An intramedullary "flame" recognized as being an intramedullary spinal cord metastasis from esophageal cancer

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Radiology Case. 2019 Jul; 13(7):14-20 :: DOI: 10.3941/jrcr.v13i7.3555

ABSTRACT

Intramedullary spinal cord metastases are rarely encountered in patients suffering from extra - central nervous system primary cancer, with only 2 described cases reported in the literature deriving from esophageal cancer. Intramedullary spinal cord metastases may occur at any level of the spinal cord but cervical location is the most frequent. We report the first case of intramedullary metastasis affecting the thoracic spinal cord from esophageal squamous cell carcinoma in a 35-year-old patient.

CASE REPORT

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A 35-year-old female patient presented with involuntary weight loss >10% in two months and solid food dysphagia.

Due to the worsening of symptoms and the onset of hematemesis, she underwent upper gastrointestinal endoscopy which revealed an ulcerative lesion of the inferior third of thoracic esophagus. The histological diagnosis was a poorly differentiated carcinoma characterised by squamous and pseudo-glandular cells which infiltrated the muscularis mucosae.

A total body computed tomography (CT) scan showed pulmonary metastases, mediastinal lymphadenopathies and osteolytic vertebral lesions.

She underwent chemotherapy with folinic acid, 5-fluorouracil and oxaliplatin (Folfox), vertebroplasty and spinal radiotherapy.

Seven months after the diagnosis, a follow-up CT study showed volumetric reduction of two of the pathologic lymph nodes described before, but an additional pathologic cervical enlarged lymph node, and new osteolytic vertebral lesions [Figure 1].

She continued chemotherapy with Folfox. One month later, because of the occurrence of headaches and vomiting, a magnetic resonance imaging (MRI) brain study revealed a right occipital and a left parietal brain metastatic lesion. For this reason, the patient began a new chemotherapy (folinic acid, 5-fluorouracil and irinotecan - Folfiri) and stereotaxic radiotherapy was performed for brain lesions.

After five months, about one year after the first diagnosis of esophageal cancer, her condition worsened due to the appearance of paraplegia and neurogenic bladder, therefore a spine MRI study was performed.

Spinal MRI study showed an intramedullary oval shaped lesion (1 cm) at T9 level which appeared hypo-isointense on T2 weighted imaging, surrounded by a thin hyperintense rim and a faint and widespread hyperintensity of the surrounding spinal cord [Figure 2a]. Post-Gadolinium T1 weighted MRI images showed patchy intense enhancement of the intramedullary lesion with an ill-defined flame shaped enhancement at the superior and inferior margins suggesting an intramedullary spinal cord tumor [Figure 2 b-d]. Because of both the appearance of new metastases and the very rapid progression of the disease, the diagnosis was intramedullary spinal cord metastases (ISCM) from esophageal cancer, rather than primary spinal cord tumor. That MRI study also showed an increase in both volume and number of osteolytic vertebral bone lesions, one of which developed components into the spinal canal compressing the dural sac [Figure 3].

Due to the poor general condition of the patient there was no indication for surgery and, on the basis of a multidisciplinary evaluation, oncologists started a palliative radiotherapy integrated with supportive care [4]. The patient died two months later.

DISCUSSION

Etiology & Demographics:

ISCMs are infrequently reported as one of the manifestations of generalized metastases from various primary malignancies. They are estimated to represent 4,2-8,5% of central nervous system (CNS) metastases [1]. In the literature it is reported that more than half of ISCMs derive from lung cancer (54%) whereas they less frequently derive from breast cancer (11%), renal cell carcinoma (9%), melanoma (8%) and lymphoma (4%) [1,2]. Rarely reported sources included colorectal (3%), ovarian (2%), gastric, thyroid, cervix, epithelial, endometrial, esophageal, parotid, and bladder malignancies. [1] To the best of our knowledge there are only 2 reported cases of ISCMs from esophageal cancer [2,3].

