

## Sinonasal Metastatic Tumors in Taiwan

Hsueh-Hsin Huang<sup>1,2</sup>, MD; Tuan-Jen Fang<sup>1,2</sup>, MD; Po-Hung Chang<sup>2</sup>, MD; Ta-Jen Lee<sup>2</sup>, MD

**Background:** To analyze the incidence of the metastatic tumors within sinonasal tract in Taiwan and review the data in the English literature.

**Methods:** Retrospective reviewed of patients from 1990 to 2005 with a histologically proven diagnosis of metastatic malignancies in the sinonasal tract.

**Results:** Among seventeen enrolled patients, 9 were men and 8 were women, with ages ranging from 24 to 76 years old, with a mean of 50.8 years. In order of frequency, sinonasal metastatic tumors originated from the gastrointestinal tract (30%), liver (18%), kidney (18%), breast (18%), thyroid gland (12%) and lung (6%).

**Conclusion:** The incidence and characteristics of metastatic neoplasms in Taiwanese patients are comparable to other countries in East Asia, except for Japan. However, our data are very different when compared with European and North American reports. Different incidences of malignant neoplasms in the primary site may explain the result of different incidences of sinonasal metastatic tumor.

(*Chang Gung Med J* 2008;31:457-62)

**Key words:** paranasal sinus, nasal cavity, metastasis, breast cancer, hepatoma, kidney cancer

Malignant tumors of the sinonasal regions constitute less than 1% of all malignancies, and most of them are primary in origin.<sup>(1)</sup> Metastasis of malignant tumors to the sinonasal area occurs infrequently and usually presents at the late stage of primary disease. Based on Bernstein's study,<sup>(2)</sup> the most common primary sources in decreasing order are the kidney (49%), lung (12%), urogenital ridge (12%), breast (9%), and gastrointestinal tract (GI tract) (6%). (Table 1) The most common metastatic sites are the maxillary sinus (50%), followed by the ethmoid sinus (18%) and nasal cavity (15%).<sup>(2)</sup> Epistaxis, rhinorrhea, cheek pain and nasal obstruction are the major presenting symptoms of metastatic tumors in the nasal cavity and maxillary sinus; headache, visual impairment and diplopia are more common with

tumors in the sphenoid sinus.<sup>(2-4)</sup> The most common symptom of metastatic tumors in the sinonasal regions is epistaxis, which accompanies some of the other aforementioned symptoms, characteristic of primary sinus disease.<sup>(2-4)</sup> The mean age of patients with sinonasal metastases varies in different primary origins. After sinonasal metastasis occurs, palliative treatments are given to release obstructive, or compressive symptoms and pain.

In addition to Bernstein's report,<sup>(2)</sup> Friedmann<sup>(3)</sup> proposed tumors metastatic to the sinonasal regions arise most commonly from the kidney (77%) and the most common site is the maxillary sinus.<sup>(2,3)</sup> Because of the different incidences of various malignancies between Asia and Occidental areas, and the fact that the cancer incidence varies with time, the incidence

From the <sup>1</sup>Department of Otolaryngology, Chang Gung Memorial Hospital, Keelung; <sup>2</sup>Department of Otolaryngology, Chang Gung Memorial Hospital, Taipei, Chang Gung University College of Medicine, Taoyuan, Taiwan.

Received: Jun. 22, 2007; Accepted: Nov. 8, 2007

Correspondence to: Dr. Tuan-Jen Fang, Department of Otolaryngology, Chang Gung Memorial Hospital, No. 5, Fusing St., Gueishan Township, Taoyuan County 333, Taiwan (R.O.C.) Tel.: 886-3-3281200 ext. 3967; Fax: 886-3-3979361;

E-mail: fang3109@cgmh.org.tw

**Table 1.** Incidence of Malignant Tumors Metastatic to the Sinonasal Regions

Author	Case No.	Primary tumor origin							
		Kidney	Breast	Thyroid	GI tract	Lung	Urogenital ridge	Liver	Others
Bernstein et al. <sup>(2)</sup>	82	49%	9%	4%	6%	12%	12%	0	7%
Friedmann et al. <sup>(3)</sup>	31	77%	3%	0	3%	6%	10%	0	0
This presentation	17	18%	18%	12%	30%	6%	0	18%	0

of sources of sinonasal metastatic tumors may be different from previous reports. The purpose of this study is to present our data and to compare the frequency of sinonasal metastases in Taiwan with previously reported studies.

