CASE REPORT

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Microcystic Meningiomas : Its Immunohistochemical and Genetic Aspect

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The authors report three microcystic meningiomas with its characteristic immunohistochemical findings and chromosomal pattern. Three patients with surgically treated microcystic meningioma were studied for its radiological, histopathological findings, and chromosomal analysis was done in the one patient. Tumors were convexity meningioma in the frontal area. The tumors were enhanced homogenously in the two, and enhanced inhomogenously with multiple small cysts in the other one on preoperative magnetic resonance image. Pathological examination showed marked nuclear pleomorphism, many small cysts, hyaline thickening in blood vessel wall, and mucinous background, compatable to microcystic type. EMA and vimentin were positive on the immunohistochemical stain. Chromosomal analysis showed tetrasomies of chromosome 5, 13, 17, and 20, and trisomies of chromosome 6, 7, 9, 11, 12, 16, 19, and 21, which are quite different from those of benign meningioma.

KEY WORDS : Microcystic · Meningioma · Immunohistological stain.

Introduction

Meningiomas are common benign tumors accounting for 13% to 18% of intracranial neoplasms[15]. They are known to be solid tumors and their gross appearance at operation usually leads to a correct diagnosis. Most of them are biologically benign, but prognosis is poor in WHO grade II and III tumors. The use of CT and MRI have generally improved our ability to identify and locate the tumor with a histological predictive accuracy approximately 90 percent.

Grade I meningiomas have been subdivided into a variety of types, including meningotheliomatous, fibrous, transitional, psammomatous, angiomatous, and etc. Microcystic meningioma is a rare variant of WHO grade I meningioma, accounting for 1.6~7% of intracranial meningioma[12,16]. It is characterized by microscopically myxoid appearance as defined by the new World Health Organization classification of brain tumors[5]. The authors experienced three cases of microcystic meningioma. So, we report three cases with clinicopathological features and genetic analysis.

Case Report

Patient 1

A 55-year-old man was admitted to the hospital because of

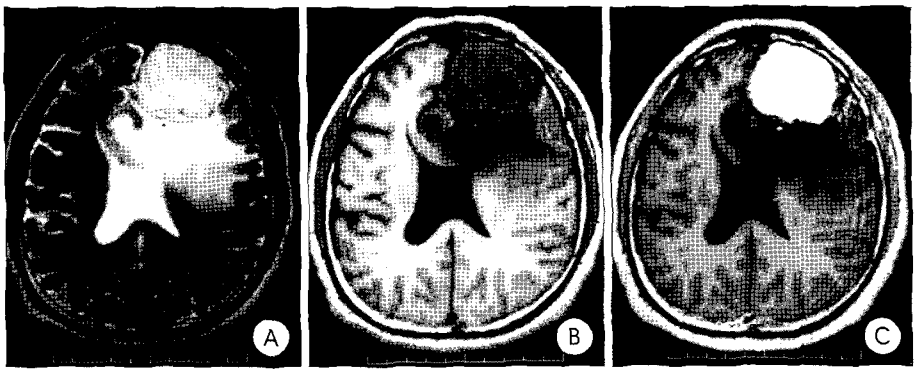

Fig. 1. Preoperative magnetic resonance(MR) image showing 4×4cm sized mass on the left frontal area, attached to the convexity dura. It is iso-signal on T2-weighted image with surrounding edema (A), low signal intensity on T1-weighted image (B), homogeneously enhancement on T1-weighted gadolinium-enhanced MR image (C).

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generalized tonic seizure. Neurological examinations were normal. He did not have any other past medical history. MRI of the brain revealed 4×4cm sized mass on the left frontal area, attached to the convexity dura (Fig. 1). It was iso-signal on T2-weighted image with surrounding edema, and was low signal intensity on T1-weighted image with homogeneous enhancement. The tumor was removed totally as Simpson Grade one. On histopathological examination, the tumor cells have elongated process nuclei. The background is loose mucinous with many small cysts formed by cytoplasmic process and contents of cysts are transudate. Hyaline thickening of blood vessel is observed (Fig. 2). Postoperative course was uneventful.

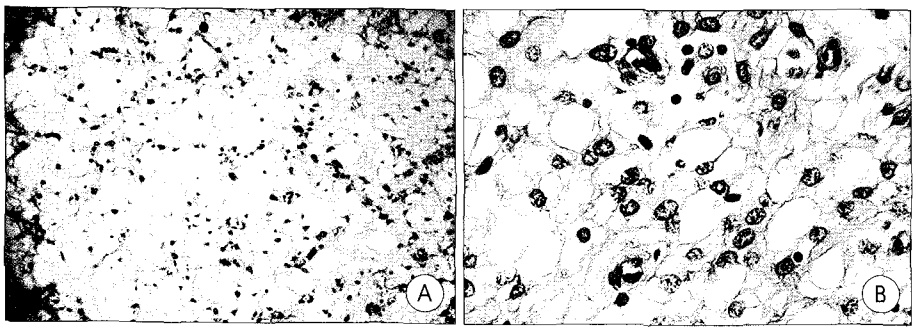

Fig. 2. A : The background is loose mucinous with many small cysts formed by cytoplasmic process and contents of cysts are transudate (H & E, ×100). B : The tumor cells have elongated process nuclei. Hyaline thickening of blood vessel is observed (H & E, ×200).

