

Multiple intracranial metastases from postoperative giant sarcomatoid malignant pleural mesothelioma: A case report and literature review

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Abstract. Sarcomatoid malignant pleural mesothelioma (SMPM) is a rare tumor with poor response to treatment and a dismal prognosis. Distant metastases are not uncommon and usually appear at the late stages of the disease. However, cerebral metastases have rarely been documented. We herein report a case of a giant sarcomatoid carcinoma of the pleura in a 41-year-old male patient with no history of exposure to asbestos, who presented with a chief complaint of left-sided chest pain for 1 month. Extrapleural pneumonectomy and rib excision were performed. At 5 months after the surgery, the patient was diagnosed with multiple intracranial metastatic neoplasms and succumbed to the disease soon thereafter. The aim of the present case report was to emphasize this rare metastatic pattern and aggressive clinical course of SMPM, with a supplementary review of the previously published literature.

Introduction

Malignant pleural mesothelioma (MPM) is relatively rare (1-5). The World Health Organization has classified MPM into three types, namely epithelioid, sarcomatoid and biphasic types. Only 10% of MPMs are classified as sarcomatoid malignant

pleural mesothelioma (SMPM), which is associated with a worse prognosis (6).

Distant metastases usually appear during the late stages of the disease. However, reported cases of intracranial metastases are extremely rare, with only few published articles to date on intracranial metastases from MPM (7-11), and only 1 reported case of multiple intracranial metastases from SMPM (8).

We herein report a case of multiple intracranial metastases from a giant SMPM in a 41-year-old male patient with no history of asbestos exposure, and review previously published cases of SMPM (Table I).

Case report

A 41-year-old male patient presented to the Department of Cardiothoracic Surgery of the Affiliated Hospital of North Sichuan Medical College (Nanchong, China) in May, 2016 with a chief complaint of left-sided chest pain for 1 month. The patient's height was ~178 cm and he weighed 70 kg, he was a non-smoker and had no past history of exposure to carcinogenic chemicals, such as asbestos. The past medical history was unremarkable and there was no family history of cancer. There was no history of cough, fever, or hemoptysis, and the vitals on admission were normal. Physical examination revealed no lymphadenopathy. The findings on lung function tests were within the normal range [forced expiratory volume in 1 sec (FEV1) 4.41 l, forced vital capacity (FVC) 5.28 l, and a FEV1/FVC ratio of 0.83]. A chest computed tomography (CT) scan revealed locally thickened left visceral and parietal pleura, associated with intermingled pulmonary infiltrative shadowing. The tumor had smooth margins with a wide tumor base. A cranial CT scan revealed no abnormal masses in the brain (Fig. 1B). A bone scan using positron emission CT detected no invasion or distant metastasis. On three-dimensional CT imaging, the ribs were not invaded. Doppler ultrasound of the abdomen and cervical area revealed no lymph node or distant metastatic lesions in other organs. The findings on CT-guided percutaneous biopsy of the mass were not significant.

The patient underwent surgery on April 10, 2016. A 20-cm incision was made at the left 6th intercostal space and a mass originating from the pleura was identified. Extrapleural pneumonectomy (EPP) was performed as the tumor invaded

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Abbreviations: MPM, malignant pleural mesothelioma; SMPM, sarcomatoid malignant pleural mesothelioma; CT, computed tomography; ECT, emission computed tomography; EPP, extrapleural pneumonectomy; CNS, central nervous system

Key words: sarcomatoid carcinoma, pleura, malignant tumor, mesothelioma, intracranial metastasis

Table I. Previously published cases of sarcomatoid malignant pleural mesothelioma.

