Metastatic Leiomyosarcoma of the Brain Manifesting as Multiple Hemorrhages

—Case Report—

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Abstract

A 74-year-old man presented with a rare metastatic leiomyosarcoma of the brain manifesting as subacute development of multiple cerebral hemorrhages. Cerebral angiography demonstrated no tumor staining or vascular malformation. Whole body computed tomography revealed abnormal masses in the liver, left adrenal gland, and duodenum. Histological examination of an open biopsy specimen identified the lesion as metastatic leiomyosarcoma. Whole brain irradiation controlled the intracranial lesions, but the patient’s general condition progressively deteriorated and he died of pneumonia. Metastatic leiomyosarcoma is a very uncommon tumor in the central nervous system with a poor response to existing treatment options. Consequently, new approaches to the treatment of this disease are needed.

Key words: leiomyosarcoma, cerebral metastasis, intratumoral hemorrhage

Introduction

Intracranial hemorrhage occasionally originates from a brain tumor, usually a malignant tumor such as glioblastoma or metastatic brain tumor,18,35) and pituitary adenoma.25,34) Brain tumor may manifest as the sudden onset of symptoms caused by intratumoral hemorrhage. However, frequent episodes of bleeding from malignant tumors rarely occur in different intracranial regions in the subacute period. We present a case of metastatic leiomyosarcoma in the brain, which is uncommon, associated with bleeding in four separate intracranial regions over a period of about 1 month.

Case Report

A 74-year-old man was admitted to another hospital on July 3, 2002, with a 2-day history of nausea and vomiting. Computed tomography (CT) revealed cerebellar hemorrhage. At that time, the patient was not receiving antiplatelet or anticoagulation therapy, and coagulation studies including platelet count were within normal limits. The patient was managed conservatively, but dysphagia and dysarthria developed 9 days after admission. CT disclosed further high density masses in the left frontal and right temporal regions in addition to extension of the cerebellar hemorrhage (Fig. 1). Therefore, the patient was transferred to Hiroshima City Asa Hospital on the same day.

On admission, CT revealed no abnormally en-
Enhanced intracranial mass. Magnetic resonance (MR) imaging performed on the same day confirmed the presence of hematoma with both acute and chronic components in the cerebellar lesion, and relatively fresh bleeding in the left frontal and right temporal regions (Fig. 2). Cerebral angiography showed no tumor staining or vascular malformation, and whole body CT revealed abnormal masses in the liver, left adrenal gland, and duodenum. Serum levels of the alpha-fetoprotein, carcinoembryonic antigen, and carbohydrate antigen 19-9 were within normal limits. The preoperative differential diagnosis included metastatic brain tumor, malignant lymphoma, and malignant melanoma.

Left frontal craniotomy was performed. Abnormal minute blood vessels were observed on the surface of the brain. Removal of part of this abnormal tissue revealed underlying hematoma. However, we could not detect a definitive neoplastic mass at this stage, so surgery was limited to biopsy. Histological examination revealed atypical spindle cells with hyperchromatic nuclei and multinucleated giant cells surrounding areas of recent hemorrhage and necrosis (Fig. 3 upper). Immunohistochemical staining showed that the lesion expressed alpha-smooth muscle actin (Lot 028; Dakocytomation Co. Ltd., Kyoto) and p53 protein (Lot 108; Dakocytomation Co. Ltd.), but not glial fibrillary acidic protein (Lot 096; Dakocytomation Co. Ltd.), CD34 (Lot 044; Dakocytomation Co. Ltd.), or c-kit protein (Lot 0D010A; Dakocytomation Co. Ltd.) (Fig. 3 lower). The Ki-67 labeling index of the specimen was 34.7%. Histological and immunohistochemical examination thus pointed to a diagnosis of metastatic leiomyosarcoma of the brain, and histopathology and whole body CT suggested that the primary lesion was located in the duodenum.

