Long-Term Survival After Surgical Resection of Primary Spinal Malignant Melanoma
—Case Report—

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Abstract
A 49-year-old man was admitted suffering from headache persisting for a month. He had a history of primary spinal intramedullary malignant melanoma at the T6 level 18 years previously, which had remained stable for 18 years. Magnetic resonance imaging revealed central nervous system (CNS) dissemination of malignant melanoma. Whole brain radiation therapy (30 Gy), local radiation therapy (15 Gy), and routine intrathecal injection of interferon beta were performed. The progression of CNS dissemination of malignant melanoma was controlled without neurological deterioration for 38 months. The prognosis for primary CNS malignant melanomas better than that for cutaneous melanoma. However, the clinical course is still unknown, and CNS dissemination is regarded fatal. The unusually long survival in the present case indicates the effectiveness of the combined radiotherapy and interferon therapy.

Key words: dissemination, spinal cord tumor, malignant melanoma

Introduction
Central nervous system (CNS) primary malignant melanoma accounts for approximately 1% of all cases of melanoma. Primary spinal malignant melanoma is unusual, with the first case reported by Hirschberg in 1906, and only 40 cases since then.4–6,10,11,19,26) The prognosis is poor, but primary CNS malignant melanoma including primary spinal malignant melanoma has a better prognosis than cutaneous melanoma. We treated a patient who presented with CNS dissemination 18 years after first treatment for primary spinal malignant melanoma.

Case Report
A 49-year-old man was admitted to our hospital (Hyogo Cancer Center) for headache persisting for a month on March 1, 2005. He had a history of primary spinal intramedullary malignant melanoma at the T6 level which was partially removed 18 years previously when he was 31 years old. Local radiation therapy up to 50 Gy was then administered to the spinal tumor at Kyoto University Hospital. Subsequently, systemic interferon beta (2.0 × 10⁸ IU/mg) therapy (total dose, 2.2 × 10⁸ U) was begun. No evidence of a primary origin outside the CNS was found. Immunohistochemical cytological study of the CNS verified melanoma cells. Chemotherapy with intrathecal administration of dacarbazine (dimethyltriazenoimidazole carboxamide: DTIC) was then initiated. Bilateral lower extremity paresis and sensory disturbance under the navel level subsequently occurred. He had been well without relapse for 18 years. The initial treatment was reported in 1989.26)

On admission to our institute, cranial nerve paresis was not identified. Urinary sphincter dysfunction was present. T₁-weighted magnetic resonance (MR) imaging demonstrated a hyperintense mass in the left cerebellopontine cistern and prepontine cistern. T₂-weighted MR imaging demonstrated a mixed hypointense and isointense mass within the lesion. MR imaging also revealed multiple lesions and leptomeningeal lesions in the cistern around the brainstem, with mild homogeneous enhancement (Fig. 1). Spinal MR imaging revealed diffuse leptomeningeal enhancement (Fig. 2). Whole body computed tomography did not reveal any other lesions. Dermatologists searched all extremities, the perianal, rectal, and pubic regions, the lymph nodes, and the uvula, but found no lesions indicative of malignant melanoma. Cytological examination of the cerebrospinal fluid (CSF) revealed dissemination of malignant melanoma cells (Fig. 3). Positron imaging tomography (PET) with [18F]FDG did not detect disease.

Whole brain radiation therapy (30 Gy, 3 × 10), local radiation therapy (15 Gy, 3 × 5), and routine intrathecal injection of interferon beta (750 000 IU every month) were begun. No neurological deterioration was seen and CNS
dissemination of malignant melanoma was stable for 38 months. However, after the adjuvant radiotherapy and interferon beta administration were completed, MR imaging demonstrated regrowth of multiple disseminated tumors after 39 months.

**Discussion**

Primary melanoma of the CNS may originate from aberrant pigment cells from the neural crest or melanocytic elements of the pia mater. The criteria of primary CNS malignant melanoma are as follows: No malignant melanoma tumor outside the CNS, involvement of the leptomeninges (spinal or cranial), intramedullary spinal lesion, hydrocephalus, tumor in the pituitary or pineal gland, and a single intracerebral lesion. Only necropsy findings can provide the final diagnosis. Most cases of CNS malignant melanoma are metastases from other origins outside CNS. Our case was diagnosed as primary spinal malignant melanoma according to the above criteria.

Primary CNS malignant melanoma has occurred in the spine, suprasellar region, cerebral region, pineal region, cerebellopontine angle, spinal nerve root, and leptomeninges. Forty cases of primary spinal malignant melanoma have been reported, including 14 with dissemination from the primary CNS malignant melanoma. One case had liver and spleen metastases.

The mean survival time with primary spinal malignant melanoma is 6 years 7 months after onset of symptoms. In contrast, the survival time with common melanoma of the skin with metastases to the CNS was only 6 months. One patient survived for 9 years 6 months after removal of primary intracranial malignant melanoma in the right frontal lobe, followed by radiation therapy and
chemotherapy (DTIC), although the effect of radiation and DTIC was unknown. In the present case, progression of tumor was controlled for 21 years, which is an unusually long survival. The factors in this successful control are unclear. There is no established treatment for CNS dissemination of malignant melanoma, but additional whole brain radiation therapy and intrathecal injection of interferon beta or DTIC may be effective for a certain period. Further investigation is necessary.

Study of the clinicopathologic features of 33 cases found no cases of melanocytoma recurred after surgical resection. The MIB-1 index was low (< 1–2%). On the other hand, the MIB-1 index for melanoma was higher (mean 8.1%) than that for melanocytomas. Eight of 13 lesions recurred after resection of melanoma. Certain histopathologic features are helpful in predicting biologic behavior. Recently, reverse transcriptase-polymerase chain reaction assay can be used to detect melanoma cells in the CSF. MR imaging is useful for the diagnosis of melanoma and evaluation of CNS dissemination. Hyperintensity on T2-weighted MR images indicates the presence of melanin. The MR imaging characteristics may depend on the amount of melanin or previous hemorrhage within the lesion. However, PET with [18F]FDG was not helpful in this case. Small volume lesions and leptomeningeal disease may be difficult to detect. The present case of long-term survival after treatment for primary spinal malignant melanoma, with CNS dissemination 18 years after the first treatment, was controlled for 38 months, suggesting the effectiveness of additional whole brain radiation therapy and routine intrathecal injection of interferon beta.

### References


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