Multiple Meningiomas Characterized by Benign and Malignant Tumor Entities

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Meningiomas are the most common intracranial tumors, accounting for about 30% of all reported brain tumors [1]. Most meningiomas are benign sporadic solitary, and multiple meningiomas (MMs) occurs in 1–9% of all meningiomas [2]. However, MMs consisting of both benign and malignant meningiomas are extremely rare [2–4]. Here, we presented a unique case of an adult who exhibited both intraparenchymal fibrous meningioma and anaplastic meningioma.

A 67-year-old man presented with hemiparesis of the right limbs, associated with a 2-month history of aconuresis and a 1-month history of intermittent fever and vomiting. Neurological examination revealed bilateral moderate papilledema, a mild mental confusion, and right hemiparesis with a positive Babinski sign. He had no family history of neurofibromatosis, and no evidence of café au lait spots. A CT scan revealed a mixed-dense tumor at the left frontal lobe and a mixed-density lesion with a surrounding edema at the left insular lobe (Figure 1A). Magnetic resonance imaging (MRI) confirmed the presence of an oval-shaped cystic tumor ($43 \times 52 \times 45 \text{ mm}^3$) in the left insular lobe. The lesion appeared to be nonhomogeneous, hypointense on the T1-weighted images, and hyperintense on T2-weighted images with surrounding edema. There was strong ring enhancement of the cyst wall following gadolinium administration, and dural tail sign was not noticed. We observed the cyst within the tumor that was isointense to cerebrospinal fluid. Magnetic resonance imaging also showed a small ($40 \times 21 \times 52 \text{ mm}^3$) strongly enhanced tumor that was hyperintense in both T1-weighted and T2-weighted images and was attached to the superior sagittal sinus in the left frontal lobe (Figure 1B).

A bifrontal craniotomy approach was performed. First, a grayish white and poor-defined solid tumor was excised at the left frontal lobe. The tumor tightly adhered to the dura mater approaching central line, and the dura infiltrated by the tumor was also removed. Then, through Sylvian fissure, a slightly gray tumor with slightly rich vascularity was excised. After the insular tumor totally removed, a yellow fluid flowed out from the tumor. No connection between the surface of the insular lobe tumor and the dura was found. Postoperatively, the patient remained neurologically intact.

Histological examination showed that the tumors were in two different histological types, which were fibrous meningioma at the left insular lobe and anaplastic meningioma at the left frontal lobe. The insular tumor was composed of fibroblast-like spindle-shaped cells and showed fascicular growth pattern (Figure 1C). The left frontal tumor revealed obvious malignant cytology, focal necrosis, and high mitotic rate (>20 mitosis/10 HPF), which is similar to sarcoma. Immunohistochemical staining showed both tumors were positive for vimentin, epithelial membrane antigen (EMA), and S-100 protein, but negative for glial fibrillary acidic protein (GFAP) and cytokeratin (CK), suggesting meningiomas. The MIB-1 labeling index of the insular lobe tumor was less than 1%, while the index of the frontal tumor was about 20%. In addition, the insular tumor did not express mutant-p53-positive cells, whereas the frontal lobe tumor did. The frontal tumor was negative for progesterone receptor (PR), while the insular lobe tumor positive. Moreover, the frontal tumor was positive for sox-2, musashi, and nestin, while the insular lobe tumor was negative (Figure 1C).

Figure 1 Adjuvant examination of this patient with multiple meningiomas. (A) Plain CT shows two lesions with a mixed density at the left frontal lobe and the left insular lobe. (B) Magnetic resonance imaging (MRI) of head also revealed both of masses. The one at the left frontal lobe was hyperintense in both T1-weighted and T2-weighted images. The other one at the left insular lobe was hypointense in T1-weighted image and hyperintense in T2-weighted image. After contrast enhancement, coronal and sagittal MR images shows uniform enhancement on the left frontal mass and strong ring enhancement on the left insular mass. Note the large cyst in left insular mass. (C) Histopathological examination was obtained. The left insular tumor shows typical features of fibrous meningioma with predominant of spindle-shaped cells. The left insular tumor expressed progesterone receptor (PR), but was negative for sox-2. The left frontal tumor has features of malignancy (geographical necrosis and nuclear pleomorphism) and high nuclear–cytoplasmic ratio, mitoses, and “sarcoma-like” morphology. The left frontal tumor did not expressed PR, whereas it was positive for sox-2.

