

Intramedullary Spinal Cord Metastases: Report of Five Cases and Review of the Literature

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Abstract

Case Report

Intramedullary spinal cord metastasis (ISCM) is a rare but severe complication of advanced malignant disease and is associated with a poor prognosis. The incidence of ISCM appears to be increasing, possibly because of advances in diagnostic imaging and the growing availability of cancer treatments that prolong patient survival. Early and accurate recognition is crucial, as neurological deterioration may become irreversible. However, the optimal management of ISCM remains uncertain because treatment decisions must be individualized according to the patient's neurological status, extent of systemic disease, primary tumor, and overall clinical condition, while comparative controlled studies remain lacking. Greater clinical awareness may facilitate diagnosis before irreversible neurological deficits develop and thereby improve the effectiveness of palliative treatment. Therefore, we carried out this retrospective research of 5 observations of ISCM, associated with a detailed review of the literature.

Keywords: Intramedullary spinal cord metastases, Radiotherapy.

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INTRODUCTION

Intramedullary spinal cord metastases are rare but clinically significant, accounting for approximately 8.5% of central nervous system metastases and 1–3% of all intramedullary spinal cord neoplasms. Despite their low incidence, ISCMs warrant clinical attention because neurological deterioration may progress rapidly, potentially resulting in irreversible deficits. Lung cancer is the most common primary malignancy associated with ISCMs, followed by breast cancer, lymphoma, leukemia, and melanoma [1]. ISCM is rarely encountered in the clinical setting, and easily ignored by clinicians, owing to a lack of awareness and related research. In fact, as the diagnosis and treatment of cancer improve and more cancer patients survive, the incidence of ISCM keeps rising [1,2]. ISCM is often associated with rapid deterioration of neurological function and devastating outcomes. Prompt identification and appropriate intervention is urgent to prevent neurological deficit and prolong patient survival.

OBSERVATIONS

Case 1

A 64-year-old man, without medical history; the beginning goes back up to 2 months by the rapid installation of bilateral lumbosciatalgia more important on the left, complicated by bilateral paresthesias, gait disorders and intermittent neurological claudication associated with genito-sphincter disorders. In the examination, we noted paraparesis and hypoesthesia with a sensitive level at L1–L2. The patient benefited from a spinal cord magnetic resonance imaging (MRI), which objectified a hypo intense T1 and hyper intense T2 intramedullary lesion process taking the contrast at the L1–L2 level (Fig. 1). A decompressive laminectomy with biopsy of the intramedullary process was indicated, the anatomopathologic examination concluded an intramedullary metastasis of a bronchopulmonary adenocarcinoma, an extension workup requested showed a right lung tumor associated with cerebral, bone and adrenal metastases, the patient benefited from local radiotherapy at L1–L2 levels and palliative encephalic radiotherapy followed by chemotherapy. The evolution

was marked by the improvement of his neurological state; the patient died 6 months after diagnosis.

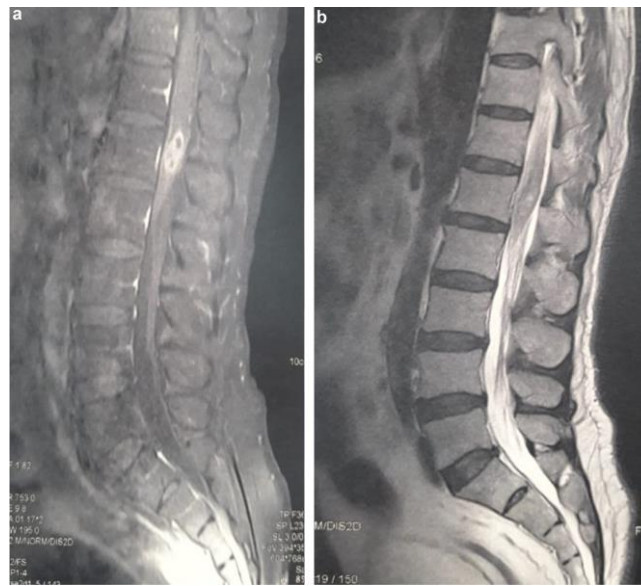


Fig. 1. (a): Sagittal T1 WI injected spinal MRI showing the enhancement of conus medullaris nodule; (b): Sagittal T2 sequence of an intramedullary metastasis of an unknown lung cancer.