### METHODS

In this retrospective study, we reviewed all patients who presented to Chang Gung Memorial Hospital in Taiwan from 1990 to 2005 (Institutional Review Board approved) with a histologically proven diagnosis of metastatic malignancy in the paranasal sinuses and nasal cavity. Of the nineteen patients identified by a search of databases provided by the Department of Pathology and and the Department of Patient Studies, 2 were eliminated because no known primary tumor was found. The two cases were both mucinous adenocarcinoma of the intestinal type. The remaining 17 patients were the subjects of this study.

The medical records of these 17 patients were reviewed. The following patient data were collected and analyzed: age, gender, clinical symptoms, site of sinonasal metastasis at time of presentation, other distant metastatic sites discovered later in the clinical course, histologic reports, radiographic findings, sinonasal scopic findings and treatment modalities.

### RESULTS

Nine of the seventeen enrolled patients were men and 8 were women, with ages ranging from 24 to 76 years old. with a mean of 50.8 years. In order of frequency, metastatic tumors of the sinonasal regions arose from the liver (18%), kidney (18%), breast (18%), small intestine, colorectal area, thyroid gland (12%) and lung. (Table 1) The sites of metastasis of these tumors were the maxillary sinus (42%),

nasal cavity (42%), and ethmoid sinus in decreasing order. The sphenoid sinus and nasopharynx were less commonly involved. The most common presenting symptom was epistaxis (60%), followed by nasal obstruction and a nasal mass. At the time the sinonasal metastatic tumors were diagnosed, 9 of 17 patients (53%) had metastatic disease at other sites, most of which were bone (6), lung (6) and brain (2). Five patients had more than one extra-sinonasal metastasis. Most (15) of these primary malignant diseases were diagnosed prior to the presentation of sinonasal metastatic tumors in these patients, and 7 cases (41%) presented with the first manifestation of metastasis. Seven patients had known extra-sinonasal metastasis before the diagnosis of sinonasal metastasis was established. The mean interval between diagnosis of the primary tumor and presentation of sinonasal metastasis was 12.9 months. Table 2 shows the tumor characteristics in our patients.

### DISCUSSION

Bernstein's review of the world literature described 82 cases of metastatic foci to the paranasal sinuses in which the maxillary sinus was the most common cavity involved.<sup>(2)</sup> Tumors metastatic to the nose and paranasal sinuses arise most commonly from the kidney.<sup>(2,3)</sup> Most of the reviewed studies came from Europe (German, Italy and France) and North America.<sup>(2,3)</sup>

The most common sites of metastasis from kidney malignancies are the lungs (75%), regional lymph nodes (65%), bone (40%) and liver (40%).<sup>(5,6)</sup> About 15% of kidney cancers metastasize to the head and neck region, specifically to the paranasal sinuses.<sup>(6,7)</sup> Kidney cancer contributes 1.9% of the world's total malignancies and the crude cancer incidence is 3.4 per 100,000 persons in the male population.<sup>(8)</sup> The highest rates are in North America (males 13.2

**Table 2.** Characteristics of Sinonasal Metastases in Our Patients

No.	Age/ Sex	Primary tumor	Symptoms	Involved sinuses	Other metastases	Status of primary	Histology	Duration before metastasis
1	38/F	Breast	Epistaxis	Ethmoid sinus, nasal cavity	Bone	Known previous metastasis	Ductal carcinoma	Unknown
2	76/F	Breast	Epistaxis	Ethmoid sinus, nasal cavity	Lung, Parotid gland	Primary not diagnosed	Ductal carcinoma	
3	42/F	Breast	Epistaxis	Nasal cavity	Lung	Known previous metastasis	Ductal carcinoma	41 ms
4	59/F	Duodenum	Purulent rhinorrhea	Maxillary sinus	Lung, Bone, Brain	Known previous metastasis	Adenocarcima	14 ms
5	61/M	Rectum	Nasal obstruction	Maxillary sinus	None	First metastasis	Adenocarcima	24 ms
6	29/M	Colon	Nasal obstruction	Maxillary sinus	None	First metastasis	Adenocarcima	7 ms
7	53/M	Small intestine	Epistaxis	Ethmoid sinus	None	First metastasis	Adenocarcima	13 ms
8	73/M	Colon	Nasal obstruction	Nasal cavity	None	First metastasis	Adenocarcima	4 ms
9	55/M	Lung	Epistaxis	Maxillary sinus	Bone, Brain	First metastasis	SCC*	2 ms
10	30/F	Thyroid	Epistaxis	Nasal cavity	None	Primary not previously diagnosed	Papillary carcinoma	
11	49/F	Thyroid	Nasal mass	Nasopharynx	Bone metastasis	Known previous carcinoma	Papillary	8 ms
12	24/F	Kidney	Epistaxis	Nasal cavity	None	First sign of metastasis	TCC†	14 ms
13	74/F	Kidney	Epistaxis	Maxillary sinus	None	First sign of metastasis	TCC†	3 ms
14	63/M	Kidney	Epistaxis	Maxillary sinus	Unknown	Unknown	TCC†	Unknown
15	42/M	Liver	Diplopia	Sphenoid sinus	Lung, Rib	Known previous metastasis	Hepatoma	12 ms
16	55/M	Liver	Nasal mass	Nasal cavity	Lung, Mediastinum	Known previous metastasis	Hepatoma	12 ms
17	41/M	Liver	Epistaxis	Maxillary sinus	Lung, clavicle	Known previous metastasis	Hepatoma	14 ms

