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Case Report

Multiple Extracranial Metastases of Atypical Meningiomas

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Meningiomas are usually benign neoplasms in which extracranial metastases occur very rarely. We report a case of multiple extracranial metastases of an atypical meningioma following a local recurrence. A 68-year-old man presented with left-side motor weakness and dysarthria for two weeks. A computed tomography (CT) scan and magnetic resonance imaging (MRI) showed an intraventricular tumor. We performed a total mass removal, and the histopathologic findings were consistent with benign meningioma. Eight months later, the meningioma recurred. We performed a reoperation and whole brain radiation therapy postoperatively. The histopathologic findings showed atypical meningioma. Six months later, CT and MRI revealed metastases to multiple vertebrae, lung, ribs and perirenal soft tissue so a decompressive laminectomy with mass removal was performed. The histopathologic findings of the spinal tumors showed atypical meningioma. The results from perirenal biopsies were consistent with metastatic meningioma. In conclusion, extracranial metastasis as well as local recurrence must be considered in atypical or anaplastic meningioma. There must be regular follow-ups. Finally, an evaluation of the chest, abdomen and bone is necessary, especially when related symptoms or signs develop.

KEY WORDS : Extracranial metastasis · Atypical meningioma · Anaplastic meningioma.

INTRODUCTION

Meningiomas are slow-growing benign neoplasms that constitute 14% to 19% of all primary intracranial and intraspinal tumors[19]. Although these tumors are typically benign, they may occasionally behave aggressively in atypical or malignant meningiomas. The reported metastatic rate of atypical meningioma is 5%[4]. However, multiple extracranial metastases are very rare. Here, we report a case of multiple metastases to the spine, lung, ribs and perirenal soft tissue from an atypical intracranial meningioma after local recurrence.

CASE REPORT

A 68-year-old man was admitted with left-side motor weakness (grade III) and dysarthria which had lasted for 2 weeks. A computed tomography (CT) scan and magnetic resonance imaging (MRI) revealed a mass lesion at the lateral ventricle that was approximately $5.5 \times 5.7 \times 3.6$ cm in size (Fig. 1). We performed a gross total surgical resection (Simpson's grade 1) of the tumor mass via a right temporoparietal transcortical approach that provided the shortest trajectory. The mass near the cortex was fragile and its margin was poorly defined, but the deep portion of the mass was hard and its margin well defined from the adjacent normal tissue. The histopathologic findings were consistent with benign meningioma (Fig. 2A). After the operation, his left-side motor weakness was improved to grade IV and he also recovered from the dysarthria.

After 8 months, the patient complained of a headache that had arisen 2 weeks earlier. Two days before his visit, the dysarthria returned and he complained of drowsiness, which resulted in his admission. CT and MRI revealed multiple recurred masses in the right lateral ventricle as well as the temporal cortex on the previous operation route (Fig. 3). We performed additional histopathologic studies with biopsy speciman from the former operation, focusing on immunohistochemical analyses. The patient was rediagnosed as having atypical meningioma because the Ki-67 labeling index was 20%, and the p53 labeling index was

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focally positive in the immunohistochemical staining. The patient and his family refused any treatment and he was discharged, but readmitted after a month for an operation. A gross total removal of the tumor through a right temporoparietal craniotomy was carried out as the initial operation. The histopathologic findings of the tumor demonstrated mild cytologic atypia and two mitoses in 10 high power fields (HPF) (Fig. 2B). It was consistent with a borderline rather than atypical meningioma. However, we concluded atypical meningioma, because immunohistochemical analysis showed 20% of Ki-67 and 10% of P-53. The patient was discharged as the neurologic symptoms improved. Whole brain radiation therapy at a total dose of 5,940 cGy was followed.

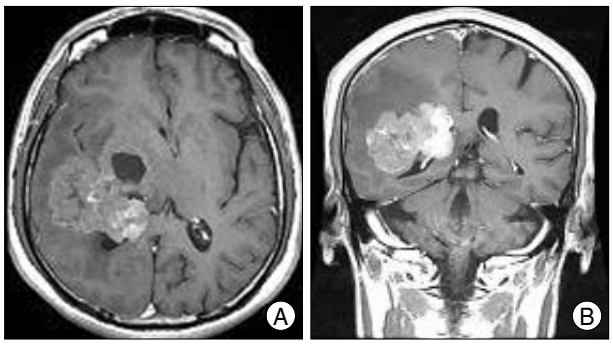

Fig. 1. Axial (A) and coronal (B) T1-weighted magnetic resonance imaging with gadolinium enhance-mnent demonstrates a mushrooming, non-homogenous, peritumoral edematous intraventricular mass with a cyst-like area and periventricular extension.