Authors	Year of publication	MPM	SMPM	Sex	Age, years	Intracranial metastasis	Survival time, months	(Refs.)
Makimoto <i>et al</i>	2014	-	1	Male	74	No	8	(2)
Mah <i>et al</i>	2004	-	1	Male	67	Yes	≥3	(10)
Winfrey <i>et al</i>	2004	-	1	Female	71	Yes	8	(11)
Balduyck <i>et al</i>	2010	329	28	M/F (26/2)	65.6	No	5	(14)
Brenner <i>et al</i>	1982	123	31	-	56	No	12	(18)
Law <i>et al</i>	1982	115	25	-	59	No	-	(20)
Hillerdal <i>et al</i>	2007	-	1	Male	57	No	-	(26)
Kim <i>et al</i>	2016	-	1	Female	65	No	≥7	(27)

MPM, malignant pleural mesothelioma; SMPM, sarcomatoid MPM; M, male; F, female.

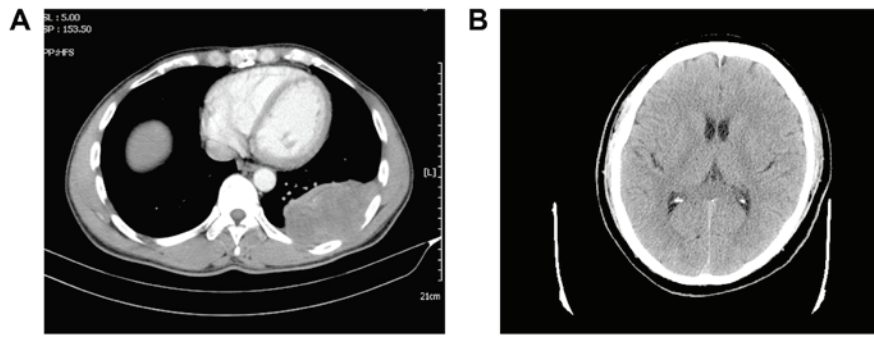


Figure 1. (A) Contrast-enhanced computed tomography (CT) scan revealed a solitary sharp homogeneous enhancing mass on the left chest wall, abutting the pleura, sized 12x10x8 cm. Pleural effusion was not observed. (B) The preoperative cranial CT scan revealed no masses in the brain.

the left inferior lobe. The solid tumor was sized ~12x10x8 cm and it was yellowish-white on cross-section. To confirm the ribs were not invaded, part of the left 5th and 6th ribs was removed for intraoperative frozen section biopsy, and the results was negative for invasion. The duration of entire procedure was ~2 h. The intraoperative blood loss was ~500 ml and the patient received a transfusion of 2 units of whole blood.

Pathological examination of the pleural mass was performed. The examination of hematoxylin and eosin-stained sections revealed papillary formations or sheets of spindle cells. Cellular atypia and nuclear fission were observed on high magnification. Bubble-like cells were also identified focally. On immunohistochemical examination, the tumor was pan-cytokeratin (CK)⁺, CK7⁺, CK18⁺, epithelial membrane antigen⁺, calretinin⁺, CK5/6⁺, P63⁺, there was no obvious loss of INI-1 expression, CD34⁺, Wilms tumor-1⁺, CD31⁺, ERG⁺, leukocyte common antigen⁺, Ki-67⁺ (30%) and S-100⁺ (partially). These characteristics were consistent with the diagnosis of SMPM (Fig. 2).

Postoperative adjuvant chemotherapy was not performed due to financial difficulties. Five months after the surgery, the patient visited our hospital with new complaints of paralysis of the left leg and chest pain. A follow-up chest contrast-enhanced CT revealed recurrence at the site of the excision. A cranial CT scan was also performed and revealed 4 intracranial metastatic lesions: A 0.5-cm mass located in the posterior horn of the lateral ventricle of the left temporal lobe, and

three more lesions in the frontal lobe, parietal lobe and basal ganglia region of the right cerebrum, sized ~1, 2 and 2 cm, respectively. There was edema surrounding the mass lesions (Fig. 3A-C). The patient was discharged without any treatment and succumbed to the disease 1 week later.

The present case report was approved by the Ethics Committee of the Affiliated Hospital of North Sichuan Medical College, and written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Discussion

Approximately 80% of patients with MPM have a history of asbestos exposure (12). The period between asbestos exposure and the onset of MPM is reported to be ~30-40 years (13). MPM originates from the mesothelium of the parietal pleura and is associated with a poor prognosis (2,12), with a median survival period of 11.5-15.3 months. However, SMPM carries a significantly worse prognosis, with a median survival of 4.2-5.0 months (14,15). Only early-stage EPP may prolong the survival of patients with MPM (16); however, as MPM is either asymptomatic or associated with a non-specific presentation, early diagnosis is usually difficult (2,12).

