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한국인 구강악안면 영역의 전이 암종

조선대학교 대학원

치의학과

고 금 출

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METASTATIC TUMOR TO THE JAWS AND ORAL SOFT
TISSUES: A RETROSPECTIVE ANALYSIS OF 41 CASES IN
KOREAN INDIVIDUALS

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이 논문을 치의학 석사학위신청 논문으로 제출함.

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Abstract

METASTATIC TUMOR TO THE JAWS AND ORAL SOFT TISSUES: A RETROSPECTIVE ANALYSIS OF 41 CASES IN KOREAN INDIVIDUALS

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This article describes a pooled analysis of Korean individuals with 41 cases of metastatic oral tumors. The data on this review are based on the retrieved published case reports from the Korean dental and medical literature between the years 1983 and 2004. The mean age was 55.2 years and the male to female ratio was 1.9:1. There were more jawbone metastases than in oral soft tissues. Comparing with the western literatures which report the breast as the most common primary site, the most common primary site was the liver followed by the lung, and thyroid. The lung was the most common primary site for the jawbone metastases, whereas the liver was for the oral soft tissues. This discrepancy may be caused by underestimation or exclusion of the jawbone in surveying for the breast tumor metastasis. Another reason is that a relatively high incidence rate of hepatocellular carcinoma occurs in Korean, especially in male.

Key words: metastasis, jawbone, oral soft tissue, Korean

I. Introduction

Metastatic tumors to the oral region occupy about 1% of oral malignant tumors. They are mostly located in the mandible, where a majority occurs in the molar region. According to the western literature, metastatic tumors in the oral region mainly originate from the breast, followed by the lung, kidney, thyroid gland, intestine, prostate gland, stomach, testis, and bladder^{7,9,10,33,34}.

Recent improvements in the diagnosis and treatment of malignant tumors have served to increase the average length of the patient survival. Therefore, it has been considered as important medical practice to detect metastasis as early as possible. Especially in the oral metastasis, early diagnosis is very important because prognosis is poor in most cases. Most of the patients die within one year following the diagnosis of the oral metastasis while the four-year survival is estimated to be 10%^{2,34}. As a result, general practitioner's role must be emphasized as the first encounter of the patients who might have malignancies somewhere else or metastatic oral tumors with known primaries.

Despite a considerable volume of literatures written about metastatic oral tumors from different countries, metastatic oral tumors in Korean individuals have not been thoroughly analyzed yet. In this study, we present a pooled analysis of patients with metastatic oral tumors retrieved from the Korean dental and medical literature.

II. Patients and Methods

Well-documented case reports of metastatic oral tumors published between the years 1983 and 2004 were collected from the Korean dental and medical literatures using Korea Medline and from cross-reference. The search was made using the key words 'metastatic oral tumor', 'metastatic jaw tumor' and 'oral metastatic tumor'. A total cases were selected which including the cases registered at the Oral Biology Research Institute, School of Dentistry, Chosun University during 1990 and 2004. However, 7 cases were excluded from the current study because they were not clinical nor radiographic and the histological evidence could not confirm the diagnosis as well as primary sites^{1,3-6,8,11,13-28,31,32}. In this article, 41 histopathologically confirmed cases were reviewed regarding the primary sites, metastatic region, clinical presentation and histopathologic features.

III. Results

A. Age and Gender

The age ranged from 23 to 70 years with a mean of 55.2 years. The mean age for women was 50.2 years and 57.8 years for men. Twenty eight patients (68%) were in their fifth and sixth decades. With the exception of one case in which gender was not mentioned, our review consisted of 26 males and 14 females with a male to female ratio of 1.9:1. Metastasis to the jawbone occurred more frequently than to the soft tissues in both gender. Comparing the two genders, jawbone metastasis in male had 2.3 times higher incidence than female (Table 1).

B. Primary site

Most common primary sources of the metastatic oral tumors are shown in Table 2. We found 11 oral metastatic cases from the liver (26.8%), which was the most common primary site in this analysis. The second common primary site was the lung (9 cases, 22%) followed by the thyroid, female genital organs and colo-rectum. There was one case each from the kidney, breast, urinary bladder, stomach, gall bladder, pancreas, esophagus and lower extremity.

