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

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Global Spine J 2014;4:115–120.

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.

Keywords
- positron emission tomography
- laminoplasty
- radiotherapy
- Brown-Séquard syndrome
- Radiculopathy
- dissemination

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.

received
June 14, 2013
accepted after revision
October 24, 2013
published online
November 22, 2013

DOI http://dx.doi.org/10.1055/s-0033-1361589.
ISSN 2192-5682.

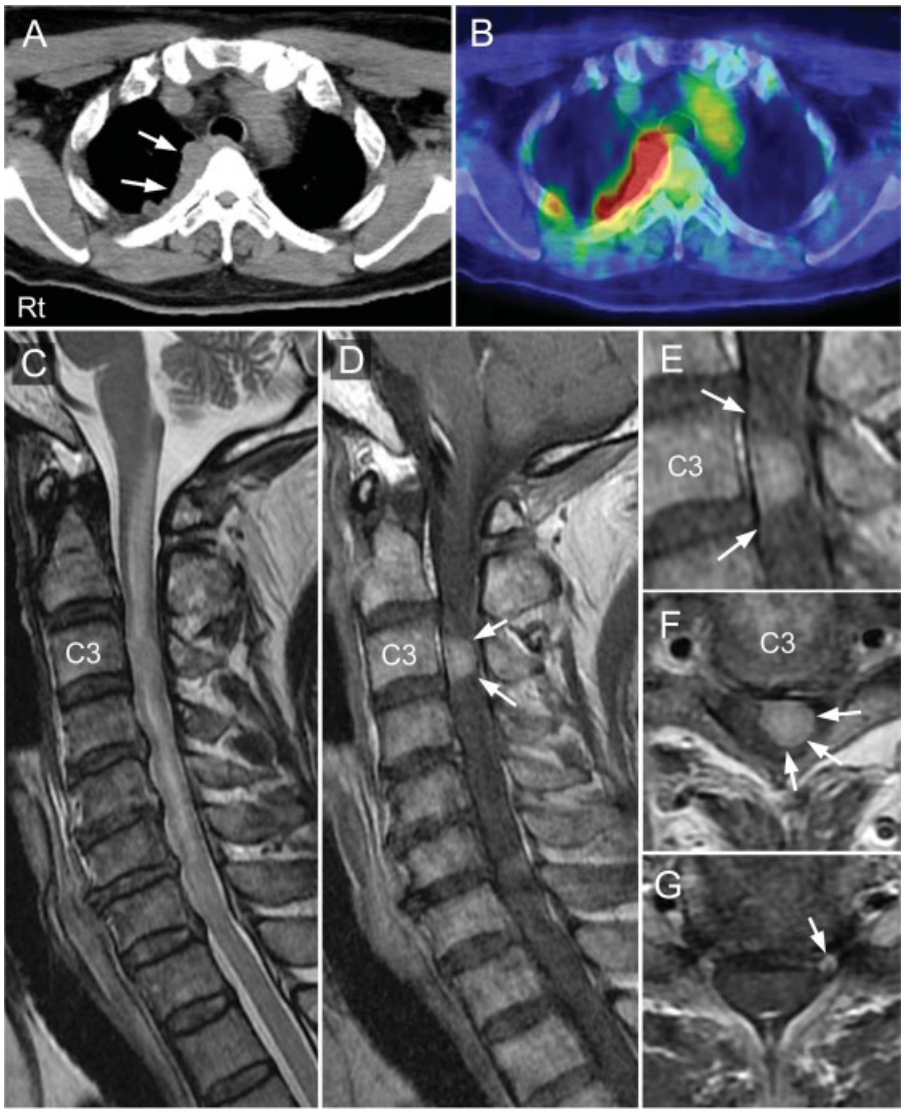

Fig. 1 Axial co-registered positron emission tomography (PET)-computed tomography (CT) images before thoracoscopic chest wall biopsy (A, B) and magnetic resonance imaging (MRI) scans obtained upon the patient's presentation of Brown-Séquard syndrome and left C5 radiculopathy (C, D, E, F, G). Sagittal (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.

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 (FDG) uptake (SUV_{max} 19.9) within the pleural mass and the adjacent chest wall (►**Fig. 1B**). However, no abnormalities were noted within the spinal canal on PET-CT. Thoracoscopic chest wall biopsy was performed and raised the suspicion of biphasic MM. Three weeks later, the patient underwent right thoracotomy with partial pleurectomy and partial decortication of the right lung. Pathologic examination of the surgically 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