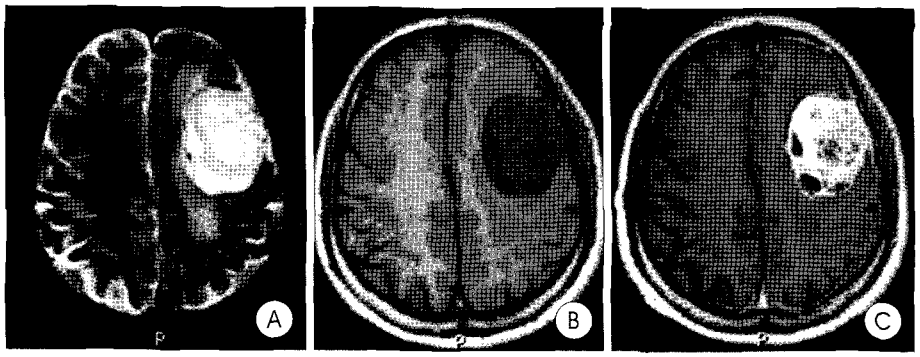

Fig. 3. Magnetic resonance(MR) image showing a mass on the left frontal area, which is 4×5cm in size. Small multiple cysts are noted and dural tail sign is not prominent. It is mixed-signal on T2-weighted MR image(A), low signal intensity on T1-weighted MR image(B), inhomogeneously enhancing on T1-weighted gadolinium-enhanced MR image(C).

Patient 2

A 61-year-old man was admitted with a history of memory disturbance for 1 month. Neurologic examinations were normal. MRI of the brain showed inhomogenously enhancing mass on the left frontal area, which was 4×5cm cm in size (Fig. 3). Small multiple cysts were noted but typical dural tail sign was not prominent. Differential diagnosis include metastatic tumor or high grade glioma. On surgery, vascularity was marked, and frozen section diagnosis could not exclude glioblastoma. But, the tumor was attached to the dura and arachnoid dissection plane was clear. The tumor was removed totally.

On histopathological examination, the tumor cells have hyperchromatic, pleomorphic nuclei. The background is loose mucinous with many small cysts formed by cytoplasmic process and contents of cysts are transudate (Fig. 4A, B). The tumor cells reveal immunoreactivity for epithelial membrane antigen (EMA) along the cytoplasmic membrane (Fig. 4C). Postoperatively, he was discharged 9 days later without neurologic deficit.

Patient 3

A 51-year-old woman was admitted with a progressive headache. No neurological abnormalities were noted. MRI of the brain revealed 2×2cm sized mass on the right frontal convexity, which was iso-signal on T2-weighted image. It was enhanced homogenously (Fig. 5). The tumor was removed totally, and histopathological examination confirmed microcystic meningioma with hyperchromatic, pleomorphic nuclei. The background is loose muci-

Fig. 4. A : The background is loose mucinous with many small cysts formed by cytoplasmic process and contents of cysts are transudate (H & E, ×100). B : The tumor cells have hyperchromatic, pleomorphic nuclei (H & E, ×400). C : The tumor cells reveal immunoreactivity for epithelial membrane antigen along the cytoplasmic membrane (EMA, ×100).

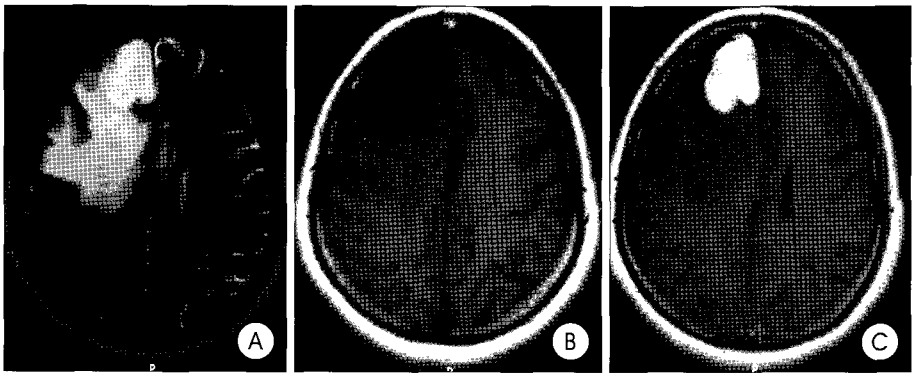

Fig. 5. Magnetic resonance(MR) image of the brain revealing 2×2cm sized mass on the right frontal convexity, It is iso-signal on T2-weighted MR image (A), low signal intensity on T1-weighted MR image (B), inhomogeneously enhancing on T1-weighted gadolinium-enhanced MR image (C).

