Sarcomatoid Malignant Mesothelioma Presenting with Intramedullary Spinal Cord Metastasis: A Case Report and Literature Review

Junkoh Yamamoto1 Kunihiro Ueta1 Masaru Takenaka2 Mayu Takahashi1 Shigeru Nishizawa1

1 Department of Neurosurgery, University of Occupational and Environmental Health, Kitakyushu, Japan
2 Second Department of Surgery, University of Occupational and Environmental Health, Kitakyushu, Japan

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Abstract

Study Design Case report.

Objective Malignant mesothelioma (MM) is an uncommon tumor of the pleural epithelium with a predilection for local spread into adjacent tissues. The sarcomatoid type accounts for ~10% of MM cases and is associated with poorer survival than the epithelioid, desmoplastic, and biphasic types. MM commonly presents with involvement of the vertebral body or epidural space. However, intradural spinal extension of MM is extremely rare. Only eight cases of intradural spinal extension have been reported. We report this rare case and discuss the clinical manifestations of intradural spinal extension of MM with literature review.

Methods This report describes the case of a 62-year-old man with Brown-Séquard syndrome and radiculopathy of the left C5 nerve root detected during treatment for pleural sarcomatoid MM. Magnetic resonance imaging (MRI) showed an intramedullary lesion at the C3 level and a small nodule at the left C5 nerve root with cervical canal stenosis.

Results The patient underwent surgery, and intramedullary metastasis of sarcomatoid MM was diagnosed. Subsequently, radiotherapy was administered, resulting in temporary improvement of the patient’s condition. Thereafter, his condition gradually deteriorated, and follow-up MRI showed a more extensive residual C3 intramedullary lesion. Thus, a second surgery was performed after chemotherapy, but the patient died 5 months after the initial diagnosis.

Conclusion We present this rare case, and emphasize intramedullary spinal cord metastasis of MM as differential diagnosis in primary cord lesion.

Introduction

Malignant mesothelioma (MM) is an uncommon but aggressive tumor with a median survival time of 9 to 12 months, despite multimodal therapy.1 Previous studies have shown that MM incidence in many countries such as Australia has increased by as much as 50% since the mid-1970s.2 MM usually arises within the pleural or peritoneal cavity and has a predilection for local spread into adjacent tissues.3 However, tumor extension into the spinal cord is extremely rare in cases of MM, although this is more commonly seen with other types of carcinoma.4 Here, we report a rare case of an adult patient with intramedullary spinal cord metastasis from sarcomatoid MM.
Case Report

A 62-year-old man presented with right chest pain. Chest computed tomography (CT) showed the presence of focal pleural thickening of the right medial aspect of the lung apex (Fig. 1A). Axial co-registered positron emission tomography (PET)-CT showed hypermetabolic fluorodeoxyglucose uptake (SUV max 19.9) within the pleural mass and adjacent chest wall (arrows in A). MRI showed extended abnormal hyperintensity on T2WI (C) and a left C3 intramedullary lesion (arrows in D) and a small nodule at the left C5 nerve root (arrow in G). An ill-defined flame-shaped region of enhancement at the superior/inferior lesion margins (flame sign; arrows in E) and a more intense thin rim of peripheral enhancement around an enhancing lesion (rim sign; arrows in F) were observed.

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Fig. 1 Axial co-registered positron emission tomography (PET)-computed tomography (CT) images before thoracoscopic chest wall biopsy (A, B) and magnetic resonance imaging (MRI) scans obtained upon the patient’s presentation of Brown-Séquard syndrome and left C5 radiculopathy (C, D, E, F, G). Sagittal (C) T2-weighted image (T2WI). Sagittal (D) and axial (E, F, G) contrast-enhanced T1-weighted image. PET-CT showed hypermetabolic fluorodeoxyglucose uptake (SUV max 19.9) within the pleural mass and adjacent chest wall (arrows in A). MRI showed extended abnormal hyperintensity on T2WI (C) and a left C3 intramedullary lesion (arrows in D) and a small nodule at the left C5 nerve root (arrow in G). An ill-defined flame-shaped region of enhancement at the superior/inferior lesion margins (flame sign; arrows in E) and a more intense thin rim of peripheral enhancement around an enhancing lesion (rim sign; arrows in F) were observed.