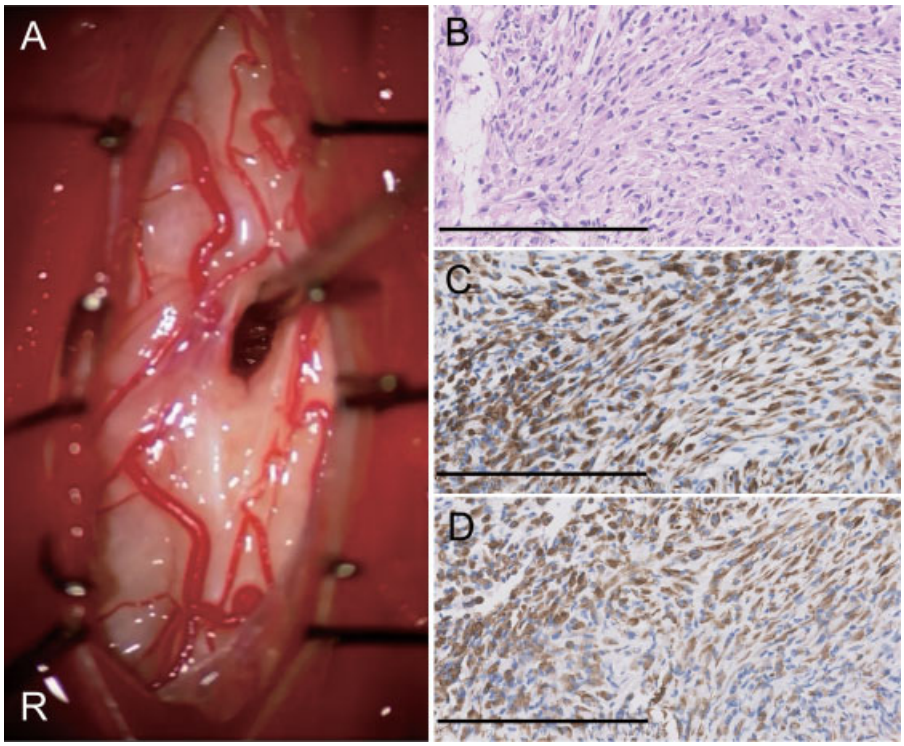

Fig. 2 Intraoperative photograph (A) and pathologic findings from the specimen of the intramedullary spinal cord tumor (B, C, D). A poorly circumscribed grayish tumor was observed (A). Hematoxylin and eosin staining indicated sarcomatoid malignant mesothelioma consisting of spindle cells arranged in fascicles or with a haphazard distribution (C). These atypical cells were positive for CAM 5.2 (C) and AE1/AE3 (D). Scale bar: 200 μm.

(►**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**).[5] 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 K_i-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/m^2) 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 K_i-67 labeling index had increased to 40%. Nonetheless, weakness in his extremities gradually progressed, and the patient presented with

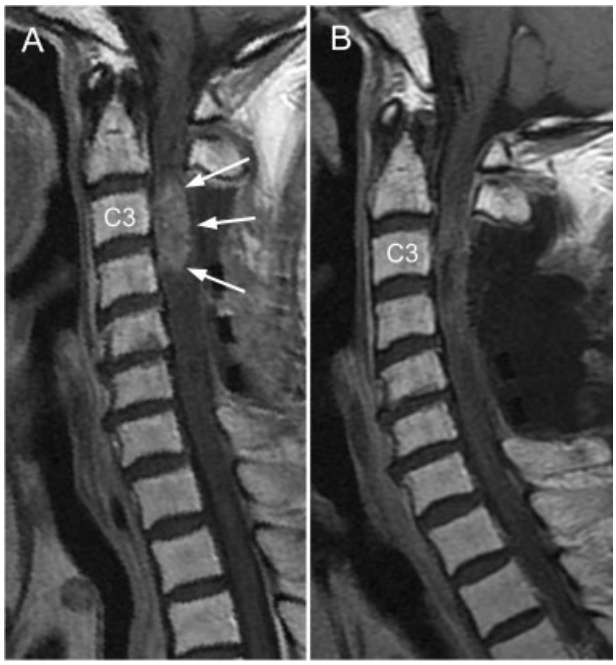

Fig. 3 Follow-up magnetic resonance imaging (MRI) scans before (A) and after (B) the second surgery (sagittal contrast-enhanced T1-weighted image). MRI before the second surgery showed extension of the C3 intramedullary lesions (arrows in A). Gross removal of the lesion after the second surgery (B).