Case 2

A 38-year-old patient without medical history, treated for metaplastic carcinosarcoma of the breast, underwent a mastectomy with axillary dissection followed by chemotherapy and adjuvant radiotherapy. Three months after the end of treatment, the patient presents cervical pain associated with paraparesis. A medullary MRI showed a cervical intra-medullary process at the height of C6–C7; it was in isosignal T1, hypersignal T2, enhanced intensely with gadolinium (Fig. 2), a thoraco-abdomino-pelvic CT, bone scan and

cerebral MRI were normal. After discussion in a multidisciplinary consultation meeting, the decision was to operate on the patient, but she refused the surgery. Hence, the indication of a palliative radiotherapy with a total dose of 30 Gy, the evolution was marked by the rapid alteration of her neurological functions with installation of a complete neurological deficit associated with visceral syndrome and genito sphincterian disorder, palliative chemotherapy is administered, but the patient died after 3 months after the diagnosis of the metastasis.



Fig. 2. A. Sagittal T1 WI injected spinal MRI, heterogeneous enhancement of nodules at C1C2. B. Axial T2 WI spinal MRI, showing spinal cord compression by an intramedullary spinal cord metastasis of a known breast cancer.

Case 3

A 62-year-old patient with a smoking history of 30 years, who has respiratory symptoms (cough, hemoptysis), underwent thoracic CT, which objectified an 85 mm left apical pulmonary process. The CT-guided biopsy is in favor of an undifferentiated adenocarcinoma, following the progressive appearance of a paresis of the lower limbs, a medullary MRI showed an enhanced intramedullary lesion with syringomyelic cavity sitting

at the height of C6–C7 and measuring 10 × 9 mm and extended over 19 mm (Fig. 3). Work-up assessment showed bone, hepatic, and brain metastases, following the onset of a complete neurological deficit; no medullary radiotherapy was indicated, encephalic radiotherapy with palliative dose was administered. The patient was then admitted to palliative care and died 4 months after diagnosis.



Fig. 3. A and B. Sagittal T1 WI injected spinal MRI, nodules enhanced intramedullary tissue lesion with syringomyelic cavity sitting at the height of C6 C7 and measuring 10 × 9 mm and extended over 19 mm.

Case 4

This 59-year-old man had been followed since October 2017 for locally advanced squamous cell carcinoma of the right lung, for which he received concomitant chemoradiotherapy. In March 2019, he presented progressively worsening paraparesis of the lower limbs. Spinal cord MRI revealed an intramedullary lesion at the level of the conus medullaris, measuring 8 mm in the axial plane and extending over 28 mm. Positron emission tomography combined with computed tomography demonstrated intense pathological hypermetabolism within the spinal cord, with a

maximum standardized uptake value of 23, extending from D11 to L1. The examination also showed hypermetabolism in the right lung, corresponding to the primary tumor, as well as mediastinal lymph node involvement. The patient received systemic corticosteroids and palliative radiotherapy at a total dose of 30 Gy, delivered in 3-Gy fractions, five fractions per week for two weeks. His clinical course was initially favorable, with improvement in paraparesis and lower limb paresthesias. However, three months after the diagnosis of the intramedullary spinal cord metastasis, and after three cycles of chemotherapy, the patient died.



Fig 4. A. Sagittal T1 WI injected spinal MRI showing an intramedullary process at the level of T1 (yellow arrow). B. Sagittal PET-CT fusion image showing an intense intramedullary hyper metabolism (yellow arrow).

Case 5

We present the case of a 44-year-old male patient with no notable prior medical history, in whom a melanoma of the left thigh with inguinal and pelvic lymph node metastases was diagnosed in 2020, and who was treated with immunotherapy using pembrolizumab. Six months later, he developed right-sided lumbar and sciatic radicular pain. Magnetic resonance imaging of the spinal cord revealed a nodular intramedullary lesion at the level of the first lumbar vertebra (L1), with enhancement after gadolinium injection (Fig 5). Cerebral

magnetic resonance imaging disclosed multiple supra- and infratentorial metastases. In view of the disseminated nature of the disease, the therapeutic strategy was palliative in intent and combined locoregional and systemic treatments: radiotherapy was delivered to the intramedullary lesion at a dose of 20 Gy in five fractions, providing partial relief of the pain, followed by whole-brain radiotherapy at a dose of 30 Gy in ten fractions. Systemic treatment with temozolomide was subsequently initiated.



