

Craniospinal Metastasis from a Metastasizing Mixed Tumor of Salivary Gland : Unusual Presentation

Hyun-Hee Ye, M.D.,¹ Chang-Won Cho, M.D., Ph.D.,¹
Mi-Young Jeon, M.D., Ph.D.,² Dae-Jo Kim, M.D., Ph.D.¹

Departments of Neurosurgery,¹ Pathology,² Maryknoll Medical Center, Busan, Korea

Metastasizing mixed tumors (MMT) of salivary glands are inexplicably metastasize maintaining benign histology. There is no pathologic and flow cytometric analysis criteria to predict the metastasis. MMT is known to metastasize by local implantation, vascular and lymphatic embolization after multiple surgery to local recurrences of primary tumor. However, multiple metastasis including cranium and spine occurred even without surgery to the primary tumor in this case. No pathological evidence of malignancy could be found in both primary and metastatic tumor. MMT is considered as an low grade malignancy based on clinical behavior rather than histologic evidence, such as low mortality rate, long delay of metastasis after primary lesion. Cranial metastasis is also extremely rare and only two cases have been reported. We report this unusual case with a literature review.

KEY WORDS : Metastasizing mixed tumors · Metastasis · Primary tumor · Cranial.

Introduction

Benign mixed tumors, also termed as benign pleomorphic adenomas are the most common tumors of salivary gland. Very few of benign mixed tumors metastasize inexplicably maintaining benign histology. These are named as metastasizing mixed tumors and considered as unrecognized or low grade malignancy even though they have benign histology. We present a case of multiple metastasis including cranium and spine from a metastasizing mixed tumor of salivary gland.

Case Report

A 68-year-old female patient visited dermatology department due to multiple nodules at back and arm that developed recently and left submandibular mass, 8 × 10cm in size which developed

40 years ago. She had no facial palsy and the mass was not painful but found to be growing in size. The result of forearm skin biopsy was benign chondroid syringoma. One and half year later, she visited dermatology again due to multiple scalp nodules recently developed. The otolaryneal specialist operated on the left submandibular mass and biopsied the multiple scalp nodules as well (Fig. 1A, B). The histopathologic examination

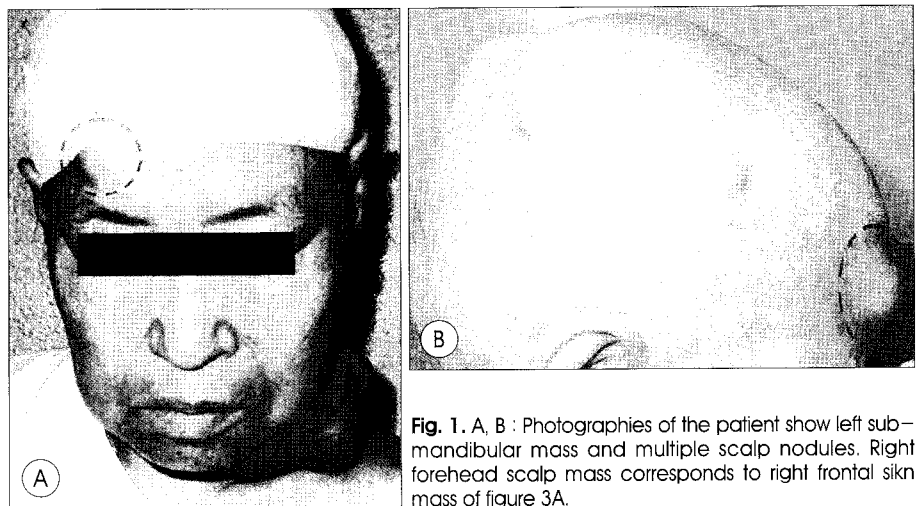


Fig. 1. A, B : Photographies of the patient show left submandibular mass and multiple scalp nodules. Right forehead scalp mass corresponds to right frontal skin mass of figure 3A.

