8 [2]	3	1	4 [1]		
13	7	4	2	4	4		1
14	6	9 [1]	5	5	1		1
15	11	9	5		4		2
16	9	3	7	7	3	3	
17	5		6	2	1	2	
18	7 (2)	2 (1)	2	3 (1)	1		
19	5	2	3 (2)	2 (1)	1		
20	1	1 (1)	1 (1)	1 (1)			
21	2 (2)	1 (1)		2 (2)			
22	2 (2)						
23	1 (1)		1 (1)	1 (1)			
24	1 (1)		2 (1)				

[]: well-differentiated and verrucous type
 (): anaplastic type

5 cases revealing diffusely marked lymphatic invasion, of which 4 cases belonged to this anaplastic type). Little evidence of cellular response of plasmolymphocytic infiltration in the surrounding tissue could be demonstrated in the majority of anaplastic epidermoid carcinoma. Of the 24 cases, there were merely 5 cases presenting moderate plasmolymphocytic infiltration in the region surrounding the lesion. The total points of histologic malignancy for 23 cases (one specimen was not available for evaluation of stage of invasion) varied from 18 to 24, and the average was 20.8 (Table 6).

There were 13 cases of well-differentiated epidermoid carcinoma. They entirely

have a distinct order of tumor cells with remarkable intercellular bridge, high cytoplasmic differentiation, and marked tendency toward keratinization as same as that observed in papilloma (Fig. 7,8,9). Their nuclei appeared nearly uniform in shape and size, and nuclear pleomorphism was very rare. Prominent mitotic figure was scarce, but dyskeratosis was not uncommon. Although, invasion of basement membrane developed already, the lesion usually infiltrated into the underlying connective tissue by growing papillomatous nodules and appeared well-demarcation with the adjacent innocent tissue (Fig. 7,9). Therefore, it might be sometime with some dif-

difficult to make differential diagnosis between well-differentiated epidermoid carcinoma and papilloma under light microscope with low power vision. Moderate to marked plasmolymphocytic infiltration in the surrounding tissue was found in 9 cases and minimal cellular response in 4 cases. The total points of malignancy was counted from 8 to 14 with an average of 10 (Table 6). The so-called verrucous carcinoma was disclosed to be 5 cases in this material, of which 4 cases were located in the lip and one case in the buccal mucosa. Many aspects of their histological appearances such as order of tumor cells, cytoplasmic differentiation, nuclear pleomorphism and mitosis even mode of tumor invasion were as the same as those found in well-differentiated epidermoid carcinoma. It merely differed histologically from a well-differentiated epidermoid carcinoma in that it evidently contained a keratin layer of a considerable amount on the papillary projected tumor surface (Fig. 10). They also revealed moderate to marked infiltration of plasmolymphocytes as showed in well-differentiated epidermoid carcinoma with an exception of a case in which mild round cells infiltration was noted.

By use of the traditional monofactorial grading system, more than four-fifth (203 cases) of oral epidermoid carcinoma were classified as moderately differentiated epidermoid carcinoma in this material. The carcinoma of this class were composed of several distinct types of tumor cells (Fig. 11,12). But their morphological pictures differed among individual lesions and so did the ratio of various types of tumor cell population. It seemed to appear some-

what an order among different cells, but it was really not so distinctive or so thorough completely as that occurred in well-differentiated epidermoid carcinoma, the different cells were always disorder and ordinarily intermingled with one another (Fig. 13). Though, tendency toward keratinization and epithelial pearls could be seen in every tumor, the degree of keratinization and the amount of pearl formation were diverse. The mitotic figure was also in the same condition, it surely occurred that numerous mitotic figure could be discovered in lots of cases under high power field (Fig. 14), but only single mitotic figure presenting under high power field was not the minority. Of the 203 cases, only 188 cases were adequately available for evaluation by the multifactorial grading system (Table 7). More than 60% of this group, the lesion revealed diffuse invasion into the underlying tissue. And about two-third (66%) of the cases, the lesion have reached the deep portion of the local tissue (Fig. 15). Minimal or even nearly no cellular response could be found (Fig. 11), but 75% of the cases revealed moderate to marked plasmolymphocytic infiltration (Fig. 12,14,15). Partially well-defined of the lesion was seen in a certain cases. The distribution of the total point of malignancy was broad from 10 to 20 (Table 6), of the 21 cases clinically with lymph node enlargement during the first visit, 17 cases belonged to this moderately differentiated epidermoid carcinoma and the remaining 4 cases were anaplastic epidermoid carcinoma. Foci of pseudo-adenoid structure very like that of adenocarcinoma were disclosed in a few cases (4 cases), but the tumor cells circling the

