

Primary Intracranial Malignant Melanoma with Extracranial Metastasis

Kengo Hirota, M.D., Chika Yoshimura, M.D., Osami Kubo, M.D., Hidetoshi Kasuya, M.D.

Department of Neurosurgery, Tokyo Women's Medical University Medical Center East, Tokyo, Japan

We report a case of primary intracranial malignant melanoma (PIMM) with extracranial metastases. The patient was an 82-year-old woman diagnosed with PIMM under the left cerebellar tentorium. We performed a tumor resection followed by gamma knife surgery. An magnetic resonance imaging at 11 months after surgery showed a local intracranial recurrence. At 12 months, vertebral metastasis was suspected, and 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT) showed multiple extracranial metastases. She died at 13 months after surgery. Although extracranial metastases of PIMM are extremely rare, we should carefully follow up extracranial metastases together with intracranial ones, especially by FDG-PET/CT, even at an early asymptomatic stage.

Key Words : Intracranial malignant melanoma · Extracranial metastasis · Positron emission tomography.

INTRODUCTION

Primary intracranial malignant melanoma (PIMM) is a rare tumor of the central nervous system (CNS)²⁾. Metastatic intracranial malignant melanoma (MIMM) from cutaneous malignant melanoma (CMM) is a frequent occurrence. PIMM is difficult to diagnose because PIMM and MIMM are similar in radiological and pathological appearance^{6,15)}. On the other hand, extracranial metastasis of PIMM is extremely rare. Both timing and sites of recurrent PIMM are unpredictable. Here, we report a case of PIMM with extracranial metastasis.

CASE REPORT

History and examination

An 82-year-old women came to the department because magnetic resonance imaging (MRI), followed up every one year for asymptomatic cerebral infarction, showed mass lesion under the left cerebellar tentorium (Fig. 1). One month later, on her admission, she had cerebellar symptoms such as nausea and gait disturbance, and the mass lesion showed as rapidly enlarged on the MRI. Past medical history was unremarkable. There was no mucocutaneous or ocular pigmented lesion on the skin. No mass lesion was shown one year before admission. The mass lesion with niveau formation and a

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• Address for reprints : **Kengo Hirota, M.D.**

Department of Neurosurgery, Tokyo Women's Medical University Medical Center East, 2-1-10 Nishiogu, Arakawa-ku, Tokyo 116-8567, Japan
Tel : +81-3-3810-1111, Fax : +81-3-3819-8680, E-mail : k2bumps@gmail.com

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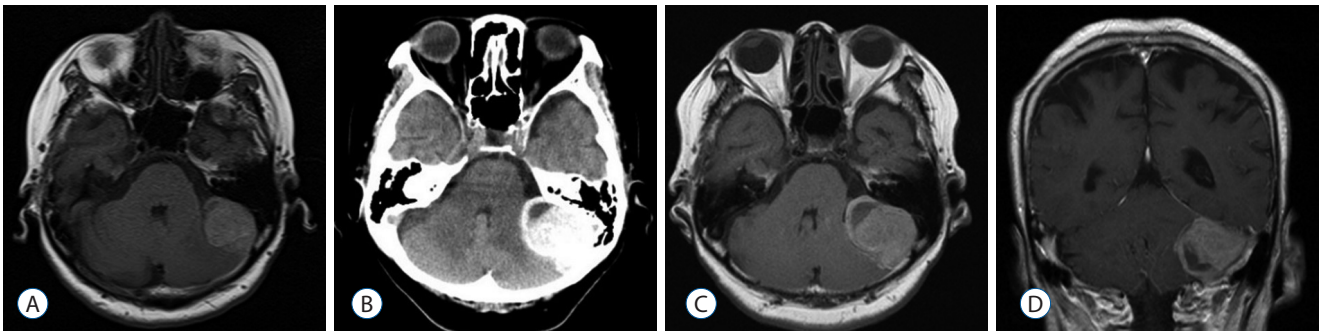


Fig. 1. Axial T1-weighted MRI (A) shows an extra-axial mass lesion under the left cerebellar tentorium one month before admission. Axial CT (B), T1-weighted MRI (C) and Coronal Gd-enhanced T1-weighted MRI (D) on admission show the enlarged mass lesion with niveau formation at one month later. MRI : magnetic resonance imaging, CT : computed tomography.

maximum diameter of 5 cm showed high density on computed tomography (CT), a slightly high intensity on T1 MRI and a low intensity on T2 MRI. It did not show enhancement after gadolinium administration (Fig. 1). 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography (FDG-PET/CT), chest and abdominal enhanced CT did not detect any malignant lesion such as an extracranial malignant melanoma (Fig. 2).