Distant metastases of MPM by hematogenous spread are estimated to occur in >10% of the cases at later stages of the

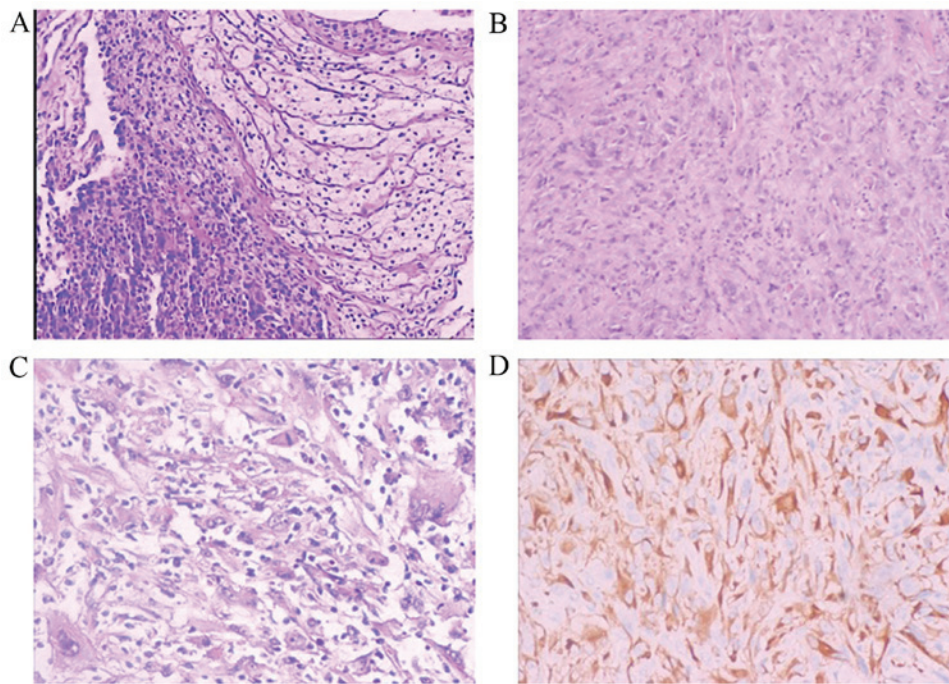


Figure 2. Pathology results of the pleural mass. Papillary formations or sheets of spindle cells were observed, with cellular atypia, nuclear fission and focal bubble-like cells observed on high magnification. Hematoxylin and eosin staining, magnification (A) x50, (B) x100 and (C) x200. (D) Immunohistochemical examination revealed that the tumor cells were positive for PCK, CK7, CK18; magnification, x100. The tumor cells were negative for epithelial membrane antigen, calretinin, CK5/6, P63, CD34, Wilms tumor-1, CD31, ERG and leukocyte common antigen.

