Brain Metastasis in Malignant Pleural Mesothelioma Presenting as Intratumoral Hemorrhage
—Case Report—

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Abstract

A 51-year-old man presented with a rare case of brain metastasis of malignant pleural mesothelioma (MPM) manifesting as intratumoral hemorrhage. He had undergone several treatments such as left pneumonectomy, pleurectomy, chemotherapy with cis-diaminedichloroplatinum and gemcitabine hydrochloride, and irradiation. Five years later, computed tomography revealed right parietal metastasis with intratumoral hemorrhage and the patient was treated by surgery and irradiation. Six months after the surgery, recurrent intratumoral hemorrhage occurred and a second surgery was performed. MPM has a poor prognosis and brain metastasis is rare, but long-term survival has recently improved through the application of multi-modality approaches. Therefore, the number of opportunities for treating MPM metastasis will increase in the near future. Intratumoral hemorrhage may occur in patients with solitary brain metastasis of MPM, so surgery should be considered as a general candidate treatment for metastatic tumors.

Key words: malignant pleural mesothelioma, brain metastasis, surgery, tumor bleeding, tumor

Introduction

Malignant pleural mesothelioma (MPM) is an uncommon membrane-based neoplasm mainly derived from the mesoderm of the pleura or peritoneum,1) and is a refractory disease with poor prognosis. MPM usually spreads by local extension and causes death in the large majority of cases. Brain metastasis is rare and the majority of reported cases were identified by autopsy.7,9) Furthermore, only 6 operative cases of brain metastasis have only been reported.3,5,7,9,16,17) We report a case of brain metastasis of MPM presenting as recurrent intratumoral hemorrhage and treated by surgery.

Case Report

A 51-year-old male was admitted to our hospital with dyspnea and pleural effusion in November 2003. He was a non-smoker and had worked in a textile factory for 20 years with no occupational exposure to asbestos. He was diagnosed with epithelial type MPM and underwent left pneumonectomy and pleurectomy. Postoperatively, he underwent two courses of chemotherapy with cis-diaminedichloroplatinum (CDDP) and gemcitabine hydrochloride, and a total of 54 Gy of irradiation. Metastatic tumor of the right lung was found and the patient underwent right partial pneumonectomy and received four courses of chemotherapy with CDDP and pemetrexed (Alimta; Eli Lilly and Co., Indianapolis, Ind., U.S.A.) in June 2007.

He presented with general convulsive attack in November 2008, and computed tomography (CT) revealed a high density lesion measuring 1.5 cm in diameter with minimal surrounding edema in the right parietal lobe (Fig. 1A). Magnetic resonance (MR) imaging demonstrated a well-circumscribed lesion with heterogeneous enhancement (Fig. 1B–D). He exhibited no neurological deficit. Gross total resection of the mass lesion was performed and identified metastatic MPM with hemorrhage. Histological examination confirmed that the tumor was malignant mesothelioma with spindle and sheet-like pattern of epithelial cells (Fig. 2A). Additionally, another histological variant was also present which included sarcomatous patterns (Fig. 2B). Immunohistochemically, calretinin (Fig. 2C) and epithelial membrane antigen were positive, and carcinoembryonic antigen, CD31, and CD34 were negative. Postoperatively, the patient underwent a total of 54 Gy whole brain irradiation. MR imaging again revealed a heterogeneously enhanced mass in April 2009, but the patient refused surgery (Fig. 3).

The patient suffered sudden onset of headache, nausea, and mild left hemiparesis in June 2009. CT revealed a high density lesion measuring 5 cm in diameter, consisting of two components, with perifocal edema and midline shift.
Fig. 1 A: Computed tomography scan showing a high density lesion of 1.5 cm diameter in the right parietal lobe. B, C: Axial T₁- (B) and T₂-weighted (C) magnetic resonance (MR) images showing an iso- and mixed intensity mass. D: Axial T₁-weighted MR image with gadolinium showing the heterogeneously enhanced mass.

(Fig. 4A). MR imaging detected a mass lesion as iso- to hyperintense on T₁- and T₂-weighted images, with heterogeneous enhancement (Fig. 4B–D). The lesion was clearly divided into two components on T₂-weighted images: the anterior part was mainly hyperintense and the posterior part was mainly isointense (Fig. 4C). The patient again underwent gross total resection of the lesion. The anterior component of the tumor consisted of large hematoma. Histological examination resulted in almost the same findings, but the sarcomatous component was much larger than that previously observed (Fig. 2D). The patient was discharged without recognizable neurological deficit.

Discussion

Asbestos exposure was first closely related to mesothelioma in 1960, and patients with asbestos-related mesothelioma have increased in number over the last few decades. Case-control studies have indicated that almost 90% of males with MPM have reported prior exposure to asbestos. A textile factory is a possible location for occupational exposure to asbestos. Our patient worked in a textile factory but no other workers have been affected by MPM.

MPM involves tumors of mesothelial origin, and CD34 is helpful in the differential diagnosis of MPM and solitary fibrous tumor. MPM is classified into four histological types: fibrous or sarcomatous, epithelial, undifferentiated, and mixed. Generally, the epithelial type is the most common and the sarcomatous type is the most rare. The sarcomatous type appears to be predominant in brain metastasis. One of the most reliable prognostic factors for metastasis is the histological subtype of mesothelioma, and the sarcomatous type carries a more favorable prognosis. Our patient had already been diagnosed with the epithelial type, but a sarcomatous component may also be present in the brain metastasis. Histological change is potentially relevant to distant metastasis.

MPM typically spreads by local extension, but metastasis to the brain is rare. Review of 171 cases of MPM with intracranial metastases found the most frequently involved organs were the liver (55.9%), adrenal glands (31.1%), kidneys (30.1%), and the contralateral lung (26.8%). Intracranial metastases were observed in only 3% of cases. The majority of MPM brain metastases were reported in autopsy cases, and only 6 patients with brain metastasis have undergone surgery (Table 1). Two of these 6 patients survived for more than 36 months. One patient died 10 days postoperatively of constructive pericardial disease, and one patient died of cardiopulmonary arrest secondary to intrathoracic disease 8 months after surgery. The outcomes were not reported in two cases. No previous deaths were due to surgery for brain metasta-
In general, the frequency of intracranial hemorrhage of metastatic tumor is about 2.9–24.4%, depending on the histological type. Brain metastases of choriocarcinoma, liver cancer, kidney cancer, and malignant melanoma are well known causes of intratumoral hemorrhage. Our very rare case of brain metastatic MPM presented with recurrent intratumoral hemorrhage. The cause of hemorrhage was suspected to be rupture of abnormal blood vessels in the tumor based on the histological findings.

MPM has a poor prognosis with a median survival time of 9 months, but long-term survival is expected to improve through the application of multi-modality approaches. The incidence of MPM is predicted to reach a peak between 2010 and 2020. Therefore, the number of opportunities for treating brain metastasis from MPM will increase in the near future. Cases of tumor bleeding also appear to be increasing in number, so surgical treatment should be considered for patients with solitary brain metastasis of MPM.

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References


11) Peto J, Hodgson JT, Matthews FE, Jones JR: Continuing in-

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