Surgery and pathological examination

We performed a near total resection, but some residual tumor attached to the sigmoid sinus and the petrosal vein remained. A black solid and encapsulated nodular tumor was found under the left cerebellar tentorium and appeared to originate from the pia mater of the cerebellum (Fig. 3). The tumor tissue was stained with H&E and other immunohistochemical stains. The aggregates of melanin were contained in the cytoplasm. H&E after decolorization of melanin showed atypical cells, necrosis and abnormal mitosis. Immunohistochemical examinations were positive for HMB-45, Melan-A and S-100 protein. The MIB-1 (Ki-67) staining index was approximately 8% (Fig. 3). The final pathological diagnosis was PIMM.

Postoperative course

She became ambulatory and was discharged. We performed gamma knife surgery at a total dose of 21 Gy for the residual tumor of the sigmoid sinus and the petrosal vein. An MRI at 11 months after surgery showed local recurrence at

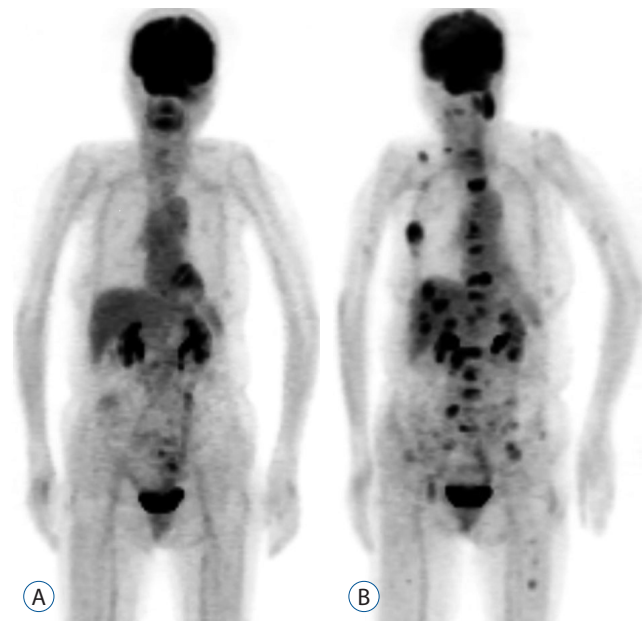


Fig. 2. Whole body FDG-PET/CT (A) on admission shows no malignant lesions such as extracranial malignant melanoma. FDG-PET/CT (B) at 12 months after the surgery shows FDG uptake in multiple metastatic lesions. FDG-PET/CT : 2-[fluorine-18]-fluoro-2-deoxy-D-glucose positron emission tomography/computed tomography.

the anterolateral edge of the left cerebellar tentorium. We performed gamma knife surgery at a total dose of 24 Gy for the recurrent tumor. At 12 months, she experienced back pain, and vertebral metastasis was suspected after MRI. Therefore, FDG-PET/CT, chest and abdominal CT for a whole body examination was performed and showed multiple metastases in the left neck, the right latissimus dorsi muscle, the right collarbone, the liver, multiple vertebral bodies and the left thigh bone (Fig. 2). Recurrence in the brain and brainstem was difficult to distinguish in the FDG-

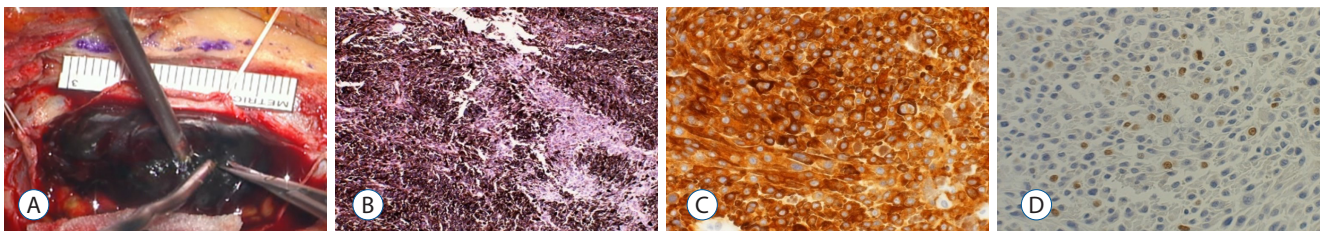


Fig. 3. Intraoperative image (A) shows the black colored tumor on the left cerebellar tentorium. Photomicrographs. The tumor cells arranged in fascicles intersperse with melanin-containing cells (B, H&E, ×200). The tumor cells are positive for Melan-A (C, ×400). The MIB-1 (Ki-67) staining index is approximately 8% (D, ×400).

