Brain Metastasis of Pleural Mesothelioma after a Subarachnoid Hemorrhage

Aya Hirooka1, Akihiro Tamiya1, Masaki Kanazu1, Junichi Nonaka2, Taiji Yonezawa3, Kazuhiro Asami1 and Shinji Atagi1

Abstract

Malignant pleural mesothelioma (MPM) is an uncommon, fatal neoplasm induced by asbestos exposure. Brain metastases from MPM are extremely rare, with most such cases diagnosed only at the time of autopsy. This report describes what we believe to be the first case of MPM metastasizing to the brain after a subarachnoid hemorrhage, as well as the subsequent surgical removal of the brain metastasis.

Key words: malignant pleural mesothelioma, subarachnoid hemorrhage, brain metastasis

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Introduction

Malignant pleural mesothelioma (MPM) is a malignancy that is associated with a very poor prognosis, a median survival period of ten months, and an incubation period of approximately 40 years (1, 2). The disease, which is caused by asbestos exposure, is difficult to diagnose in the early stage by pleural effusion and needle biopsy. The symptoms of MPM only manifest when it has progressed to its end stage, at which point the patients are not able to receive any treatment. MPM exhibits high resistance to chemotherapy and few patients are candidates for radical surgery. Metastatic sites typically include the pleura and occasionally, the peritoneum, pericardium, genital tract, and the tunica virginalis. Falconieri et al. reported that intracranial metastases were observed in only 3% of autopsy cases (3).

There have been no previous reports of brain metastasis from MPM after subarachnoid hemorrhage (SAH), yet the present case suggests that this was a developmental mechanism.

To the best of our knowledge, this is the first reported case of brain metastasis from MPM in a patient who underwent resection after an SAH.

Case Report

A 57-year-old man was urgently admitted to a neurosurgical hospital with an SAH in May 2010 (Fig. 1). Surgery was performed to clip the ruptured internal carotid aneurysm, remove hematomas, and to perform coil embolization of the basilar artery. Three months after the neurosurgical procedure, the patient was admitted to our hospital because of left pleural fluid effusion, and he underwent an open pleural biopsy. A histological examination of the biopsy specimen revealed the features of biphasic mesothelioma, which was predominantly sarcomatoid in nature. Contrast-enhanced magnetic resonance imaging (MRI) revealed a brain tumor near the SAH-induced hematoma in the right occipital lobe (Fig. 2). Thus, it was necessary to definitively diagnose whether it was a metastatic brain tumor. In October 2010, the patient underwent surgery to remove the brain tumor because of its rapidly increasing size and its potential to cause epilepsy. A complete resection was achieved. A subsequent immunohistopathological examination of the resected brain tumor revealed that it had metastasized from an MPM (Fig. 3). The patient’s Eastern Cooperative Oncology Group (ECOG) Scale of Performance Status score remained at 1 after removal of the brain tumor; this indicates that he had difficulty with strenuous activity but he remained ambu-
Figure 1. A brain computed tomography scan showing a subarachnoid hemorrhage in the right occipital lobe.

Figure 2. Contrast-enhanced T1-weighted MRI showing an enhanced mass lesion in the right lateral cortex.

Figure 3. A: A photomicrograph of the surgical brain tumor specimen showing malignant cells with necrosis (Hematoxylin and Eosin staining, ×100). B: A positive immunohistochemical staining of the brain tumor for AE1/AE3 (×200). C: A positive nuclear immunohistochemical staining of the brain for WT-1 (×400).

The majority of brain metastases originate from lung cancer (4). In contrast, there have only been seven previously reported cases of brain metastasis from pleural mesothelioma following surgery (5-10). Distant metastases such as brain metastases are rare in MPM, as it commonly metastasizes to an organ in close proximity along the serosa membrane. In this case, as it appeared that the brain metastasis might have followed the SAH, we speculated that the SAH might have been involved.

Under experimental conditions, previous studies have found that SAH causes marked damage to the blood-brain barrier (BBB) in cat and rat models, and that it induces disruption of the BBB (11-17). For example, Trojanowski used Evans blue to detect discrete, diffuse spots in the cerebral cortex an hour after the occurrence of an SAH. Four hours after the bleeding, they found that the extravasations and tissue staining had become more widespread (18). Previous studies have reported an association between metastasis to the central nervous system (CNS) and the influence of molecular factors such as vascular endothelial growth factor and metalloproteinase (5-10, 19, 20).

In present case, we propose that the BBB dysfunction occurred as a result of the SAH, which facilitated the invasion by mesothelioma cells, eventually leading to tumor cell colonization of the brain parenchyma near the SAH-induced hematoma lesion. Thus, it is possible that the SAH caused the MPM metastasis in the CNS. If subarachnoid bleeding causes BBB dysfunction, this would enable migration, and the ensuing pathological changes might be disseminative in
Figure 4. A working hypothesis explaining the development of CNS metastasis in MPM.

nature (Fig. 4). Although no brain tumor was identified when the patient of the present case underwent surgery to treat his SAH, we cannot deny the possibility that the microscopic metastasis from the MPM had already manifested.

In the present case, we hypothesize that the subarachnoid bleeding led to the failure of the BBB, which in turn served to promote the brain metastasis from the MPM.

Despite this assertion, the details of the mechanism underlying MPM metastasis in the CNS remain unclear. A key event in brain metastasis is the migration of malignant cells through the BBB. However, brain capillary walls are difficult to penetrate because of their tight layer of endothelial cells, tight junctions, and the astrocyte foot processes (21, 22). Accordingly, the brain endothelium might play an important role in brain metastasis; however, the details of such transmigration and the molecular mechanisms that facilitate BBB penetration by malignant cells remain poorly defined. To confirm this hypothesis, additional studies would be required to determine whether the SAH or the act of surgery itself caused the rupture of the BBB. We believe that this case is important because it highlights the possible development of brain metastasis due to cerebrovascular disease or brain surgery in patients with MPM.

The authors state that they have no Conflict of Interest (COI).

References