A review of the literature by Kalayci showed that the average age of presentation of ISCM is 58 (23–79) years and that more than half (57%) of affected patients are male while 43% are female [1].

ISCMs may occur at any time during the course of oncologic diseases and may affect any level of the spinal cord, but they are rare; however, according to the literature, the cervical spinal cord is the most involved (42% of patients; thoracic and lumbar spinal cord are respectively involved in 26% and 32% of cases) due to its richer vascularization and increased thickness [1,2,5-7].

There are three theories on the pathogenesis of ISCMs. Hematogenous spread is believed to account for the majotity of cases. The second one concerns the meningeal carcinomatosis; tumor cells originating from carcinomatous meningitis may infiltrate the perivascular spaces, penetrating the pial membrane and invading the spinal cord tissue. The third potential dissemination pathway is through a possible direct extension of tumor cells via nerve roots or cerebrospinal fluid. Hematogenous spread is believed to account for our case because brain metastases coexisted in our patient, which was probably partly due to the low effectiveness of chemotherapy in the CNS for the blood-brain barrier [1,2,8,9].

Clinical & Imaging findings :

The most common clinical manifestations of ISCMs are sudden onset and rapid progression of neurological deficits and symptoms such as weakness, which is the most frequent one, sensory loss, backache, urinary incontinence and Brown-Séquard syndrome [1,2,10]. It is reported that radicular pain occurs in 25-33% of patients, but this is related with extramedullary tumors rather than intramedullary ones [6]. When vertebral metastases extend out to the epidural space of the spinal canal, they may cause spinal cord compression resulting in asymmetrical neurological deficit in 1-8% of cases [6]. Moreover, the primary malignancy has not always been diagnosed at the time of ISCM symptom onset or MRI; patients can be asymptomatic, even in the case of multiple ISCMs [6].

Plain radiography is not useful for the diagnosis of ISCM. CT is sensitive and specific for the diagnosis of extramedullary metastases, in particular bone metastases. MRI is the diagnostic imaging technique of choice for ISCMs, and it is especially effective when it is performed after intravenous Gadolinium-contrast administration [6].

There are three MRI features of ISCM reported in the literature: typical patterns of enhancement after Gadolinium-contrast administration, the associated extensive spinal cord hyperintensity surrounding the lesion, and the rarity of hemorrhage and intra-peritumoral cystic-necrotic changes [1, 11].

There are two peripheral enhancement patterns on post-Gadolinium MRI which are reported to be typical for non-CNS-origin of ICSMs compared with spinal cord primary tumors: a more intense thin rim of peripheral enhancement around the enhancing lesion (rim sign) and an ill-defined flame-shaped region of enhancement at the superior-inferior margins (flame sign) [6]. The rim and flame signs, singularly or together, are seen more frequently in ISCMs than in primary cord masses [6]. When one or both of these two signs are associated with an acute onset of symptoms in a cancer patient without previous evidence of spinal tumor, the diagnosis of

ISCM is strongly suggested [1,2,5,6,10,11]. According to this, even if in our case pathological specimens could not be obtained, the clinical course and imaging findings (flame sign) strongly suggested the diagnosis of ISCM. However, our diagnosis of ISCM is hypothetical, due to the lack of sampling from autopsy, but the clinical and neuroradiological features in our case, in agreement with the literature, highly confirmed it.

Furthermore, according to the literature, the ISCM is frequently associated with additional intra or extra-axial brain and spinal extramedullary metastases or, more commonly, with a known primary CNS tumor and/or other non-CNS metastases. The prevalence of other CNS/spinal extramedullary metastases in case of multiple ISCMs is especially high [1, 11].

Treatment & Prognosis:

Actually, there are no established guidelines for the treatment of ISCMs. Radiotherapy is the therapeutic gold standard especially when it is implemented very early in radiosensitive tumors [2,10]. Our patient underwent radiotherapy given the presence of epidural component of osteolytic metastasis spreading into spinal canal [6]. Chemotherapy is generally ineffective because many anticancer drugs do not cross the blood-brain barrier [2,12]. Surgery can be performed in selected cases. It is reported that a patient with cervical ISCM by esophageal cancer, with no evidence of skeletal or organ metastases, underwent a C5-C7 laminectomy and resection of the tumor. However, his neurologic status improved marginally [3].