Jawbone metastases (23 cases) were more frequently reported than oral soft tissues (18 cases). In the jawbone, 8 out of 9 lung tumors metastasized to the jaws so that the lung was the most common primary site in the jawbone metastases, followed by the liver (6 cases), thyroid (4 cases). Additionally the colon, uterus, ovary, urinary bladder, esopaghus also showed the jaw metastasis in our review. On the other hand, the liver was

the most common primary site followed by female-genital organs, and thyroid in the soft tissue. The other soft tissue lesions originated from the lung, kidney, breast, stomach, gall bladder, pancreas, and lower extremity.

The common primary site differed between genders for women, the thyroid, followed by the female genital organs were most common; for man, it was the lung and liver. It is interesting that all lung tumor metastases to the oral region (9 cases) reported only in the male and all cases from the thyroid (6 cases) were reported in female. Histologically, hepatocellular carcinoma (HCC, 11 cases) showed the highest rate of metastasis and the next frequent type was adenocarcinoma (8 cases) which originated from the lung, female-genital organs, colo-rectum, stomach, and gall bladder. The follicular carcinoma (5 cases) was the third. In 32 cases, the oral metastasis was the only one found at the time the metastasis was recorded. Nine cases had other metastases as well. Histologically, most of the cases were carcinoma. Two sarcomas were found which were known as being extremely rare occurrence of oral metastases. In 11 (26.8%) out of 41 cases, metastasis to the oral region was the first indication of the existence of a primary somewhere else. The tumor types of the 11 cases were HCC (5), small cell carcinoma (2), follicular carcinoma (2), choriocarcinoma (1) and germ cell tumor (1).

Table 1.Comparison between cases metastatic tumors to the jawbone and oral soft tissue.

	M : F Ratio	Mean Age (range)		Most Common Primary Site	Most Common Oral Site
		M	F		
All (n=41)	1.9:1	57.8 (35-70)	50.2 (23-70)	Liver(11, 26.8%) Lung(9, 22.0%) Thyroid(6, 14.6%)	
Jawbone (n=23)	2.3:1	55.7 (35-70)	50.3 (29-69)	Lung(8, 34.8%) Liver(6, 26.1%) Tyroid(4, 17.4%)	Mandible (20)
OST (n=18)	1.1:1	61.1 (50-70)	48.3 (23-70)	Liver(5, 27.8%) Female-genital organ(3, 16.7%) Thyroid(2, 11.1%)	Gingiva (10)

M: Male, F : Female, T : total, OST : Oral soft tissue

Female-genital organs : Uterus, Ovary, Vagina

C. Oral site

In the jawbones, it was reported that 20 out of 23 cases metastasized to the mandible with the molar area being the most frequently involved site, followed by the ramus, mandibular angle, retromolar trigone, and condyle (Table 3). In the oral soft tissues, gingiva especially in the lower anterior region was the most affected sites (Table 4). The other oral soft tissue lesions were in the tongue, submandibular gland, masticator space, mouth floor, palate, vestibule, and cheek.

Table 2. Correlation between site of origin and gender in jawbone and oral soft tissue.

Primary site	Total (%)	Jawbone			Soft tissue	
		M	F	U	M	F
Liver	11(26.8)	5		1	4	1
Lung	9(22.0)	8			1	
Thyroid	6(14.6)		4			2
Female genital organs	4(9.8)		1			3
Colo-rectum	3(7.3)	1	1			1
Kidney	1(2.4)				1	
Breast	1(2.4)					1
Urinary bladder	1(2.4)	1				
Stomach	1(2.4)				1	
Gall bladder	1(2.4)					1
Pancreas	1(2.4)				1	
Esophagus	1(2.4)	1				
Lower extremity	1(2.4)				1	
Total	41(100)	16	6	1	9	9

M: male, F: female, U: unknown

Table 3. Sites of metastases in the jawbone.