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The removed specimen indicated sarcomatoid MM. Subsequently, radiotherapy for the right chest was planned. After a few days, the patient experienced decreased sensation in his right upper and lower extremities and a gradual progression of weakness in his left upper and lower extremities. At this point, he consulted our department for further examination. Neurologic examination led to the diagnosis of Brown-Séquard syndrome with analgesia to pinprick on the right side and hemiparesis below the C3 level on the left side. Radiculopathy of the left C5 nerve root was also observed. Joint position sense and vibration sense were intact on both sides. Whole spinal MRI showed extensive abnormal T2 hyperintensity of the cervical cord, associated with a left enhancing C3 intramedullary cord lesion, and cervical canal stenosis.
Fig. 1C, D. MRI also showed the presence of a small nodule on the left C5 nerve root that was enhanced on contrast enhancement T1-weighted imaging (CE-T1WI) (Fig. 1G). In addition, the C3 intramedullary lesion presented a more intense thin rim of peripheral enhancement around an enhancing lesion (rim sign) and an ill-defined flame-shaped region of enhancement at the superior/inferior lesion margins (flame sign) on CE-T1WI (Fig. 1E, F). Neither tumor encasement of the cervical spine by the lung lesion nor continuity between the spinal and lung lesions was observed on MRI. Brain MRI showed no abnormal findings. Radiologic findings led us to suspect malignant lymphoma, sarcoidosis, multiple sclerosis, or intramedullary spinal cord metastasis (ISCM). The patient's condition rapidly deteriorated, and therefore, pulse corticosteroid therapy was administered as diagnostic treatment. However, MRI on the day after steroid therapy showed no change in the spinal lesions. Therefore, surgery was performed immediately for positive diagnostic confirmation and to decompress the cervical cord. Laminectomy at the C3 level and laminoplasty at the C4–C6 level were performed through a midline skin incision. On opening the dura, there was no evidence of tumor dissemination within the dura. After partial myelotomy at the left swollen dorsal column, the tumor was easily detected (Fig. 2A). However, a clear plane of dissection between the tumor and the cord was difficult to identify. A biopsy specimen of the tumor was pathologically examined. After surgery, left-sided hemiparesis and radiculopathy at the left C5 level improved, and the patient became ambulatory. However, slight right-sided sensory disturbance persisted.

Histopathologic Examination
Pathologic examination of the spinal cord tumor obtained during the first surgery indicated sarcomatoid MM corresponding to the previous pleural lesion (Fig. 2B). Immunohistochemically, the atypical cells were positive for cytokeratins (AE1/AE3 and CAM 5.2; Fig. 2C, D) and faintly positive for D2-40 but negative for thrombomodulin, calretinin, Ber-EP4, carcinoembryonic antigen, desmin, CD34, and S-100. The Ki-67 labeling index was ~20%.

Postoperative Course
The patient underwent subsequent radiotherapy and was transferred to the hospital's inpatient rehabilitation facility. Two weeks later, the patient's condition deteriorated. He presented with weakness in his left upper and lower extremities. The first course of combined chemotherapy consisted of carboplatin (590 mg) and pemetrexed (500 mg/m²) with dexamethasone. However, weakness in his extremities continued to progress gradually. Although chest CT revealed no recurrence of pleural lesions, whole central nervous system MRI showed an obvious extension of the previous C3 intramedullary lesion without the appearance of any additional new lesions (Fig. 3A). Thus, the patient underwent a second surgery for gross removal of the C3 intramedullary lesion by laminectomy (Fig. 3B). Examination of the tumor specimen obtained during the second surgery also revealed sarcomatoid MM, but the Ki-67 labeling index had increased to 40%. Nonetheless, weakness in his extremities gradually progressed, and the patient presented with
tetraplegia 2 weeks after his second surgery. Ventilator support with tracheostomy was required. Eventually, the patient developed septicemia leading to pneumonia and succumbed to disease progression 5 months after the first surgery for ISCM.

Discussion

Spinal involvement of a pleural MM is uncommon, but when it does occur, vertebral body or epidural space involvement is the most common, either due to direct extension through the intervertebral foramen, via hematogenous spread to the meninges, perineurally, or by “neurotrophic” growth along nerve roots. Intradal spinal mesothelioma is extremely rare, and only eight cases have been reported to date (Table 1). In most of these cases, metastases were considered to result from direct perineural spread into the dura of the spinal cord, with continuity of the pleural lesion. In only two cases (case 1 and the present case), intramedullary tumors were considered to result from hematogenous or leptomeningeal spread, without continuity with the pleural lesion. Case 1 (autopsy case) showed multiple discrete foci of tumor deposits within the spinal cord, which seemed to result from hematogenous spread via the spinal branches of the posterior intercostal arteries. Similarly, in the present case, an intramedullary lesion and a small nodule at a nerve root without continuity with the pleural lesion were noted on MRI. Previous autopsy studies reported that 50 to 67% of patients with pleural MM showed evidence of distant spread. Although extremely rare, metastasis should be considered in the differential diagnosis of discrete intramedullary spinal lesions in patients with pleural MM.