The general medical condition of the patient, the stage of the primary tumor, the presence of leptomeningeal metastases or more than one metastases are the main factors influencing the decision for surgery [1,7,8,10,13]. Although in the literature it has been described that patients may survive for nearly twice as long after surgery than patients treated conservatively, our patient could not undergo surgery because of her poor clinical condition. The overall prognosis of ISCM is in any case very poor; the mortality rate is 80% within 3-4 months after the appearance of the first symptoms [1,2,7,13].

Differential Diagnosis:

One of the main problems in diagnostic imaging is to differentiate an ISCM from a primary spinal cord tumor. If the patient has not an underlying cancer, the pre-operative clinical diagnosis will likely be a primary spinal tumor, such as astrocytoma or ependymoma [1]. It is sometimes difficult to differentiate between primary spinal cord tumor and an ISCM, only based on imaging studies. The previously described MRI patterns of contrast enhancement, known as “rim sign” and “flame sign”, strongly suggest the diagnosis of ISCM. At the time of the diagnosis most of ISCM patients have systemic metastases, and about a half of all ISCM cases have brain metastases.

Once an intramedullary neoplasm is excluded by MRI, in a patient suffering from a primary known cancer it is required to differentiate the ISCM from other spinal cord lesions including radiation myelopathy, paraneoplastic myelopathy, inflammatory myelopathy and vascular myelopathy. Identifying characteristics of pain at presentation may be useful for diagnosis: radiating myelopathy and necrotizing myelopathy typically do not present pain. An acute painful presentation, instead, is consistent with metastatic disease and should be considered in differential diagnosis [1,11,13].

TEACHING POINT

Intramedullary spinal cord metastases are rare in patients with primary non-central nervous system cancer and mainly affect the cervical spinal cord. Their typical Gadolinium enhancement patterns on magnetic resonance imaging are represented by an intense thin enhancing rim around the lesion (rim sign) and an ill-defined flame-shaped region of enhancement at the superior-inferior margins of the metastasis (flame sign).