• Received : August 23, 2006 • Accepted : December 15, 2006

• Address for reprints : Chang-Won Cho, MD., Ph.D., Department of Neurosurgery, Maryknoll Medical Center, Daecheong-dong 4-ga, Jung-gu, Busan 600-730, Korea Tel : +82-51-461-2458, Fax : +82-51-466-6164, E-mail : braincwc@hotmail.com

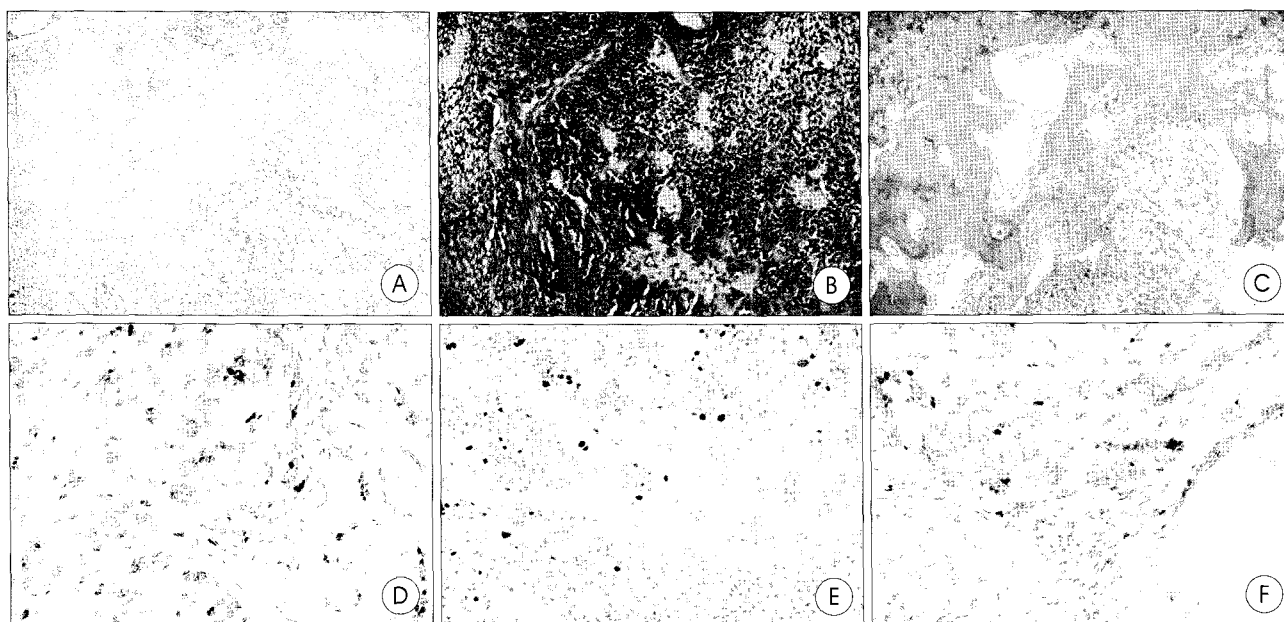


Fig. 2. A : Pathologic finding of submandibular mass shows admixture of glandular epithelium and myxochondroid stroma. Right lower area shows high cellularity and similar finding with metastatic lesion (H&E, x40). B : Pathologic finding of cranial mass shows markedly hypercellular appearance without cytologic atypia and scanty myxoid stroma (H&E, x100). C : Pathologic finding of spine mass shows benign appearing tumor cell infiltrating bone (H&E, x40). D : Photography shows section of submandibular mass immunostained MIB-1, 6.2% (x400). E : Photography showing section of brain metastatic mass immunostained MIB-1, 6.5% (x400). F : Photography demonstrating section of spine metastatic mass immunostained MIB-1, 6.2% (x400).