After 6 months, he was admitted with motor weakness of both legs (grade II), back pain and chest pain that had lasted for two weeks. CT and MRI revealed multiple spinal metastases in T5, T10, L1, L3, L4, S1, S2 and especially T7. At T7, a posterolateral epidural mass compressing the cord as well as multiple osteolytic lesions were observed (Fig. 4). Abdominal CT revealed two well-marginated enhancing retroperitoneal masses. The larger one was approximately 7.9×5.9×7.7 cm in size and the smaller one, medial and superior to the large one, was about 3.7×3.9×3.7 cm in size with an inner non-enhancing necrotic portion between the left kidney and spleen. There was medial displacement of the left kidney due to the abutting left perirenal and pararenal masses (Fig. 5). Chest CT and X-ray revealed multiple nodules in the both lungs. Among these, the largest one was about 1.7×1.5 cm in size, in the lingular segment of the left upper lobe (Fig. 6). First, we performed a decompressive total laminectomy of T7 and subtotal T6 with removal of the epidural mass. The mass compressed the cord in the epidural space, and it adhered tightly to the dura. We removed the epidural mass and metastasized bone including the pedicle and transverse process. The metastasized bone was fragile and bled profusely. According to the histopathologic findings, it was an atypical meningioma with bone invasion (Fig. 2C). Paraparesis did not improve significantly after the surgery. Four weeks after the operation, a percutaneous biopsy of the perirenal masses was done and the histopathologic findings showed metastatic malignant meningioma (Fig. 2D). In the immunohistochemical staining, the Ki-67 labeling index was 30%. The patient refused any other intensive treatments and wanted conservative management, so he was transferred to a local clinic and died after a few months.

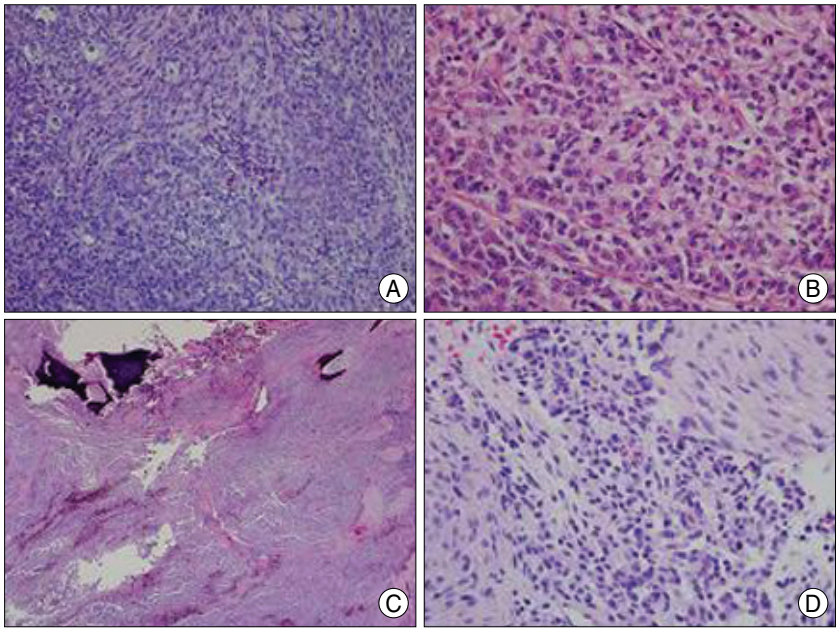

Fig. 2. Histopathologic findings. A : First resected tumor consists of spindle cells with whorling or fascicular patterns (Hematoxylin-Eosin, ×400). B : Second resected tumor shows mild cytologic atypia and a few mitoses : mitotic count : 2/10 high power field (Hematoxylin-Eosin, ×400). C : Resected vertebral tissue reveals invasion to the bone (Hematoxylin-Eosin, ×12.5). D : Resected perirenal soft tissue shows a morphologic appearance similar to conventional meningiomas (Hematoxylin-Eosin, ×400).