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FIGURES

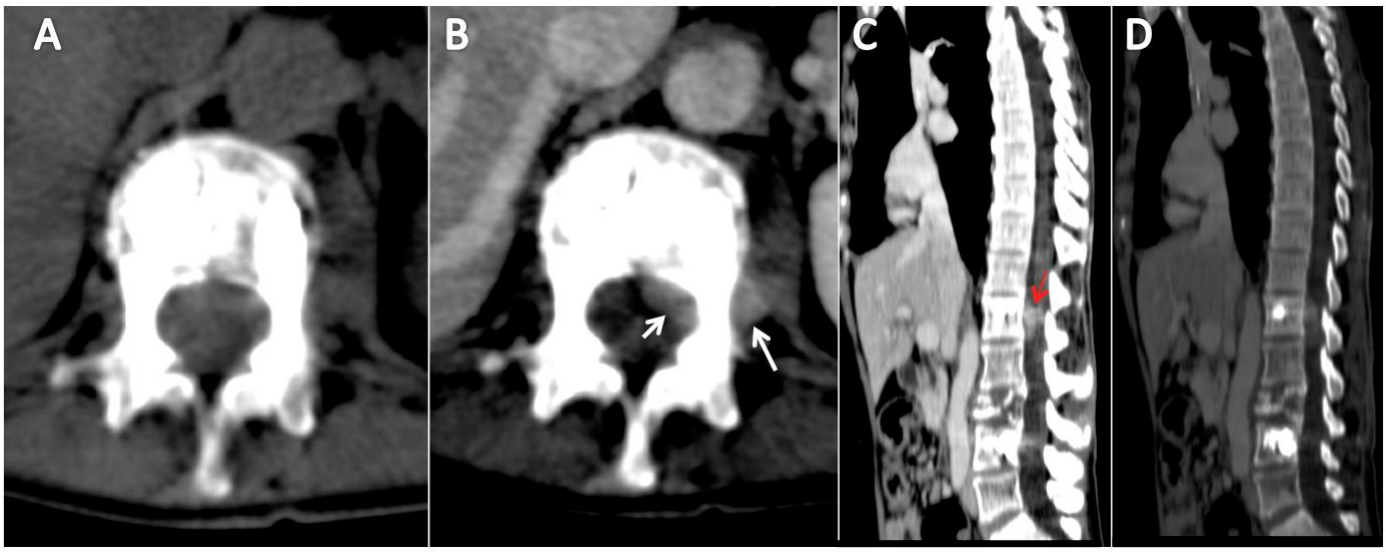

Figure 1: 35-year old female with thoracic intramedullary spinal cord metastasis from esophageal squamous cell carcinoma.

Findings:
A) Unenhanced and (B) contrast-enhanced axial CT images at L1 level show epidural metastatic contrast enhanced tissue (arrows in B), filling the anterior spinal canal at the same level, which extends across the intervertebral foramen on the left side. (C-D) Sagittal reformatted contrast-enhanced CT images reveal the enhancing epidural pathologic tissue at L1 level (red arrow in C), osteolytic vertebral bone metastasis at L3, and the vertebroplasty results at L1 and L4 levels (better recognizable in bone window reformat images (D). CT scan is not feasible to assess the spinal cord.

Technique:
4 detector row CT, Aquilion; Toshiba Medical System, Japan.
A) Unenhanced CT scan (1 mAs, 120 kV, 3 mm slice thickness) and (B) contrast enhanced CT scan (1 mAs, 120 kV, 3 mm slice thickness) acquired 60 seconds after intravenous contrast injection (120 mL of nonionic contrast medium; Ultravist 370, Schering AG, Berlin, Germany). A, B, C) window level: 174 and window width: 355; D) window level: 407 and window width: 930.