results were benign mixed tumors and the same histologic finding with previous biopsy from skin lesion (benign chondroid syringoma) (Fig. 2A). Two months later, she was referred to neurosurgical department due to change in mentality as confused state. The Gadolinium-enhanced magnetic resonance image (MRI) of brain revealed the left frontal mass involving skull and compressing the left frontal lobe, 6 × 4cm in size with two additional lesions involving occipital bone (Fig. 3A). The left frontal mass was removed with involved bone which showed the same pathology with left submandibular mass, benign mixed tumor (Fig. 2B). Whole body bone scan with Tc99m-HDP demonstrated the multiple metastatic lesions to spine, rib, and scapula (Fig. 3B). Enhanced computed tomography scan of chest revealed multiple metastatic nodules to both lungs (Fig. 3C). One month after craniotomy, she complained of leg weakness. The Gadolinium-enhanced MRI of spine revealed the bone tumor compressing the spinal cord at T10 level and thecal sac at L3 region which were then surgically removed (Fig. 3D). Pathology of spine mass was also the same with previous ones, benign mixed tumor (Fig. 2C). The patient gained normal cognitive function and improved to become ambulatory. Even though the pathologic finding was benign, radiation therapy was given to the resection bed of brain, two additional lesions at occipital bone with 5800 rad and the spine resection bed with 2500 rad each. The brain and spine lesions showed no change on recent follow up MRI (Fig. 3E, F) but the left submandibular gland mass recurred one year after first re-

section, although in small size. The recent follow up of chest CT shows slight mass enlargement in compared with previous ones from one year earlier (Fig. 3G). Submandibular mass was again removed recently and the pathologic finding was also the same with previous ones maintaining benign histology.

Discussion

Benign mixed tumors are the most common neoplasm of salivary glands and are composed of an admixture of benign glandular epithelia and mesenchymal component such as myxochondroid, mucoid or hyalinized fibrous stroma^{1,11}. Some of these 2-9% are known to undergo malignant change³. The malignant mixed tumors of salivary glands include carcinoma ex-mixed tumor and carcinosarcoma (true malignant mixed tumor). In both cases, clinical and histopathological criteria for malignancy are usually present. In carcinoma ex-mixed tumor, focus of carcinoma arises from the epithelial component of benign mixed tumor in association with residual benign mixed tumor. Clinically, they show recent, rapid growth or development of facial nerve palsy from a long standing salivary gland mass. In carcinosarcoma, simultaneous foci of carcinoma and sarcoma are present with residual mixed tumor. The sarcomatous component is usually chondrosarcoma. Clinically, they are presented with painful, enlarging mass, sometimes associated with facial palsy. The third category is metastasizing mixed tumor which metastasize inexplicably mai-