Sites of involvement	Cases (%)
Max molar region	2 (8.7)
Max incisor region	1 (4.3)
Man maloar region	8 (34.8)
Ascending ramus	6 (26.1)
Man angle	2 (8.7)
Condyle	1 (4.3)
Retromolar trigone	1 (4.3)
Man (not specified)	2 (8.7)
Total	23 (100)

Max: Maxilla, Man: Mandible

Table 4. Sites of metastases in the oral soft tissue

Sites of involvement	Cases (%)
Gingiva upper anterior	1 (5.6)
upper posterior	2 (11.1)
lower anterior	4 (22.2)
lower posterior	2 (11.1)
lower unknown region	1 (5.6)
Tongue	1 (5.6)
Submandibular gland	1 (5.6)
Masticator space	1 (5.6)
Cheek	2 (11.1)
Mouth floor	1 (5.6)
Palate	1 (5.6)
Vestibule	1 (5.6)
Total	18 (100)

D. Signs and symptoms

The most common symptoms were painful swelling, paresthesia, bleeding, and increasing tooth mobility. Delayed healing of extraction socket, pathologic fracture, masticatory difficulties, trismus, dysphagia and dyspnea were reported as additional symptoms in 10 cases. Interestingly, all 5 patients showing paresthesia (21.6%) had mandibular ramus metastatic lesion.

Radiographically, a radiolucent or lytic lesion with ill-defined margins was shown in most jawbone metastases, but one case of the jawbone had positive technetium scans in spite of negative x-rays. On the other hand, there were no abnormalities in most soft tissue lesions. However, 3 cases out of 18 soft tissue metastatic cases showed radiographically cortical bone erosion.

IV. Discussion

It has been reported that most metastatic oral tumors were found in patients in their fifth to seventh decades^{9,10,29,33}. Our analysis also had same frequent age ranges with a mean of 55.2 years. The mean age of female patients were a little younger than male in the current study. The difference between the two genders is probably due to the cases of metastatic germ cell tumor and choriocarcinoma, which more frequently occur in younger aged women. However, there is a controversy whether men or women have tendency to affect more frequently. According to Hirshberg et al.⁹, metastases to the jawbones have a slight female predilection, while metastases to the oral mucosa have male to female ratio of 1.6:1. Schwartz et al.³³ reported that females were more likely to develop jawbone metastases. Their results attributed to the preponderance of primary breast lesion. However, Nishimura et al.²⁹ showed 1.5 times higher incidence in female than in male due to the high incidence of choriocarcinoma of the uterus. In our review, male had higher incidence rate than female, especially in the jawbone metastasis. The liver and lung were the most common primary sites for male, whereas the breast was much less common for female in this study. This may account for the difference in the gender ratio.

There is a difference between the western literatures and our analysis in the common primary sites. Contrast to the western reviews that the breast was the most common primary site, we found that the most common primary site was the liver followed by the lung and thyroid. Especially, the thyroid was the most common primary site for Korean women not the breast. Even though breast carcinoma has been one of the most common tumors among

Korean women and the most preferred site of metastasis is bone³⁰, there is no case report to the jawbone metastasis except for the one case to maxillary anterior gingiva in this review. One reason may be attributed that case reports have been mainly of unusual cases, which could cause some bias in favor of primary sites and oral sites⁹. The incidence of metastatic jawbone tumor, especially multiple metastases, is difficult to assess accurately since the jaws are seldom included in the radiographic skeletal survey¹⁰. Additionally, previous literatures have not been considered different ethnic origins as a factor in the metastatic process in the oral region. A review of the Japanese literature revealed that the uterus was the most common primary site in Japanese women, not the breast²⁹.

The liver and lung were the most frequently metastasizing tumors for Korean man. Although the high metastatic frequency from the lung is consistent with western literatures, the incidence rate from the liver was particularly higher than western reports. The HCC is one of the most common cancers among Koreans, especially in males¹². Huh et al.¹² reported that the crude annual incidence rate in Seoul from 1991 to 1992 was 21.1 per 100,000 for males and 7.0 for females. The mortality rate of HCC among Koreans was one of the highest in the world and was reported as 35.4 per 100,000 for males and 12.0 for females in 1990¹². As a result, due to the high incidence of HCC, oral metastases from the liver also reported frequently in Korean dental and medical literatures.