The majority of multiple meningiomas present as benign with uniform histology [4]. Young-Cho Koh [3] reported a case of multiple meningiomas with both atypical meningioma and psammomatous meningioma. Tomita [4] described a 61-year-old patient with multiple meningiomas consisting of anaplastic meningioma and fibrous meningioma. Mocker [2] introduced a case of a 36-year-old female with a transitional-atypical meningioma and a transitional-psammomatous meningioma. Therefore, there are only three cases with MMs consisting of different pathological types in the same patients in the literature nowadays. We summarized total 4 cases of multiple meningiomas consisting of both benign and malignant meningiomas in Table 1 [2–4].

One of the important features in our case is that the tumor at the insular lobe and close to Sylvian fissure is an intraparenchymal meningioma with neither dural attachments nor any relationship with the ventricles. Intraparenchymal meningioma is extremely rare [5,6], believed to arise from ectopic meningothelial cells within the stroma of the choroid plexus, tela choroidea, or

the pia mater [6]. It has been shown that the major pathological subtype is fibrous meningioma, which is benign [5,6]. We also demonstrated that the intraparenchymal meningioma in our case was fibrous type. Cyst formation is uncommon in meningiomas, but the incidence of cyst formation is relatively high in intraparenchymal meningiomas [6]. This is consistent with our case. Because of the absence of typical features on CT scans and MRI, it is extremely difficult to distinguish intraparenchymal cystic meningioma from glioma or metastatic brain tumor with cystic or necrosis changes [7]. To our knowledge, this is the fourth case with multiple meningiomas consisting of different grades of malignancy in the same patient. However, we first presented that a patient with intraparenchymal fibrous meningioma also suffered from anaplastic meningioma, which is different from the other three cases [2–4].

There are two hypotheses for the occurrence of multiple meningiomas. First, tumors originate from multicentric neoplastic foci and arise independently. Another hypothesis suggests that a single

Table 1 A comparison of three cases of previously reported multiple meningiomas consisting of both benign and malignant meningiomas with our present case

	Present study		Koh et al., 2001 [3]		Tomita et al., 2003 [4]		Mocker et al., 2011 [2]	
Sex	Male		Male		Female		Female	
Age	67		65		61		36	
Tumor location	Left frontal	Left insular	Right frontal	Left parietal	Left sphenoid ridge	Left parasagittal	Left parietal	Left occipital
Cystic meningioma	Yes	Yes	Yes	No	No	No	/	/
Histopathological subtype	Anaplastic III grade	Fibrous I grade	Atypical II grade	Psammomatous I grade	Anaplastic III grade	Fibrous I grade	Atypical II grade	Psammomatous I grade
Dural attachment	Yes	No	Yes	Yes	Yes	Yes	Yes	Yes
Intraparenchymal meningioma	No	Yes	No	No	No	No	No	No

transforming event occurs and the original clone of cells spreads through the subarachnoid space, resulting in the formation of multiple, clonally related tumors. If the benign lesion and the malignant lesion are derived from a single clone in this case, what is the reason for the difference in the two histological types? Many tumors have shown to display gene expression signatures characteristic of human embryonic stem cells [8]. There may be stem-like cells in meningiomas [1,9]. Prakash Rath [1] had succeeded in isolating meningioma-initiating cells from atypical meningioma. Therefore, we examined the stem cell markers nestin, musashi-1, and a self-renewal transcript factor sox-2 expression in our case by using immunohistochemistry. Our results showed that nestin, musashi-1, and sox-2 in the malignant lesion are strongly positive as compared with those in the benign lesion. Although the molecular genetic study was not employed in our case, our preliminary pathological data seemingly suggest that cancer stem cells might

play a role in the progression of multiple meningiomas, supporting a common clonal origin of MMs. This hypothesis, however, is amenable to further investigation.

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Conflict of Interest

The authors declare no conflict of interest.

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