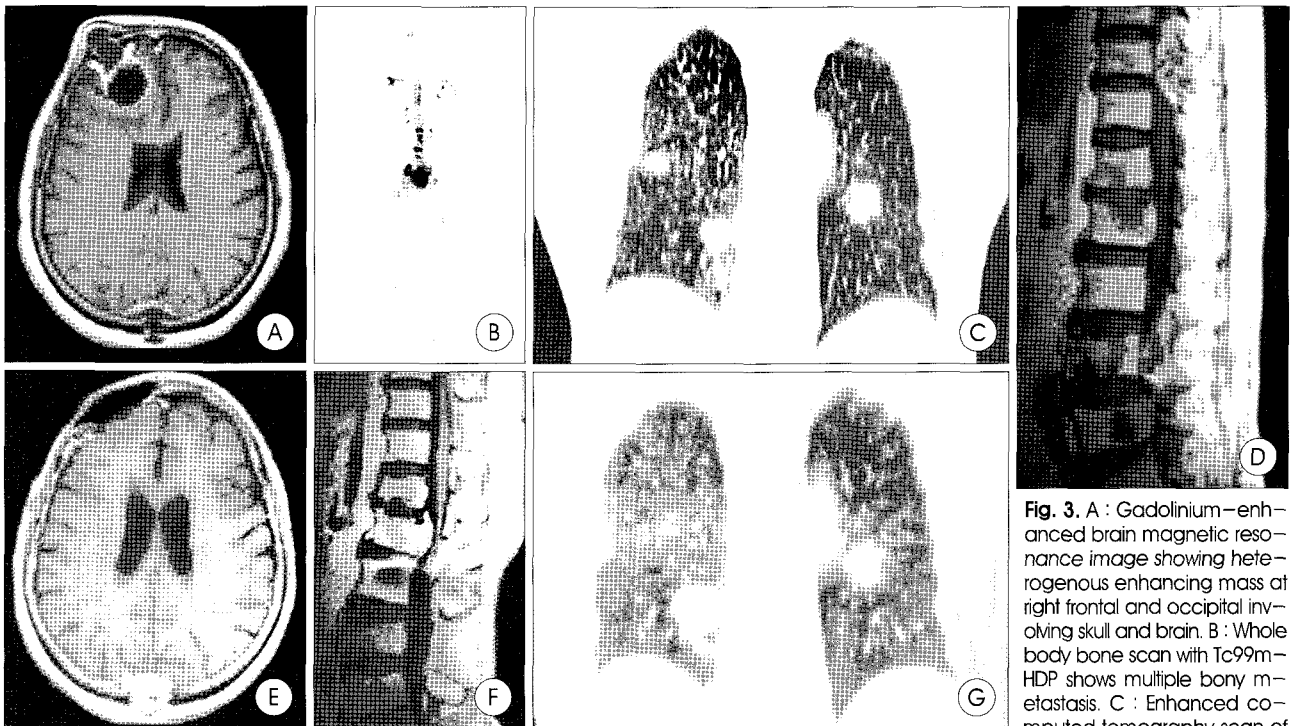


Fig. 3. A : Gadolinium-enhanced brain magnetic resonance image showing heterogeneous enhancing mass at right frontal and occipital involving skull and brain. B : Whole body bone scan with Tc99m-HDP shows multiple bony metastasis. C : Enhanced computed tomography scan of

chest revealing multiple metastatic nodules on both lung fields. D : Gadolinium-enhanced spine magnetic resonance image demonstrating multiple vertebral body invasion by tumor with heterogenous enhancing mass in spinal canal at T10 and L3 level. E : Postoperative gadolinium-enhanced brain magnetic resonance image shows no recurrence of tumor mass. F : Postoperative gadolinium-enhanced spine magnetic resonance image shows no recurrence of tumor mass. G : Follow-up enhanced computed tomography scan of chest shows slight mass enlargement compared with previous ones.

maintaining benign histology. Marioni et al found out approximately 60 cases since 1942 in their exhaustive literature review in 2003⁸. The metastasis developed usually after long indolent course, with a maximum of 52 years following occurrence of primary tumor reported¹³. Clinically, no facial palsy and pain are associated with MMT. There are several authors who have tried to characterize the pathological criteria of MMT. Chen stated that infiltrative growth pattern and limited mitotic activity in an otherwise typical mixed tumor is indicative of MMT¹. Cresson et al postulated that myoepithelial predominance should be considered in diagnostic criteria of MMT⁹. El-Naggar et al postulated that the only common feature to all MMT was stromal, often myxoid preponderance in the tumors⁴. However, Wenig et al presented in their 11 cases that epithelial component predominate rather than myxochondroid stromal component¹³. However, they could not find out any pathologic criteria including mitotic rate, cellular pleomorphism, infiltrative growth, vascular or lymphatic invasion and flow cytometric analysis to predict metastasis in MMT in their extensive retrospective review. In this case, infiltrative margin and focal areas of ischemic necrosis were found in primary tumor, but there were no atypical mitosis and other findings suggesting typical anaplasia were found. The metastatic tumors showed high cellularity compared with primary tumor of salivary gland in this case. However, some benign mixed tumor may show

extremely high cellular pattern and these tumors do not behave differently from the ordinary pattern on follow up study⁷. The MIB1 results of primary tumor, cranial and spine metastasis were 6.2%, 6.5% and 6.2% each with similar proliferative potential (Fig. 2D, E, F). Thus, MMT is considered as a low grade malignancy based on clinical behavior rather than pathological evidence, such as low mortality rate, long delay of metastasis after primary lesion⁸. Most of the metastasis in MMT develop after multiple local recurrences of primary tumor^{8,13}. Hence, the mechanism of metastasis is considered as a spillage from capsular rupture during excision of primary tumor and local implantation with vascular and lymphatic access^{2,12,13}. Only three cases have been reported in which metastasis developed without local recurrences after excision of primary tumor^{11,13,14}. Also, there has not been any case report of metastasis without surgery of primary tumor through literature review. In this aspect, this case is very unique as patient presented simultaneously the huge submandibular mass of 40 years history and recent on set of nodular mass of back and arm.