DISCUSSION

Meningioma is regarded as a benign neoplasm that commonly arises along the intracranial and spinal meninges and dural extensions. These tumors constitute 14-19% of all central nervous system neoplasms[19]. The intraventricular meningioma in particular is a relatively rare neoplasm,

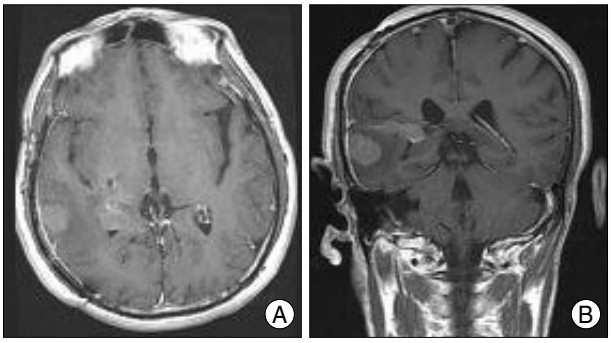

Fig. 3. Axial (A) and coronal (B) T1-weighted magnetic resonance imaging with gadolinium enhancement reveals multiple recurred masses in the right lateral ventricle and the temporal cortex on the previous operative route.

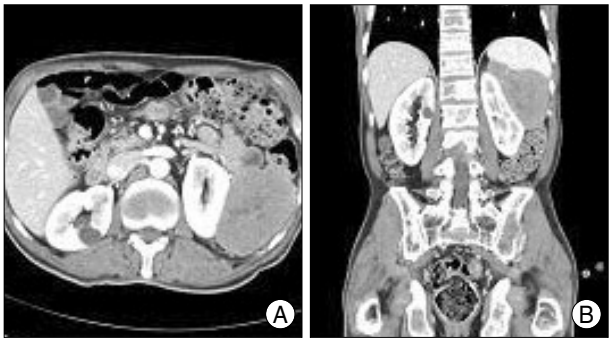

Fig. 5. Axial (A) and coronal (B) abdomianl enhanced computed tomography revealed well marginated enhancing two retroperitoneal masses between left kidney and spleen.

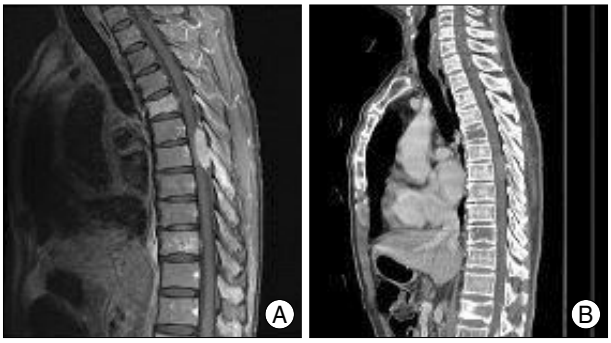

Fig. 4. Sagittal view of gadolinium-enhanced T1-weighted magnetic resonance image (A) and enhanced computed tomography (B) show multiple spinal metastases with epidural mass compressing cord posterolaterally and multiple osteolytic lesions.

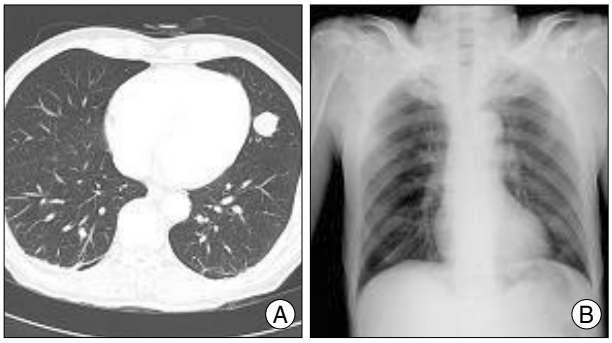

Fig. 6. Computed tomography (A) and a simple X-ray (B) of the chest revealing multiple nodules. The largest nodule is about 1.7×1.5 cm in size, lingular segment of left upper lobe.

comprising only 0.5 to 3% of all intracranial meningiomas[6]. The local recurrence rates of meningioma, even after complete resection, vary from 9 to 32%[3]. Distant metastasis is rare and has been estimated to occur in only 0.1% with patients in meningioma[15]. However, the reported metastatic rate of atypical meningioma is 5% and of malignant meningioma, 30%[2,4].

The World Health Organization (WHO) classification of tumors of the nervous system lists 15 histopathological variants of meningioma. Atypical meningiomas have increased mitotic activity, with three or more of the following features : increased cellularity, small cells with high nucleus-to-cytoplasm ratio, prominent nucleoli, uninterrupted patternless or sheet-like growth and foci of 'spontaneous' or 'geographic necrosis'. For this variant, increased mitotic activity has been defined as four or more mitosis per 10 high-power fields (defined as 16 mm^2)[11]. Anaplastic meningiomas exhibit histological features of frank malignancy far in excess of the abnormalities present in atypical menin-gioma. Such features include either obviously malignant cytology or a high mitotic index (20 or more mitoses per 10 HPF)[12]. The above criteria have also been shown to correlate with higher recurrence rates. In our case, we diagnosed benign meningioma and did not perform any other adjuvant treatment nor immunohistochemical analysis because there were few mitoses.