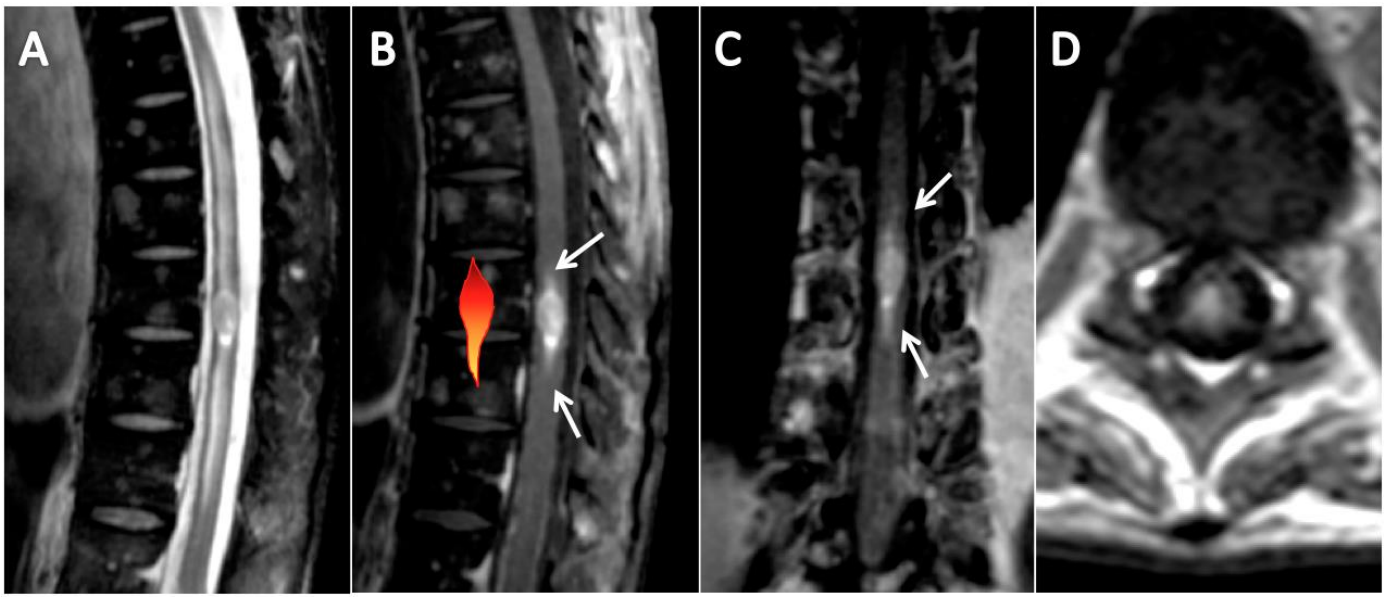

Figure 2: 35-year old female with thoracic intramedullary spinal cord metastasis from esophageal squamous cell carcinoma.

Findings:
A) Fat suppressed sagittal T2-weighted magnetic resonance imaging shows an oval shaped isointense intramedullary spinal cord lesion at T9 level surrounded by a hyperintense thin rim associated with more diffuse and faint hyperintense signal of the close thoracic spinal cord; B-D) sagittal (B), coronal (C), and axial (D) T1-weighted post-gadolinium MRI show an irregular enhancement of the intra-medullary spinal cord lesion, with an ill-defined flame-shaped enhancement of the superior and inferior margins (arrows), resembling a flame (red illustration).

Technique:
1,5T Siemens Magnetom Avanto MRI scanner.
A) Sagittal fat suppressed T2W, TR 3520, TE 116, 3.5 mm slice thickness; B) sagittal fat-suppressed T1W, TR 650, TE 13, 3 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL); C) coronal fat-suppressed T1W, TR 708, TE 13, 4 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL); D) axial T1W, TR 200, TE 17, 4 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL).