\*: SCC: squamous cell carcinoma ; †: TCC: transitional cell carcinoma.

per 100,000) and Europe (males > 10 per 100,000), whereas the incidence rates are low in Africa, Asia (except Japanese males) and the Pacific.<sup>(8)</sup> The kidney cancer incidence is especially low in eastern Asia (males 1.2; females 0.7 per 100,000).<sup>(8)</sup> In 1990, the crude rate of kidney cancer in Taiwan was 3.11 per 100,000 population in males and 1.84 in

females.<sup>(9)</sup> (Table 3)

The incidence rates in Europe and North America are much higher than in East Asia, including Taiwan. The high cancer incidence rate may be related to some risk factors, including obesity and dietary factors.<sup>(10)</sup> These predisposing factors may be the reason why the percentage of kidney cancer in

**Table 3.** Cancer Incidence in North American, Europe, East Asia and Taiwan

	Kidney (M/F)	Colo-rectal (M/F)	Breast	Liver (M/F)
North America	13.2/8.5	56.8/2.1	117.7	4.0/2.1
Europe	8.6~14.7/7.0~9.0	27.0~57.2/2.7~6.1	69.6~104.6	7.3/4.2
East Asia*	1.2/0.7	10.9/10.3	11.0	29.9/10.3
Taiwan	3.11/1.84	36.3/28.3	42.65	52.1/20.0

Crude rate of cancer incidence in 1990: per 100,000

**Abbreviations:** M/F: male/female; \*: East Asia includes China, Taiwan, Korea, Thailand ...etc, but not Japan.

sinonasal metastatic tumors is higher in Europe and North America than Taiwan.

Hepatocellular carcinoma (HCC) is among the most common malignancies in the world (5.4% of total malignancies).<sup>(8)</sup> HCC is estimated to have an incidence of between 250,000 to 1.2 million per year worldwide. The cancer incidence is low in North America (male/female: 4.0/2.1 per 100,000) and Europe (male/female: 7.3/4.2 per 100,000) and high in sub-Saharan Africa, and East Asia (China male/female: 29.9/10.3; Taiwan male/female: 52.1/20.0)<sup>(8)</sup> China (East Asia) alone counts for 53.9% of the worldwide total HCC cases.<sup>(8)</sup> HCC metastasizes easily and extrahepatic metastasis of HCC occurs in more than 50% of these patients.<sup>(11)</sup>

Chronic hepatitis B and C virus infections are well documented to have a major role in HCC development.<sup>(12,13)</sup> Chen proposed HBV could significantly increase the incidence rate of HCC and decrease the mean age of HBV-related HCC patients.<sup>(12)</sup> HBV does play an important role in chronic hepatitis in Asia as follows: China (78%), Philippines (64.5%), Taiwan (76%), Singapore (70%) and Malaysia (75.3%). The exception is Japan where HBV accounts for only 36% of chronic hepatitis, but HCV accounts for 63%.<sup>(12,13)</sup> The lower age of sino-nasal HCC - affected patients in Asia, especially in Taiwan, is related to the high prevalence of HBV-related HCC.<sup>(8)</sup> The annual crude rate of HCC has reached 36.4 cases per 100,000 persons in Taiwan (male:female = 2.5:1)<sup>(9)</sup> and hepatitis B virus causes 80-90% of HCC in Taiwan.<sup>(12,13)</sup> Although sinonasal metastatic HCC occurred infrequently in previous reports, the high cancer incidence rate, large number of cases, and lower age of affected patients has increased the frequency of HCC as the source of sinonasal metastasis in Taiwan.

### Conclusions

The cancer incidence of individual malignant tumors is variable in different areas; it may depend on genetic predisposition or exposure to environmental risk factors. The cancer distribution is similar in Taiwan and other countries in East Asia, except for Japan, but is very different from that in Europe and North America. We believe this is the reason why the proportions of sources of metastatic tumors in the sinonasal regions in Taiwan are different from that in previously reported studies.