Fig 5. Sagittal T1 WI injected spinal MRI, nodules enhanced intramedullary tissue lesion sitting at the height of L1

DISCUSSION

Intramedullary metastatic disease affects only 0.1 to 0.4% of all cancer patients and comprises only 1 to 3% of all intramedullary spinal cord neoplasms [3].

Lung cancer is the most common primary malignancy associated with intramedullary spinal cord metastasis, accounting for approximately half of reported cases, while breast cancer is the second most common primary tumor [1,2,4]. This distribution is reflected in the present series, in which three of the four fully described patients had a pulmonary primary and one had breast cancer, underscoring the need to consider ISCM when patients with these malignancies develop new spinal or neurological symptoms.

ISCM may arise at any level of the spinal cord, although the cervical region appears to be the most frequently affected site [5]. In most patients, it develops in the context of a previously diagnosed primary malignancy rather than the initial manifestation of cancer. The interval between diagnosis of the primary tumor and the detection of ISCM is generally short; in the series reported by Schiff and O'Neill, it was 17 months [6].

This relatively short interval suggests that ISCM usually represents progression of an established malignancy. Accordingly, ISCM should be considered promptly when a patient with cancer develops new spinal or neurological symptoms. Because neurological deficits may progress rapidly over days to weeks, prompt spinal MRI is warranted to enable diagnosis and treatment before substantial, potentially irreversible deterioration occurs [7].

Although intramedullary spinal cord metastasis is an uncommon manifestation of malignancy, it may be the initial presentation of cancer in approximately 25% of cases, according to a review by Kalayci *et al.*, [2]. These lesions typically produce mass effect and distortion of the spinal cord parenchyma, initially causing pain and sensory disturbances, followed by motor weakness and, in later stages, sphincter dysfunction [3]. The rapid progression of neurological symptoms over days to weeks is characteristic of ISCM and contrasts with the generally slower clinical course of primary intramedullary spinal cord tumors [1,2].

With the advent of MRI technology, ISCM has been encountered with increasing frequency, and it certainly has become the diagnostic test of choice in

patients with known malignancy and suspected spinal cord disease [8].

T2-weighted MR images are extremely sensitive in delineating intramedullary lesions because of their abnormal MR signal. The additional use of gadolinium may help demonstrate an enhancing central metastatic tumor nodule from surrounding edema. Despite advancements in MR imaging, no spin sequence exists that is capable of effectively distinguishing ISCM from primary spinal cord neoplasms or other non-neoplastic lesions, such as demyelinating plaques, radiation myelitis, or para-neoplastic myelopathy [9].

ISCM give a poor response to treatment and has a very unfavorable prognosis. Every effort should be made for effective palliation, and prevention of paraplegia. The mean survival after the diagnosis of ISCM is limited to 3 months [1,2,10]. No satisfactory guidelines for treatment of ISCM are available. More conservative approaches (radiation, steroids, and chemotherapy) have been adopted due to systemic diseases and improvement in the quality of life has been reported in certain cases.

The role of surgery in the management of ISCM is to preserve neurological function and provide optimal decompression. Although ISCMs may present as well-circumscribed focal masses amenable to gross-total resection [11], the potential benefits of complete excision must be weighed against the risk of postoperative neurological deterioration. [11;13]

However, some neurosurgeons believe that preservation of neurological function, rather than complete tumor resection, is the more prudent treatment objective. Thereby, less aggressive subtotal resection may be preferred, especially in cases in which the tumor spinal cord interface is not apparent, and more peripheral dissection may risk damaging infiltrative yet functionally viable cord tissue [14].