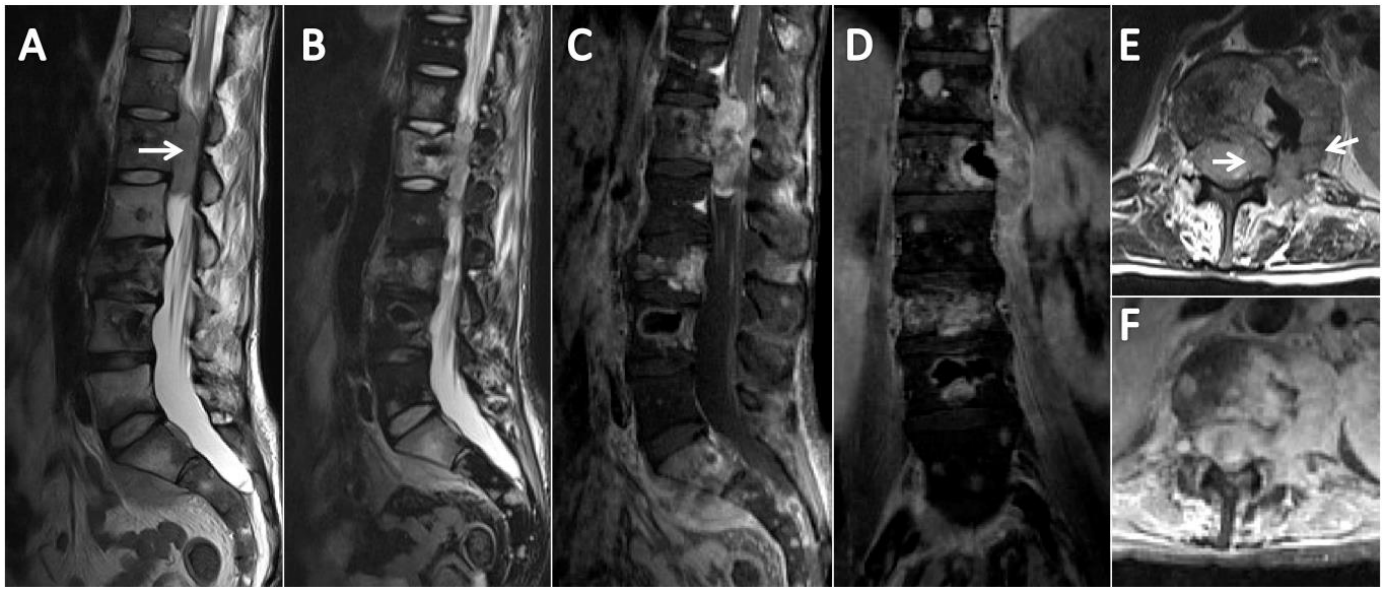

Figure 3: 35-year old female with thoracic intramedullary spinal cord metastasis from esophageal squamous cell carcinoma.

Findings:
A) sagittal T2-weighted magnetic resonance imaging, (B) sagittal fat-suppressed T2-weighted magnetic resonance, and (E) axial T2-weighted magnetic resonance imaging show the epidural pathologic tissue at L1 level (arrows), in the ventrolateral epidural space of the spinal canal on the left side, isointense to the spinal cord, which compresses the dural sac and extends into the left intervertebral foramen reaching the para-spinal soft tissues; sagittal (C), coronal (D) and axial (F) fat-suppressed T1-weighted post-gadolinium MRI images depict the inhomogeneous enhancement of the epidural pathologic tissue at L1 level on the left side, which involves the near para-spinal soft tissues. Pictures A-D show abnormal signal intensity and contrast enhancement of the vertebral bone marrow due to metastases too.

Technique:
1,5T Siemens Magnetom Avanto MRI scanner.
A) Sagittal T2W, TR 3500, TE 105, 4 mm slice thickness; B) sagittal fat-suppressed T2W, TR 3710, TE 67, 4 mm slice thickness; C) sagittal fat-suppressed T1W, TR 650, TE 13, 3 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL); D) coronal fat-suppressed T1W, TR 708, TE 13, 4 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL); E) axial T2W, TR 9130, TE 112, 3 mm slice thickness; F) axial fat suppressed T1W T1W, TR 903, TE 11, 4 mm slice thickness after intravenous contrast medium administration (Gadovist, 7 mL).

Etiology	Hematogenous dissemination, meningeal carcinomatosis and direct extension through nerve roots or cerebrospinal fluid.
Incidence	4.2-8.5% of CNS metastases
Gender ratio	57 % males; 43% females
Age predilection	Mean 58 years
Riskfactors	Oncologic diseases, especially lung cancer
Treatment	Radiotherapy, chemotherapy, surgicalresection
Prognosis	Verypoor
Imaging findings	MRI post-Gadolinium T1-hyyperintensity, “rim sign”, “flame sign”.

Table 1: Summary table of key-aspects of intramedullary spinal cord metastases (ISCMs).

	ISCM	Spinal astrocytoma	Spinal ependymoma	Post-radiation myelitis
CT	Rarely seen	Osseous remodeling: posterior vertebral body scalloping or thinning of the pedicle or laminae	Iso- to slightly hyper-attenuating compared with normal spinal cord	Rarelyseen
MRI - T1w	Isointense	Isointense to hypointense	Isointense to hypointense	Hypointense
MRI - T2w	Hyperintense prominent edema commonly surrounds the tumor nodule	Hyperintense	Hyperintense	Hyperintense
Pattern of contrast enhancement	• Avid homogeneous enhancement • Rim sign • Flame sign	Vast majority enhance patchy enhancement pattern	Inhomogeneous, strong enhancement	Focal, homogeneous contrast enhancement

Table 2: Differential diagnosis table for intramedullary spinal cord metastases (ISCMs).

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ABBREVIATIONS

CNS = Central nervous system
CT = Computed tomography
ISCM = Intramedullary spinal cord metastases
MRI = Magnetic resonance imaging

KEYWORDS

intramedullary spinal cord metastases; flame sign; rim sign; esophageal cancer; MRI

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