PET/CT. Her general condition continued to be good, and we performed an open biopsy for diagnosis of the tumor lesion in the right latissimus dorsi muscle. Pathological examination of the intramuscular tumor was the same as those previously described. The MIB-1 staining index was approximately 7%. At 13 months after surgery, the patient died from cryptogenic cardiopulmonary arrest.

DISCUSSION

PIMM accounts for approximately 0.1% of all intracranial tumors²⁾. PIMM predominantly originates from the leptomeningeal melanocytes. These cells are found underneath the brain and the brainstem, inside the ventricles, at the optic chiasm, in the grooves of the various lobes, in the substantia nigra and in the choroid¹⁶⁾. Primary spinal cord melanoma is rare, but has been reported previously⁹⁾.

It is not easy to differentiate PIMM from MIMM because they overlap in radiological and pathological appearance¹⁵⁾. It has been reported that the following factors are proposed for establishing a diagnosis of PIMM: (i) no malignant melanoma outside the CNS; (ii) involvement of the leptomeninges; (iii) intramedullary spinal lesions; (iv) hydrocephalus; (v) tumor in the pituitary or pineal gland; and (vi) a single intracerebral lesion⁶⁾. PIMM is generally a diagnosis of exclusion. In our case, there were no skin or eye melanoma, neither the FDG-PET/CT or chest and abdominal enhanced CT detected malignant lesions in the other parts of her body. It has been reported that MIMM often shows extensive necrosis, more obvious cytologic malignancy, a higher mitotic index and a higher MIB-1 staining index. An MIB-1 staining index may

provide useful information to help classification. The MIB-1 staining index of MIMM (range, 17–38 per 10 HPFs) was higher than that of PIMM (range, 2–15 per 10 HPFs)¹⁾. In our case, the MIB-1 staining index was approximately 8%. Thus, PIMM was more likely. It has also been reported that PIMM have a better prognosis than MIMM. The median survival for patients with MIMM is only 5–6 months while patients with PIMM survive 9–24 months. Individuals have been reported to survive for more than 5 years^{5,6,12–14,16)}.

Many cases with PIMM die from recurrence of intracranial lesions. Extracranial metastasis of PIMM is extremely rare³⁾. It has reported that of 168 cases with extracranial metastasis in adults 68 were cases of glioblastoma, 49 of meningeal tumors, 22 of medulloblastoma, and other cases were of ependymoma, pituitary gland, oligodendroglioma, neuroblastoma, germinoma and hemangioblastoma⁷⁾. The lungs, pleura, lymph nodes, bone, and liver are the most common sites of extracranial metastases of glioblastoma^{4,11)}.

The routes of extracranial metastasis are not clear. Risk factors for extracranial metastasis include previous craniotomy, ventricular systemic shunting, high-grade tumor histology, radiation therapy, long interval since the primary therapy and tumoral relapse¹⁷⁾. In our case, the patient received craniotomy and some residual tumor attached to the sigmoid sinus and the petrosal vein remained. It is quite possible that the residual tumor invading the venous sinus and the dural sinus was the cause of the hematogenous dissemination.

CMM can spread to any organ. The most common sites of clinical presentation are the skin, subcutaneous tissue and lymph nodes followed by lung, liver and bone. It is quite possible that CT, MRI, FDG-PET/CT and skeletal scintigraphy provide clinically useful information to detect the metastasis

of CMM. Especially, a whole body FDG-PET/CT is a non-invasive, high-resolution molecular imaging technique that can detect CMM metastasis based on abnormal cellular glucose uptake¹⁰. However, FDG-PET/CT has limitations with small (less than 1 cm), pulmonary and brain metastasis³. On the other hand, the optimal time point for detecting metastatic malignant melanoma is not certain. It has been reported that the optimal timing to perform FDG-PET/CT in high risk CMM is at 6 months after surgery because all recurrences at an early asymptomatic stage were found between 7–14 months after surgery⁸. In the case of PIMM, a head MRI is routinely performed to check for recurrent PIMM. Therefore, we concluded that whole body FDG-PET/CT should also be performed to screen for extracranial PIMM metastasis even at an early asymptomatic stage after surgery.

CONCLUSION

We reported a case of PIMM with extracranial metastasis. Although extracranial PIMM metastasis is extremely rare, we should carefully follow up extracranial metastases together with intracranial ones, especially with FDG-PET/CT, even at an early asymptomatic stage.

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