The use of radiation treatment with or without concomitant steroids is frequently described in the literature [1,2,10]. Radiation therapy usually halts the growth of the tumor and provides stabilization of further neurological deterioration [8]. However, its efficacy may be limited to patients with radiosensitive tumors, such as lymphoma, breast cancer, and small cell lung carcinoma.

Often the best responses are achieved when treatment is initiated early in the clinical course of ISCM. In a series of Lee *et al.*, [15], the outcomes of 12 patients were reported. Eleven patients were treated with steroids and external beam radiation therapy to a total dose ranging from 20 to 30 Gy, and one patient refused all treatment. Two patients reported transiently improved motor function; however, all developed progressive neurological status deterioration. The median survival was 3.9 months after the diagnosis of ISCM. However,

for radio-resistant tumors, such as renal cell carcinoma and melanoma, conventional external RT (30 Gy in 10 fractions or 40 Gy in 20 fractions) is hard for ideal control of ISCM and relief of symptoms [16].

Stereotactic radiosurgery represents a promising treatment option. Parikh and Heron [17] reported a 26-month overall survival and near-complete neurological recovery following CyberKnife treatment in a patient with renal cell carcinoma and ISCM. Nevertheless, although modern stereotactic radiotherapy techniques may offer substantial therapeutic potential, current evidence remains insufficient to establish their long-term efficacy.

Chemotherapy is generally used as an adjunct to radiotherapy or surgery rather than as a standalone treatment. Responses are most likely in chemo sensitive tumors, such as small-cell lung cancer and hematological malignancies. It may also be beneficial in patients who have not received extensive prior cytotoxic treatment or who have widespread systemic disease. However, evidence for its effectiveness in ISCM remains limited, and no survival benefit has been demonstrated [6,18].

Treatment selection must be individualized, as the aggressive course and limited prognosis of ISCM make a one-size-fits-all strategy inappropriate. The decision should integrate the patient's neurological status and rate of deterioration, lesion characteristics on MRI, histology and radiosensitivity of the primary tumor, extent of systemic disease, functional status, and expected survival. These factors determine whether the primary objective should be decompression and neurological preservation through surgery, local disease control with radiotherapy, or symptom palliation in patients unlikely to benefit from aggressive intervention [9,13].

The appearance of intramedullary metastases generally is an unfavorable sign because they frequently occur in conjunction with widespread systemic disease and signify late stages of a disease process. Kalayci *et al.*, [2] demonstrated an overall median survival of 7.3 months with the length of survival in surgical patients (9.4 months) being almost twice as long as the non-surgical patients (5 months). The better survival rate in surgical patients may have reflected patients being pre-selected as the result of their limited systemic disease and good clinical grading, and hence better chance of survival after treatment [9].

Nevertheless, more than half of the patients who underwent surgery experienced improvement in weakness, pain, or sphincter dysfunction, whereas most patients treated conservatively had unchanged neurological symptoms.

CONCLUSION

The occurrence of ISCM in the course of malignant disease is usually predictive of shortened life expectancy and is often associated with severe and worsening neurological deficit. The knowledge of prognosis of intramedullary metastasis is still very heterogeneous. It depends on the histology of the primary tumor, whether it has spread to other organs, operative and conservative treatment strategies, and the patient's overall condition. In the future, sophisticated treatment algorithms will be of great importance, as the incidence of ISCM will probably increase further and prospective studies are needed.

Conflicts of Interest:

The authors declare that there are no conflicts of interest regarding the publication of this paper.

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Ethical Approval:

As this is a case report, formal ethical committee approval is not required by our institution, provided that anonymity is maintained and consent is obtained. The study was conducted in accordance with the Declaration of Helsinki.

Patient Consent Declaration:

Informed consent was obtained from the patient's next of kin for the publication of this case report and accompanying images. The patient's identity has been fully anonymized, and no specific identifying details are included in the manuscript.

Authors' contributions

EM, MH, AB: Conceptualization, literature search, clinical data acquisition, manuscript drafting, and editing. **MB, AM, KA:** Participation in the clinical management of patients, data analysis, and manuscript review. **KH, and ME:** Supervision, critical revision of the manuscript for important intellectual content, and final approval of the version to be published.

All authors read and approved the final manuscript.

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