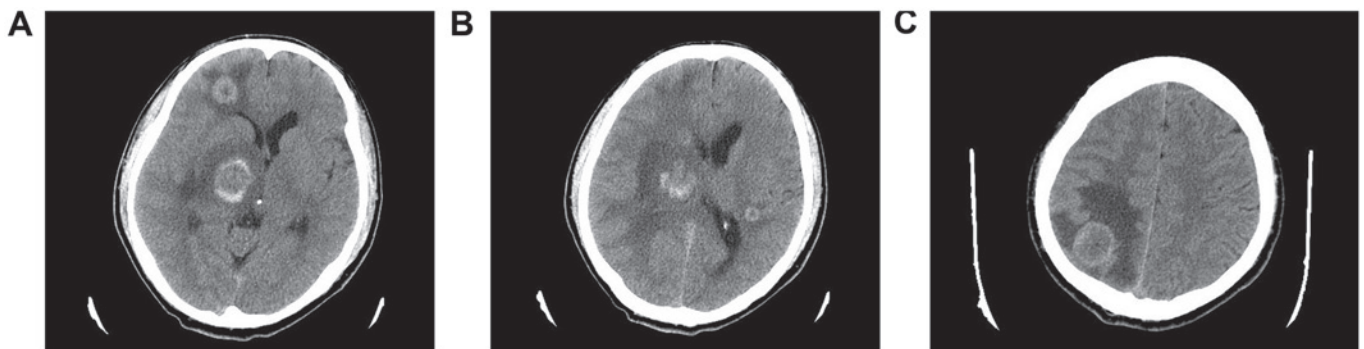


Figure 3. On postoperative computed tomography examination, masses were identified (A) in the right frontal lobe (~1 cm), (B) in the right parietal lobe (~2 cm) and (C) in the basal ganglia region of the right hemisphere (~2 cm). Edema was observed in the brain tissue surrounding the masses.

disease (17). The most frequently involved organs are the liver, adrenal gland, kidney and contralateral lung (18-22). There have only been few reports on intracranial metastasis of MPM (7-11). Hurmuz *et al* reported a case of multiple intracranial metastases from MPM, but not SMPM (9). Falconieri *et al* summarized 93 cases of MPM with distant metastases, among which only 3 intracranial metastases were observed. All 3 cases were SMPMs, and only 1 case without CNS symptoms involved multiple intracranial metastases (8).

The incidence of the three subtypes of MPM is as follows: Epithelioid subtype, ~60%; sarcomatoid subtype, ~10%; the biphasic subtype, exhibiting a mixed histological pattern, accounts for the remainder of the cases (23). The epithelioid subtype has the best prognosis, whereas the sarcomatoid has the worst (23). Wagner *et al* reported that, among 200 cases of MPM, there were only 25 SPM cases and they all exhibited short survival (24).

Pathological confirmation of SMPM is difficult preoperatively (25). With immunohistochemistry, calretinin is the most commonly used marker for MPM, which is often positive in epithelioid MPM, but negative in SMPM (26-28). In the present case, calretinin was negative, consistently with previous reports.

There was recurrence in the thorax and multiple intracranial metastatic tumors ~5 months after EPP. There is currently no widely accepted curative approach to intracranial metastases of MPM. Surgery or stereotactic radiosurgery would be considered as treatments for solitary intracranial metastasis from MPM (11); however, there has been no documented treatment for multiple intracranial metastases from MPM. Whole-brain irradiation or/and chemotherapy would be considered as reasonable treatment options.

The most common symptoms of SMPM include coughing, hemoptysis, weight loss, chest pain, dyspnea, fatigue, and fever due to recurring pneumonia (3). In the present case,

the patient presented with only chest pain. Smoking may also be a risk factor, but our patient was not a smoker. The CT findings suggested MPM, which usually affects the lungs. The recommended treatment included surgery, radiation and chemotherapy; however, only surgery was performed due to financial constraints. Supportive treatment may relieve some of the symptoms. Prognosis in MPM may be difficult to assess consistently, due to the great variability in the time before diagnosis and the rate of disease progression. Our patient only survived for ~5 months after surgery, as the disease exhibited an aggressive clinical course.

EPP appears to be the only radical treatment option for locally advanced MPM, and may be able to eradicate macroscopic disease in selected patients. However, the long-term survival remains unsatisfactory due to the high incidence of recurrence, particularly locoregional treatment failure, and more effective treatments are urgently required (16).

Cytological assessment of pleural effusion may not be sufficiently sensitive and specific (29). In addition, fine-needle biopsy is not primarily recommended, as it is associated with low sensitivity (~30%). In the present case, CT-guided percutaneous needle biopsy was performed, but the findings were not significant. Deng *et al* suggested that SMPM may only be confirmed by full-thickness biopsy (30).

In conclusion, SMPM has not been extensively investigated due to the scarcity of reported cases. We herein present a case of multiple intracranial metastases from a giant SMPM, emphasizing the rare metastatic pattern, aggressive clinical course and poor response to treatment, along with a review of the previously published relevant literature.

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