Table 7. Distribution of 188 Cases of Moderately Differentiated Epidermoid Carcinoma in the Different Point Scale Group

Point Scale	Tumor cell population			Tumor-host relation		
	Cytoplasmic differentiation	Nuclear polymorphism	Mitosis under HPF	Mode of invasion	Stages of invasion	Cellular response
1	32 (17%)	51 (27%)	117 (62%)	2 (1%)	0	27 (14%)
2	122 (65%)	116 (62%)	52 (28%)	12 (6%)	10 (5%)	114 (61%)
3	34 (18%)	21 (11%)	19 (10%)	57 (31%)	54 (29%)	46 (24.5%)
4	0	0	0	117 (62%)	124 (66%)	1 (0.5%)

adenoid spaces were polygonal in shape with intercellular bridge and arranged in single layer or more than two layers (Fig. 16). The exact cause of this appearance was not known but most likely due to central degeneration of the tumor cell nest. The cell with empty cytoplasm after stained with H.E., so-called clear cell, was rarely found in this material.

DISCUSSION

It is the fact that no matter how much the incidence of primary malignant tumors is found in oral cavity, epidermoid carcinoma is the most predominant malignant neoplasm and almost accounts for about 90% of all oral primary malignant tumors (1,2,3,4) as showed in the present materials. The carcinoma may involve any portion of the mouth, but their occurrence varies widely among different regions. In general, the tongue is the most common site of the involvement and the floor of the mouth is usually mentioned to be the site of next greatest frequent (1,2,9). However, epidermoid carcinoma arising from the buccal mucosa is also frequent in some Asian areas (3,4,15). As revealed in this study, more than 20%

of the oral epidermoid carcinoma were located in the buccal mucosa and its incidence was found just only less than that of the tongue. Srivastava (1975)⁽¹⁵⁾ has stated that in Northern India, mixing tobacco and lime with betel leaves is very common and increases the incidence of oral cancer. He has quoted the findings from an epidemiological field study done by Wahi in India. The findings were described as that cancer of the buccal mucosa was eight times more prevalent among those who chewed a special type of tobacco and lime mixed with finely cut betel nuts chips than in non-chewers, and the incidence increased in the buccal mucosa was strikingly associated with larger dose of the quid, the longer duration of the quid kept within the mouth and higher frequency of chewing per day. He has also mentioned the finding of a study by Cohen et al and stated as that the alkaloid formed within the quid may play an important role for the distribution between the epithelial connective tissue interface through which the epithelium grows down and cancer than will occur. Even the exact etiology of oral epidermoid carcinoma is still unknown and it may be considered to be multifactorial in nature,

betel nut chewing is now generally regarded to be closely related to the development of oral epidermoid carcinoma^(2,3,4,15). Chewing betel nut and leaves with lime is not unusual in this geographic region, probably this personal habit may explain the high incidence of epidermoid carcinoma in buccal mucosa in this study for somewhat extent, though there was no satisfactory record to be available. Still, the cause of a significant high prevalence ($P < 0.2$) of epidermoid carcinoma in the left side buccal mucosa in this study material is not known, but the same result has been reported in the carcinoma of the tongue by Flamant et al (1964)⁽⁷⁾ and they suggested that a detailed study of possible etiological factors, especially the use of alcohol and tobacco would be interesting to do. The age distribution and the male predominant of the lesions were nearly the same as that in several reports (1,2,7,8,9,16,17).