The chondroid syringoma of skin and mixed tumor of salivary glands share the same histological findings on light and electron microscopic finding¹⁰. The chondroid syringomas of skin of back and arm were considered to be metastasis from benign mixed tumor of submandibular gland. It is not certain that the skin biopsy procedure to the already metastasized mul-

iple skin nodule expedited the whole body metastasis including the cranium, spine, lung and bone. The frequent metastatic sites are bone and lung. Calvarial metastasis such as this case is extremely rare and only two cases have been reported with MMT^{6,9,13}. Wenig et al reported one case of central nervous system (CNS) metastasis among their cases there was no detailed description¹³. The ideal treatment is total surgical excision of primary lesion. Treatment of metastatic lesion depends on sites but surgical excision is recommended if possible. The overall mortality rate as a result of metastasis is known to be approximately 20%⁸. There is no established scientific evidence that favors the radiation therapy to MMT. In this case, brain and spine were irradiated after surgery and still shows stable condition after one year. However, small nodular submandibular mass recurred and metastatic lesion of lung increased in size during this period, which were not irradiated. Radiotherapy definitely played role to delay the recurrence in this case and this can be considered in cases of incomplete excision or as a palliative therapy^{1,4}.

Conclusion

Cranial and spine metastasis can develop from long standing benign mixed tumor of salivary gland. Metastasis usually occur after multiple local recurrences of primary tumor but also may develop simultaneously, as in this case. Thus, benign mixed tumor of salivary gland should be considered as a metastatic foci to the CNS.

• Acknowledgement

There is no funding resources and interest in this manuscript and this has never been presented in neurosurgical society until now.

References

1. Chen KTK : Metastasizing pleomorphic adenoma of the salivary gland. *Cancer* 42 : 2407-2411, 1978
2. Collina G, Eusibi V, Carasoli PT : Pleomorphic adenoma with Lymph-node Metastases Report of two cases. *Path Res Pract* 184 : 188-193, 1989
3. Cresson DH, Goldsmith M, Askin FB, Reddick RL, Postma DS, Siegal GP : Metastasizing Pleomorphic adenoma with Myoepithelial cell predominance. *Path Res Pract* 186 : 795-800; discussion 801-802, 1990
4. el-Naggar A, Batsakis JG, Kessler S : Benign metastatic mixed tumours or unrecognized salivary carcinomas? *J Laryngol Otol* 102 : 810-812, 1988
5. Fugimura M, Sugawara T, Seki H, Otawara Y, Sakuma T, Nakano Y, et al : Carcinomatous change in the cranial metastasis from a metastasizing mixed tumor of the salivary gland. *Neurol Med Chir (Tokyo)* 37 : 546-550, 1997
6. Girson M, Mendelsohn DB, Burns D, Mikey B : Histologically benign pleomorphic adenoma of the calvaria. *AJNR Am J Neuroradiol* 12 : 193-196, 1991
7. Juan R : Major and minor salivary gland : *Rosai and Ackerman's Surgical Pathology*, 9th ed. : Mosby, 2004, Vol1, pp873-916
8. Marioni G, Marino F, Stramare R, Marchese-Ragona R, Staffieri A : Benign metastasizing pleomorphic adenoma of the parotid gland : a clinicopathologic puzzle. *Head Neck* 25 : 1071-1076, 2003
9. Morrison PD, McMullin JP : A case of metastasizing benign pleomorphic adenoma of the parotid. *Clin Oncol* 10 : 173-176, 1984
10. Pinto de Moraes H, Herrera GA, Mendonca AM, Estrela RR : Metastatic Malignant Mixed tumor of the skin. *Appl Pathol* 4 : 199-208, 1986
11. Schreiberstein JM, Tronic B, Tarlov E, Hybels RL : Benign metastasizing pleomorphic adenoma. *Otolaryngol Head Neck Surg* 112 : 612-615, 1995
12. Sim DW, Maran AG, Harris D : Metastatic salivary pleomorphic adenoma. *J Laryngol Otol* 104 : 45-47, 1990
13. Wenig BM, Hitchcock CL, Ellis GL, Gnepp DR : Metastasizing mixed tumor of salivary glands. A clinicopathologic and flow cytometric analysis. *Am J Surg Pathol* 16 : 845-858, 1992
14. Youngs GR, Scheuer PJ : Histologically benign mixed parotid tumour with hepatic metastasis. *J Pathol* 109 : 171-172, 1973