In 26.8% (11 cases) of patients, metastatic oral lesion was the first indication of an undiscovered malignancy at a distant site. This is consistent with the western reports of metastatic oral disease^{9,10}. In addition, the first indicative tumor types were HCC (5 cases), small cell carcinoma (2 cases), follicular carcinoma (2 cases), choriocarcinoma (1 case) and germ cell

tumor (1 case). Since these tumor types are histologically distinctive, the undiscovered malignancies in the distant organs might be easily detected. Another comparable finding with western literatures was that the diagnosis of metastatic oral tumor indicated a wide-spread disease and poor prognosis.

There was no difference in the oral site localization of the metastatic tumors, either in the jawbone or in the soft tissues. In the jawbones, it was the mandible with the molar area and lower anterior gingiva was the most affected sites in the oral soft tissues. Early gingival metastatic lesions often confused with benign reactive lesions such as pyogenic granuloma, hemangioma, giant cell granuloma, and peripheral fibroma from their clinical appearance³¹. Variable signs and symptoms lead to an erroneous diagnosis. Major symptoms like painful swelling, bleeding, increasing tooth mobility and minor symptoms such as delayed healing of extraction socket, pathologic fracture, masticatory difficulties, trismus, dysphagia and dyspnea were indication of the malignancies. It is particularly interest that all patients with paresthesia had mandibular ramus metastatic lesion. Metastasis to the mandible with involvement of the inferior alveolar nerve occasionally produces a distinctive pattern of anesthesia termed 'numb-chin syndrome' in which there is an unexplained loss of sensation in the lower lip and chin. Schwartz et al.³³ reported that alveolar nerve anesthesia was present in 50% of the cases in their review of mandibular metastasis, while Clausen and Poulsen⁷ reported only 25% of cases which is consistent with 21.6% of in this study. This difference is most likely based on the examination for alveolar nerve anesthesia in their series, while its presence or absence was not tested usually in the earlier reports.

In summary, here we analyzed the 41 cases of Korean oral metastases.

The most frequently affected oral region was the mandible with the molar area in the jawbones and the lower anterior gingiva in the oral soft tissues. While the breast was the most common primary site in the western literatures, the most common primary site was the liver followed by the lung, and thyroid in our review. In addition, the lung was the most common primary site for the jawbone metastases, whereas the liver was for the oral soft tissues. This discrepancy may be caused by underestimation or exclusion of the jawbone in surveying for the breast tumor metastasis. Another reason is that a relatively high incidence rate of HCC occurs in Korean, especially in male.

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본인이 저작한 위의 저작물에 대하여 다음과 같은 조건아래 조선대학교가 저작물을 이용할 수 있도록 허락하고 동의합니다.

- 다 음 -

1. 저작물의 DB구축 및 인터넷을 포함한 정보통신망에의 공개를 위한 저작물의 복제, 기억장치에의 저장, 전송 등을 허락함
2. 위의 목적을 위하여 필요한 범위 내에서의 편집·형식상의 변경을 허락함. 다만, 저작물의 내용변경은 금지함.
3. 배포·전송된 저작물의 영리적 목적을 위한 복제, 저장, 전송 등은 금지함.
4. 저작물에 대한 이용기간은 5년으로 하고, 기간종료 3개월 이내에 별도의 의사표시가 없을 경우에는 저작물의 이용기간을 계속 연장함.
5. 해당 저작물의 저작권을 타인에게 양도하거나 또는 출판을 허락을 하였을 경우에는 1개월 이내에 대학에 이를 통보함.
6. 조선대학교는 저작물의 이용허락 이후 해당 저작물로 인하여 발생하는 타인에 의한 권리 침해에 대하여 일체의 법적 책임을 지지 않음
7. 소속대학의 협정기관에 저작물의 제공 및 인터넷 등 정보통신망을 이용한 저작물의 전송·출력을 허락함.

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의
년

저작자: (서명 또는 인)

조선대학교 총장 귀하