After surgery, the patient's level of consciousness fell due to new bleeding in the right occipitoparietal region (Fig. 4). Intracranial bleeding had thus occurred in four areas, the cerebellum, left frontal, right temporal, and right occipitoparietal regions, over a period of 1 month. Whole brain irradiation (30 Gy) controlled the intracranial lesions, but pneumonia gradually progressed despite medical...
treatment, and anemia also increased. The patient died on the 53rd day after the onset of symptoms.

**Discussion**

The present patient suffered sudden onset of nausea and vomiting due to cerebellar hemorrhage, and hemorrhage occurred in two further intracranial locations in the 2 weeks prior to surgery. CT, MR imaging, and craniotomy suggested no discrete mass lesion, but the presence of unusual small blood vessels on the brain surface raised the suspicion of tumor invasion and associated hematoma. Hemorrhage probably resulted from the breakdown of these unusually brittle blood vessels.

Intracranial leiomyosarcoma is a very uncommon tumor in the central nervous system. Metastases from uterine or retroperitoneal leiomyosarcoma occur more commonly than primary lesions, but primary leiomyosarcoma has recently been reported in the context of immunosuppression due to human immunodeficiency virus or radiation therapy. A recent study of 3829 patients with soft tissue sarcoma found the prevalence of brain metastases was approximately 1%, with leiomyosarcoma accounting for 20% of these metastatic lesions. Metastases from uterine leiomyosarcoma were aggressively treated and had relatively long survival periods, outcomes tend to be poor despite treatment, and lesions at other sites including the primary tumor are often not controlled effectively.

Intratumoral hemorrhage occurred prior to treatment in only one case of metastasis from a primary tumor in the colon. Another patient died of cerebral hemorrhage 5 weeks after incomplete resection of an intracranial metastasis from a primary leiomyosarcomatous lesion in the thigh. Hemorrhage presumably occurred in the area of incomplete resection in this case. This neoplasm might show a propensity to bleed, although too few cases have been reported to detect a clear tendency.

In the present case, only a small area of the lesion was sampled by biopsy, because most of the abnormal area consisted of hematoma. However, thorough histological analysis of the area of biopsied tissue with neoplastic organization detected none of the characteristics of leiomyosarcoma, such as prominent interlacing fascicles of spindle-shaped cells. The differential histological diagnosis includes malignant astrocytoma and malignant fibrous histiocytoma. Malignant astrocytoma was ruled out by negative immunostaining for glial fibrillary acidic protein. Similarly, malignant fibrous histiocytoma was considered unlikely due to the absence of storiform pattern, cell pleomorphism, or nuclear atypia, and the negative immunostaining for alpha-smooth muscle actin.

Resection of metastatic lesions is performed if possible, followed by either whole brain irradiation or chemotherapy (generally using Adriamycin). Although some patients with cerebral metastasis from uterine leiomyosarcoma were aggressively treated and had relatively long survival periods, outcomes tend to be poor despite treatment, and lesions at other sites including the primary tumor are often not controlled effectively.

Leiomyoma and leiomyosarcoma are conventionally considered to be myogenic neoplasms, but immunohistochemical staining has demonstrated that some cases appear to be derived from nervous tissue. Gastrointestinal stromal tumors (GIST) have recently been recognized as a clinical entity. However, prediction of the biological behavior is relatively difficult. Recently, the biological behavior of GIST was classified according to metastatic potential (low, intermediate, and high risk). At the present time, no effective chemotherapeutic options are available for patients with unresectable GIST. Imatinib mesylate (Glivec, formerly STI571; Novartis Pharma AG, Basel, Switzerland) inhibits the tyrosine-kinase activity of the KIT receptor. Imatinib mesylate has been effective in patients with metastatic GIST and clinical trials are in progress. Although surgery remains the treatment of choice for resectable GIST, imatinib may allow the treatment of inoperative lesions. Radiation therapy may be beneficial for controlling tumor regrowth, but is not curative. Consequently, further development of novel agents that are effective against generalized GIST is needed.
References

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