In oral epidermoid carcinoma, ulceration, induration and fungating are the main local findings and among them ulceration is quite prevalent^(2,3,4,7). The duration from symptoms onset to first visit varies greatly not only in different anatomical regions but also in the same site. It has been reported ranging from less than one month to more than 10 years with the mean between 9 and 11.9 months in a study of cancer of buccal mucosa by O'Brien et al (1965)⁽¹⁷⁾. In another study of intraoral epidermoid carcinoma by Tiecke et al (1954)⁽¹¹⁾, the average duration was 4.2 months. In some other study of tongue carcinoma by Flamant et al (1964)⁽⁷⁾, the average period was 4.6 months. Of 169 cases recorded with symptoms in this study,

113 (67%) cases revealed ulceration. The average delay between symptom appearance and first visit in 6 cases of mouth floor and the other site was 1.4 months, the shortest duration among distinct location groups. But, the average duration of the all 77 patients was 6.9 months. Therefore, from the result of such a long average delay in seeking care, it should seem that the patients did not pay considerable attention to the oral epidermoid carcinoma. In order to avoid any more delay in treatment, a clinician should take some more responsibility for early detection of oral carcinoma. As Byer (1975)⁽¹⁴⁾ has stated that a clinician should keep a high index of suspicious of cancer when an ulcer has been present on the tongue longer than three weeks, and biopsy should be taken for an unhealing ulcer as early as possible⁽¹⁸⁾. There were 21 patients with enlarged regional lymph nodes during first examination of which 17 cases belonged to moderately differentiated epidermoid carcinoma and 4 cases belonged to anaplastic epidermoid carcinoma. Of the 11 cases of tongue carcinoma clinically with enlarged cervical nodes, 7 were arising from the tongue base. Although, it has been stated that the adenopathy was more frequently found in the patient with carcinoma in the posterior portion of the tongue⁽⁷⁾. The clinically enlarged regional lymph nodes may be caused by reactive proliferation of lymphoid tissue in some cases^(5,14,15,18). In order to make the best for choice of therapy, the enlarged lymph nodes should be histologically examined as possible as the same time while the patient comes for seeking aid.

Histological grading of malignancy of epidermoid carcinoma depended on cellular

differentiation and mitosis has been discussed by Broder more than half a century before, and the degree of malignancy of the carcinoma classified by this system has been considered to be highly significant to prognosis⁽¹⁰⁾. However, another multifactorial evaluating system of malignancy of epidermoid carcinoma, as also used in this study, has been developed recently. This multifactorial system of histologic grading has been believed to be more sufficient correlate better with prognosis than traditional classification^(11,12). Two systems have been applied in this study. And from the results, it could generally be found that the well-differentiated epidermoid carcinoma including so-called verrucous carcinoma has low scale of total malignancy points and the anaplastic epidermoid carcinoma were certainly with high scale of total malignancy points, while the scale point of the moderately differentiated carcinomas was broad in distribution, it in some cases revealed as high as that of the anaplastic epidermoid carcinoma, and in some other cases it even showed lower than that of a few well-differentiated epidermoid carcinoma. Indeed, the degree of differentiation is not always parallel to the other biologic behaviour of the tumor^(11,15). Thus, to determine the histological grading of malignancy of epidermoid carcinoma, it is undoubtedly that there are the more relevant criteria included the more accurate result obtained.

The relation between the primary tumor site and prognosis is still uncertain. Carcinoma of the lip, gingiva, and buccal mucosa has been regarded as slow growing compared to those of the tongue⁽¹⁵⁾. The prognosis of lip carcinoma is found to be

quite favorable even in advanced lesion, while the outlook for the tongue carcinoma is said to be somewhat worse than that for the carcinoma of the gingiva and the mouth-floor. Still, the histologic grade of malignancy of carcinoma is of less prognostic importance than the location of carcinoma within the tongue^(4,7). However, in a study of 585 cases of oral carcinoma. Fries et al (1980)⁽⁶⁾ concluded that the "so-called organ localizations" of carcinoma in the oral cavity do not carry any prognostic significance. As seen from the results in this study, no matter what kind of grading system applied, it seemed unable to make any straight correlation between the histological grading of epidermoid carcinoma and the intraoral anatomical sites with the only one exception of verrucous carcinoma predominant in lips. It could be, therefore suggested that histologic grade of the tumor is of limited important for the significant correlation (if there is any) between the primary tumor site and prognosis. Actually, prognosis of the tumor is believed to be influenced by various factors^{1,3,4)} not only the histologic grade and location but also the duration and size of the lesion, degree of spread, patient age, sex⁽¹⁹⁾ and therapeutic method etc. Any attempt to predict this complex problem with a single factor is likely to be inadequate.