### REFERENCES

1. Carrau RL, Myers EN. Neoplasms of the nose and paranasal sinuses. In Bailey BJ, Calhoun KH, Healy GB, Johnson JT, Jackler RK, Pillsbury III HC, Tardy ME, eds. Head and Neck Surgery-Otolaryngology. 3rd ed. Philadelphia: Lippincott Williams & Wilkins, 2001:1247-64.
2. Bernstein JM, Montgomery WW, Balogh K. Metastatic tumors of the maxilla, nose and paranasal sinuses. Laryngoscope 1966;76:621-50.
3. Friedmann I, Osborn DA. Metastatic tumors in the ear, nose and throat region. J Laryngol Otol 1965;79:576-91.
4. Mochimatsu I, Tsukuda M, Furukawa S. Tumors metastasizing to the head and neck - a report of seven cases. J Laryngol Otol 1993;107:1171-3.
5. Godley PA, Stinchcombe TE. Renal cell carcinoma. Curr Opin Oncol 1999;11:213-7.
6. Som PM, Norton KI, Shugar JM, Reede DL, Norton L, Biller HF, Som ML. Metastatic hypernephroma to the head and neck. AJNR Am J Neuroradiol 1987;8:1103-6.
7. Gottlieb MD, Roland JT. Paradoxical spread of renal cell carcinoma to the head and neck. Laryngoscope 1998;108:1301-5.
8. Parkin DM, Pisani P, Ferlay J. Estimates of the worldwide incidence of 25 major cancers in 1990. Int J Cancer 1999;80:827-41.
9. Annual Report of Cancer Registry, Department of Health,

- Taiwan, 2004. (In Chinese)
10. Rubagotti A, Martorana G, Boccardo FM. Epidemiology of kidney cancer. *Eur Urol* 2006;supple 5:558-65.
  11. Izquierdo J, Armengot M, Cors R, Perez A, Basterra J. Hepatocarcinoma: Metastasis to the nose and paranasal sinuses. *Otolaryngol Head Neck Surg* 2000;122:932-3.
  12. Chen CJ, Yu MW, Liaw YF. Epidemiological characteristics and risk factors of hepatocellular carcinoma. *J Gastroenterol Hepatol* 1997;12:294-308.
  13. Lee CM, Lu SN, Changchien CS, Yeh CT, Hsu TT, Tang JH, Wang JH, Lin DY, Chen CL, Chen WJ. Age, gender, and local geographic variations of viral etiology of hepatocellular carcinoma in a hyperendemic area for hepatitis B virus infection. *Cancer* 1999;86:1143-50.

## 台灣轉移性鼻竇癌的原發腫瘤發生率

黃學信<sup>1,2</sup> 方端仁<sup>1,2</sup> 張伯宏<sup>2</sup> 李達人<sup>2</sup>

**背景：**轉移至鼻竇及鼻腔的惡性腫瘤並不常見。轉移至該處最常見的惡性腫瘤其原發部位依序為：腎臟 (49%)，肺臟 (12%)，泌尿生殖系統 (12%)。本文假設不同的惡性腫瘤盛行率會導致轉移至鼻竇及鼻腔的腫瘤之原發部位比例不同。

**方法：**本篇由 1990 到 2005 年，以回溯整理方式共報告了 17 個患有經組織病理證實為轉移至鼻竇及鼻腔之惡性腫瘤的病人。

**結果：**在 17 個病人中，9 名是男性，8 名是女性。年齡分布為 24 至 76 歲，平均年齡 50.8 歲。轉移至鼻竇及鼻腔的惡性腫瘤來源依序為：胃腸道 (30%)，肝臟 (18%)，腎臟 (18%)，乳房 (18%)，甲狀腺 (12%)，及肺臟 (6%)。

**結論：**在台灣及其他除日本之外的東亞國家，轉移至鼻竇及鼻腔的惡性腫瘤其發生率及特徵相似，但卻與歐洲及北美地區差異甚大。根據本篇研究，我們認為這可解釋為何在台灣轉移至鼻竇及鼻腔之惡性腫瘤，其原發部位比例和之前被報告過的研究不同。

(長庚醫誌 2008;31:457-62)

**關鍵詞：**副鼻竇，鼻腔，轉移，乳癌，肝癌，腎臟癌

---

長庚紀念醫院 <sup>1</sup>基隆院區；<sup>2</sup>台北院區 耳鼻喉部；長庚大學 醫學院

受文日期：民國96年6月22日；接受刊載：民國96年11月8日

通訊作者：方端仁醫師，長庚紀念醫院 耳鼻喉部。桃園縣333龜山鄉復興街5號。Tel.: (03)3281200轉3967;

Fax: (03)3979361; E-mail: fang3109@cgmh.org.tw