Prediction of, and tendency for, spinal intradural spread in cases of pleural MM remain unclear. Of the six published cases with available information on the precise histologic form, spinal intradural MM was of the sarcomatoid type (Table 1). The sarcomatoid type accounts for ~10% of MM cases and is associated with poorer survival than the epithelioid, desmoplastic, and biphasic types. In addition, the sarcomatoid type is more frequently associated with metastasis.

Table 1 Summary of cases with intradural spinal extension of malignant mesothelioma

| Case no. | First author | Age (y)/gender | Tumor location | Histologic form | Mechanism |
|----------|--------------|---------------|---------------|----------------|-----------|
| 1        | Cooper       | 67 M          | Intramedullary, T8 | Sarcomatous | Hematogenous (leptomeningeal spread) |
| 2        | Lee          | 55 F          | Intramedullary, T9 | No information | Direct perineural spread (T9 nerve roots) |
| 3        | Hillard      | 61 M          | Intramedullary, C7/T1 | No information | Direct perineural spread (C8, T1 nerve roots) |
| 4        | Payer        | 50 M          | Intramedullary, T5 | Sarcomatous | Direct perineural spread (T4 nerve roots) |
| 5        | Okura        | 61 M          | Intramedullary, T4 | Sarcomatous | Direct perineural spread (T4 nerve roots suspected) |
| 6        | Chamberlain  | 67 M          | Intramedullary, T1−T3 | Sarcomatous | Direct perineural spread (T4 nerve roots) |
| 7        | Murray       | 48 M          | Extramedullary, L3−5 | No information | Hematogenous (leptomeningeal spread) |
| 8        | Steel        | 54 M          | Extramedullary, T1 | Epithelial | Direct perineural spread (T1 nerve roots) |
| 9        | Present      | 62 M          | Intramedullary, C3 | Sarcomatous | Hematogenous (leptomeningeal spread) |
Recently, an FDG-PET study showed that the metabolic activity of the primary pleural lesions according to $S_{\text{UV}_{\text{max}}}$ values correlated with the presence of metastatic disease.\textsuperscript{20} In that study, the mean $S_{\text{UV}_{\text{max}}}$ values of the primary pleural lesions in patients with and without metastatic disease were 7.1 and 4.7, respectively. In the present case, the primary pleural lesion was diagnosed as the sarcomatoid type with an $S_{\text{UV}_{\text{max}}}$ of 19.9 on FDG-PET. The presence of the sarcomatoid type with a high $S_{\text{UV}_{\text{max}}}$ may influence spinal intradural spread. Until recently, no highly specific MRI features of ISCM that could distinguish them from primary cord masses have been described, making diagnosis of ISCM by MRI for this extremely rare case of MM difficult. A recent study reported that rim and flame signs were associated with ISCMs due to carcinoma and were rarely associated with primary cord masses.\textsuperscript{5} In the present case, rim and flame signs were observed on the initial MRI. Therefore, knowledge of these MRI findings may improve confidence when attempting to diagnose ISCMs in cases of MM spinal cord lesions.

Generally, ISCM has a very unfavorable prognosis. Mean survival after the diagnosis of ISCM is only 3 months.\textsuperscript{21} Extradural metastasis of MM can be resected safely.\textsuperscript{8} However, ISCM of MM complicates tumor removal because of diffuse tumor infiltration into the spinal cord, as observed in the present case.\textsuperscript{12} Most MMs are probably best treated with involved-field radiotherapy and concurrent dexamethasone, with the latter administered to manage cytotoxic spinal cord edema and associated signs and symptoms.\textsuperscript{15} In some instances, such as early stage cases like the one reported here, partial spinal decompression may be considered to prevent further neurologic deterioration. Thus, early diagnosis of ISCMs in cases of MM and early commencement of treatment may be essential.

**Conclusion**

Tumor extension into the spinal cord is extremely rare in cases of MM. In addition, the mechanism of spinal intradural spread is difficult to predict. Although rare, we emphasize that ISCM of MM be considered as a differential diagnosis in cases of a primary cord lesion, particularly of the sarcomatous type, with a high $S_{\text{UV}_{\text{max}}}$.

**Disclosures**

The authors report no conflict of interest concerning the material or methods used in this study or in the findings specified in this paper.

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