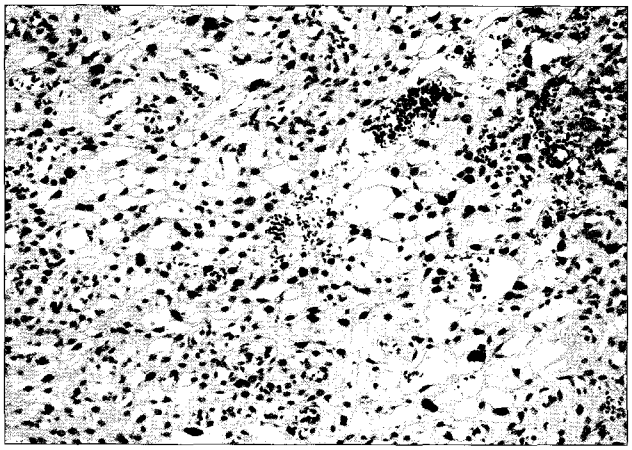

Fig. 6. The background is loose mucinous with many small cysts formed by cytoplasmic process and contents of cysts are transudate (H & E ×100).

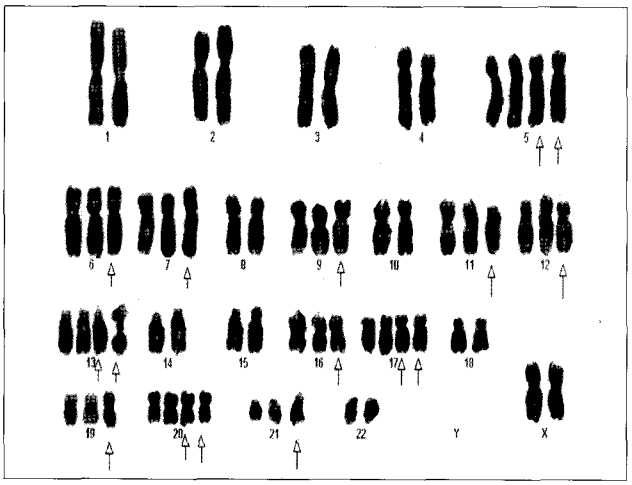

Fig. 7. Chromosomal analysis showing tetrasomies for chromosome 5, 13, 17, and 20, and trisomies for chromosome 6, 7, 9, 11, 12, 16, 19, and 21.

nous with many small cysts formed by cytoplasmic process and contents of cysts are transudate (Fig. 6). Immunoreactivity for vimentin and the cytoplasmic membrane was positive. Postoperative course was uneventful.

Chromosomal analysis was done. Classical G-banding with trypsin-EDTA was done and chromosomes were identified according to ISCN 1995. Chromosomal analysis showed tetrasomies for chromosome 5, 13, 17, and 20, and trisomies for chromosome 6, 7, 9, 11, 12, 16, 19, and 21 (Fig. 7).

Discussion

WHO classify meningiomas into three group by likehood of recurrence and grade. Microcystic variant belong to the group I[6]. Pathologically, cystic spaces within the cell cluster or sheets are characteristic findings, and cytoplasm is more abundant than that of classic meningioma, and may resemble hemangioblastoma with lipidosis, pilocystic astrocytoma with a prominent microcystic component, and metastatic adenocarcinoma[4,8]. The astrocytoma presents satellite cells and PTAH (phosphotungstic acid-hematoxylin)-positive intracytoplasmic fibrils[8]. The abscence of malignant cytological features such as mitosis, necrosis and cerebral invasion is worth mentioning as it helps to exclude clear cell malignant tumors of other cellular origin[8]. Unfortunately, sometimes even the intraoperative pathologic examination(frozen section) is unclear and only the postoperative histopathologic study will provide an accurate diagnosis.

The immunohistochemistry of microcystic meningiomas is similar to that of other meningiomas. Meningiomas are generally considered to be mesenchymal origin, arising from the arachnoid membrane and their dual mesenchymal and epithelial properties are reflected by staining for both vimentin and EMA (epithelial membrane antigen) in most major types of meningiomas[5,13].

This type of tumor has been described as one of the histological variants of meningioma under the term of microcystic, humid, myxomatous, or vacuolated meningioma. Cyst formation of the meningioma was described by Penfield[2] in 1932, and Masson described similar lesions as humid and myxomatous meningiomas in 1956. The term 'microcystic' was suggested by Kleinman et al. in 1980, and microcystic meningioma is available according to the new WHO classification of brain tumors.