The histopathological criteria for malignancy in meningiomas remain at least partly uncertain. More than three mitoses/10 HPF seems to be the most reliable indicator of malignant behavior, but that measure is also imperfect[8]. So, immunohistochemical analysis of a nuclear protein related to cell proliferation, the Ki-67 and P53 labeling index, or of molecular markers such as CDKN2A deletion, along with a 9p21 deletion, are very useful in evaluating the potential of tumors to recur or metastasize[10,16]. The Ki-67 indices especially show a highly significant increase from benign (mean 3.8%), through atypical (mean 7.2%), to anaplastic meningioma (mean 14.7%)[7].

In the assessment of a meningioma, certain radiological indicators such as mushrooming, non-homogenous enhancement, peritumoral edema, osteolysis, intrinsic cyst-like areas, and indistinct tumor-brain borders have been proposed as providing important clues about the malignancy or aggressiveness of the tumor[9]. In our case, although MRI showed aggressive characteristics including mushrooming, non-homogenous enhancement, marked peritumoral edema,

we did not doubt the histopathologic findings. This was a mistake. When multiple lesions recurred after 8 months, we analyzed once again the immunohistochemical study of the biopsy specimen from the initial operation. The Ki-67 labeling index was 20% and we rediagnosed it as atypical meningioma. After the second operation, the biopsy also revealed atypical meningioma and the Ki-67 labeling index was 20%. Thus, when meningiomas have recurred or metastasized, or radiologic findings are aggressive, analyses of immunohistochemistry such as the Ki-67 labeling index are useful in defining malignancy or aggressiveness.

Extracranial metastasis of meningiomas is rare. The most frequent sites are pulmonary and pleural, followed by the intra-abdominal organs especially the liver, lymph nodes, long bones, pelvis, skull, vertebrae and other visceral organs[13]. Therefore, in the case of recurrent or metastatic meningioma, the evaluation for multiple organs, especially the lungs, has to be made at the same time. Metastases of meningiomas are postulated to spread via the venous system, lymphatics or cerebrospinal fluid (CSF). Meningiomas commonly invade dural venous sinuses and cranial veins and can travel from there to the pulmonary circulation, the azygous and hemiazygous systems, and the vertebral venous plexus, accounting for the major sites of metastasis[18]. Surgery was initially thought to aid the formation of metastases by allowing tumor cells access to the blood and lymphatic circulation[14]. Meningiomas gain access to the lymphatic system as they spread in the skull and scalp or to the lymphatics around the cranial nerves, for instance in the cavenous sinus[14]. In our case, we think that the route of the first metastasis to the temporal lobe was "drop-metastasis" on the previous surgical trajectory, and the others represented hematogenous spread. Although meningiomas arise from arachnoid cells and are naturally exposed to the CSF in the process of their growth or at the time of surgical intervention, dissemination or seeding via the CSF is rarer than the development of hematogenous metastasis to extracranial organs[5]. However, we regret that we did not perform an analysis of CSF, because the possibility of CSF spread cannot be excluded.

There is quite a variable latency period between the diagnosis of the intracranial tumor and the appearance of the metastasis, ranging from a few months to more than twenty years[8]. The intracranial lesion usually recurs locally several times before it metastasizes. In our case, there was an intracranial recurrence before the multiple extracranial metastases were developed.

Complete surgical resection is the treatment of choice for accessible intracranial or intraspinal meningiomas[2]. Postoperative radiation therapy has been recommended for the prevention of local recurrence, especially when the resection is partial or when the histology suggests malignancy[2]. There are some reports indicating good results obtained with chemotherapy[17]. However, traditional chemotherapy has little benefit, even in histologically atypical or malignant meningiomas[1].

CONCLUSION

When meningiomas recur or metastasize, or radiologic findings are aggressive, careful histopathological examination with analyses of immunohistochemistry should be performed to differentiate atypical or anaplastic meningioma from benign. In intracranial atypical meningioma, extracranial metastasis as well as local recurrence should be considered, and regular follow-up is necessary with evaluations of the chest, abdomen and bone, especially when related symptoms or signs also develop.

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