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.[6–9] Intradural spinal mesothelioma is extremely rare, and only eight cases have been reported to date (►**Table 1**).[8–15] 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[10] 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.[10] 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.[16,17] 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.[18] In addition, the sarcomatoid type is more frequently associated with metastasis.[19]

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[10]	67 M	Intramedullary, T8	Sarcomatous	Hematogenous (leptomeningeal spread)
2	Lee[11]	55 F	Intramedullary, T9	No information	Direct perineural spread (T9 nerve roots)
3	Hillard[12]	61 M	Intramedullary, C7/T1	No information	Direct perineural spread (C8, T1 nerve roots)
4	Payer[13]	50 M	Intramedullary, T5	Sarcomatous	Direct perineural spread (T4 nerve roots)
5	Okura[14]	61 M	Intramedullary, T4	Sarcomatous	Direct perineural spread (T4 nerve roots) suspected
6	Chamberlain[15]	67 M	Intramedullary, T1–T3	Sarcomatous	Direct perineural spread (T4 nerve roots)
7	Murray[9]	48 M	Extramedullary, L3–5	No information	Hematogenous (leptomeningeal spread)
8	Steel[8]	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 SUV_{max} values correlated with the presence of metastatic disease.[20] In that study, the mean SUV_{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 SUV_{max} of 19.9 on FDG-PET. The presence of the sarcomatoid type with a high SUV_{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 carcinomas and were rarely associated with primary cord masses.[5] In the present case, rim and flame sings 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.[21] Extradural metastasis of MM can be resected safely.[8] However, ISCM of MM complicates tumor removal because of diffuse tumor infiltration into the spinal cord, as observed in the present case.[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.[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 SUV_{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.

References

1 Robinson BW, Lake RA. Advances in malignant mesothelioma. N Engl J Med 2005;353(15):1591–1603
2 Driscoll TR, Baker GJ, Daniels S, et al. Clinical aspects of malignant mesothelioma in Australia. Aust N Z J Med 1993;23(1):19–25
3 Boutin C, Schlesser M, Frenay C, Astoul P. Malignant pleural mesothelioma. Eur Respir J 1998;12(4):972–981
4 Newlin HE, Morris CG, Amdur RJ, Mendenhall WM. Neurotropic melanoma of the head and neck with clinical perineural invasion. Am J Clin Oncol 2005;28(4):399–402
5 Rykken JB, Diehn FE, Hunt CH, et al. Rim and flame signs: postgadolinium MRI findings specific for non-CNS intramedullary spinal cord metastases. AJNR Am J Neuroradiol 2013;34(4): 908–915
6 Pistolesi M, Rusthoven J. Malignant pleural mesothelioma: update, current management, and newer therapeutic strategies. Chest 2004;126(4):1318–1329
7 Ishikawa R, Kikuchi E, Jin M, et al. Desmoplastic malignant mesothelioma of the pleura: autopsy reveals asbestos exposure. Pathol Int 2003;53(6):401–406
8 Steel TR, Allibone J, Revesz T, D'Arrigo C, Crockard HA. Intradural neurotropic spread of malignant mesothelioma. Case report and review of the literature. J Neurosurg 1998;88(1):122–125
9 Murray JB, Neilly JB, Hadley D, Moran F, McKean M. Diffuse meningeal thickening associated with pleural mesothelioma. Thorax 1990;45(1):70–71
10 Cooper D. Malignant mesothelioma invading the spinal canal. Postgrad Med J 1974;50(589):718–723
11 Lee AW, Nikitins I, Pozza C, Koblar SA. Pleural mesothelioma with extension into the thoracic spinal cord. Intern Med J 2005;35(3): 195–196
12 Hillard VH, Liu JK, Kwok A, Schmidt MH. Perineural spread of malignant mesothelioma resulting in an intradural spinal cord mass: case report. J Neurooncol 2007;81(2):185–189
13 Payer M, von Briel T. Intradural pleural malignant mesothelioma. Acta Neurochir (Wien) 2007;149(10):1053–1056, discussion 1056
14 Okura H, Suga Y, Akiyama O, et al. Pleural malignant mesothelioma causing cord infiltration through the nerve root. Case report. Neurol Med Chir (Tokyo) 2009;49(4):167–171
15 Chamberlain MC, Eaton KD, Fink JR, Tredway T. Intradural intramedullary spinal cord metastasis due to mesothelioma. J Neurooncol 2010;97(1):133–136
16 King JA, Tucker JA, Wong SW. Mesothelioma: a study of 22 gases. South Med J 1997;90(2):199–205
17 Hulks G, Thomas JS, Waclawski E. Malignant pleural mesothelioma in western Glasgow 1980–6. Thorax 1989;44(6):496–500
18 Klebe S, Brownlee NA, Mahar A, et al. Sarcomatoid mesothelioma: a clinical-pathologic correlation of 326 cases. Mod Pathol 2010; 23(3):470–479
19 Wilson GE, Hasleton PS, Chatterjee AK. Desmoplastic malignant mesothelioma: a review of 17 cases. J Clin Pathol 1992;45(4): 295–298
20 Lee ST, Ghanem M, Herbertson RA, et al. Prognostic value of 18F-FDG PET/CT in patients with malignant pleural mesothelioma. Mol Imaging Biol 2009;11(6):473–479
21 Schiff D, O'Neill BP. Intramedullary spinal cord metastases: clinical features and treatment outcome. Neurology 1996;47(4):906–912