Microcystic meningioma has female predominance at the age ranging from 3 to 90 years (mean 50.5 years), similar to most other meningiomas[10]. Microcystic meningiomas are more common in the pediatric age group than in the adult. They are seen in 10~19% of all pediatric meningiomas, compared with only

2~4% in the adult. The most frequent location of microcystic meningiomas is the cerebral convexity and the parasagital region is the second most frequent location. Microcystic meningioma is considered to have a clinical course similar to those of typical meningiomas despite the morphological differences, with slowly progressive symptoms[14]. Some authors reported the rapid onset of symptoms[14], but it might be due to enlargement of cyst and edema rather than the tumor itself.

On computed tomography or magnetic resonance imaging of the brain, the tumor may be enhanced homogeneously or heterogeneously and confused with cystic astrocytoma or metastatic adenocarcinoma in the latter, resulting in incorrect radiological diagnosis about 50% of patients. Location of the tumor with broad-based dura attachment is an important radiological evidence suggesting meningioma.

As described earlier, cyst formation is the characteristic features of the microcystic meningioma, and several theories were proposed to explain the pathogenesis of the cyst formation[1]. Some studies indicated secretory activity of tumor cells or degenerative processes. Michaud and Gagne suggested that the transduction of low-protein fluid could be responsible for the cyst formation[8]. Some reports claimed that the formation of microcysts mimics the developmental process of the subarachnoid space in the embryo. But all of these reports say that the precise mechanism of microcystic formation remains unknown[8]. The several theories have been advanced to explain the microcystic changes, recapitulation of subarachnoid structure (penetration of CSF), degenerative process, and disordered vascular permeability (protein fluid transudation)[3]. The genetic abnormalities reported in meningioma are loss of heterozygosity (LOH) at 22q, abnormalities of chromosome 1p, 9q, 10q, and 14q. In a study of 208 meningiomas for LOH on chromosome 10, significant correlations were reported between chromosome 10 markers and tumor grade, that is, higher incidence of LOH and multiple loci on chromosome 10 was related with malignancy[7,11]. In this study, only one patients was analyzed and genetic subset of microcystic type was quite different from that of benign meningioma, showing tetrasomies for chromosome 5, 13, 17 and 20 and trisomies for chromosomes 6, 7, 9, 11, 12, 16, 19, and 21. Maillo et al. reported trisomy 22 predicts worse outcome. From clinical view point, trisomy/tetrasomy was associated with several adverse disease characters such as younger mean age, higher incidence of atypical and anaplastic histopathologic subtypes, greater proportion of DNA aneuploid cases, and higher proliferative rate of tumor cells. Even more, from prognotic point of view, trisomy and tetrasomy was associated with a significantly shorter disease free survival[9]. Its unique abnormal chromosomal findings that may be confusing to neurosurgeon, radiologist and pathologist alike and need to further study in the future.

Conclusion

Meningioma are most common intracranial benign tumor, and they must be differentiated from malignant tumors. But, microcystic meningiomas, though very uncommon, should be considered in the differential diagnosis of gliomas or metastatic carcinomas. Recently, we experienced this uncommon type of meningiomas, so reported it with review of literatures.

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Commentary

The authors presented three illustrative cases of microcystic meningioma with a contemporary literature review. They described characteristic MR findings of microcystic meningioma and immunohistochemical findings with a chromosomal analysis data in one case. They found tetrasomies for chromosome 5, 13, 17, and 20 and trisomies for chromosomes 6, 7, 9, 11, 12, 16, 19, and 21 in chromosomal analysis of one case. They

mentioned that microcystic meningiomas, though very uncommon, should be considered in the differential diagnosis of gliomas or metastatic carcinomas because of cystic nature and frequent association of peritumoral edema in radiological examinations.

I think this paper is very interesting and informative in that they mentioned about the chromosomal abnormalities in one case of microcystic meningioma and they stressed the differential dignosis with other malignant tumors. Microcystic meningioma is well known to have characteristic MR findings which are helpful for preoperative differential diagnosis : (1) high signal in T2-weighted images; (2) low signal in T1-weighted images; (3) dura-based enhancing mass with a "dural tail sign"[1]. However it has been unknown about the underlying mechanism of the high incidence rate of severe peritumoral brain edema and cystic nature of microcystic meningioma. As the authors empathized, I think the differential diagnosis with other malignant brain tumors such as high grade gliomas or metastastic brain tumors is very important before surgery. Regarding chromosomal abnormalities shown in one case of microcystic meningioma, however, further study seems to be mandatory for clarification of whether such chromosomal abnormalities are common findings in the microcytic meningioma.

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