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活體切片檢例口腔表皮樣癌之探討

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口腔原發性惡性腫瘤絕大多數是表皮樣癌已盡人皆知，本文即以口腔表皮樣癌之活體切片檢例及其臨床資料作其各項流行病學之統計及其組織學的研究，進而觀其組織分化型別及組織惡性度與患部之關係，藉以瞭解在台灣之中國人罹患口腔表皮樣癌之一般概況，及探討各患部之癌瘤組織惡性度分布情形，以期作為明瞭癌瘤預後與患部間關係之參考。研究材料是取自民國 54 年至民國 65 年計 12 年間台北醫學院病理學科獲自台灣各地診所醫院所送檢之口腔活體切片檢例標本及其臨床資料。所記載之臨床資料均加以分析統計之。全部標本均再次詳細鏡檢之，組織學上除傳統地將癌分成分化良好型表皮樣癌，中等度表皮樣癌及退行性表皮樣癌外，每一癌瘤還分別以其細胞群及癌與宿主間之各情形為基準以評估其組織學之惡性度，並觀其分布情形。

272 例口腔原發性惡性癌中表皮樣癌 245 例，其分布依序為舌 79 例，頰粘膜 52 例，牙齦 43 例，腭 34 例，唇 26 例，口底部 7 例，其他處 4 例。患者最年青者 27 歲，50 歲以上者共 183 例，男性居多。病發至求診期間由一星期至 4 年不等，平均 6.9 個月，在有記錄之 77 例中 50% 以上在 3 個月內。臨床以潰瘍為主要症狀，載明病狀之 169 例中述及潰瘍者 113 例。組織學屬退行性型者 24 例，多數其細胞似過渡細胞，亞基底細胞或中間型細胞成巢狀排列，不見角化亦無上皮珠，細胞間橋不易察覺，分裂像頗著。亦有由似梭形細胞所組成或含巨細胞出現多極性分裂像者。癌組織與正常組織間之境界不明，且幾呈瀰漫性浸及其下深部之結締組織，其惡性度總點數高，由 18 至 24 不等。13 例屬分化良好型，其細胞層次與分化程度頗似乳頭瘤，角化強，細胞間橋明顯，核大小均勻，分裂像較少。其往往呈乳突樣結節浸及毗鄰之結締組織，且界線分明，低倍鏡下偶易與乳頭瘤相混淆。其惡性度總點數由 8 至 14 不等。所謂疣狀癌者共 5 例（唇 4 例，頰粘膜 1 例），其組織學像與分化良好型者相近似，所不同的是其表面呈無數疣狀突起上蓋一層頗厚之角化物。餘 203 例為中等度分化型，多由數種型別細胞相互雜陳而成，各型細胞之比率及分裂像隨癌瘤而異，呈不等度之角化及上皮珠形成。絕大部分癌組織與其毗鄰之結締組織境界不清且呈廣泛性浸潤，75% 之病例呈中等度或極度圓形細胞浸潤，其惡性度總點數分布頗廣，由 10 至 20 點不等。

口腔表皮樣癌以犯舌者居首位幾各報告皆然，但本研究材料所示犯頰粘膜者之多僅次於犯舌者顯然異於一些報告，之所以如此或許與部分國人嗜嚼檳榔有關。或謂口腔表皮樣癌之預後與患部有關，然本研究中無論以何種評估方式，結果除疣狀癌好犯唇外均顯示癌之組織學惡性度之分布與患部無恒定關係，因此設若患部與預後有關之說屬實，癌組織惡性度型別似非為其單一之主因。

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