INTRAMEDULLARY SPINAL CORD METASTASES: REVIEW OF THE LITERATURE

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Aims. To review the epidemiology, dissemination, clinical presentation, diagnosis, treatment, survival and functional outcome of intramedullary spinal cord metastases (ISCM).

Methods. Literature review of all surgically treated cases of ISCM and all described cases of ISCM of breast carcinoma.

Results. 42 references to 87 surgically treated cases of ISCM were found, 13 references to 27 cases with diagnosed and treated ISCM of breast carcinoma. In only 9 cases of spinal cord metastases of breast cancer was surgical resection of ISCM done (10% of all surgically treated ISCM).

Conclusions. Three treatment modalities are available for ISCM: radiotherapy, chemotherapy, and surgery. The gold standard remains radiotherapy.

Microsurgical resection of a focal intramedullary mass appears to be feasible and should be considered in selected cases. Patients who have no evidence of widespread organ metastases or multiple intramedullary lesions and who have a life expectancy of at least a few months with tumours of non-lymphoma histology should be considered for tumor resection.

In conclusion, ISCM are difficult to treat lesions, but early diagnosis, careful surgical management and maintenance therapy may substantially contribute to a satisfactory functional outcome and prolonged survival.

INTRODUCTION

Intramedullary spinal cord metastases (ISCM) are infrequent and clinically affect only 0.1–0.4% of all cancer patients^{1–3}. Most present with rapid progressive neurological deficits and require immediate examination^{1,2,4–6}. Currently, spinal magnetic resonance imaging (MRI) is applied routinely for diagnosis^{3,7–11}. Surgery aims at decompression of functional neural tissue and histological confirmation of tumor⁶. As with other central nervous system (CNS) metastases, patients with ISCM have a very short life expectancy, with a median survival of 3 to 4 months from the time of diagnosis^{3,4,12}. I review here all surgically treated patients series in the literature.

DISCUSSION AND REVIEW OF THE LITERATURE

Epidemiology

Of all spinal tumor locations, extradural (ED) is the most common (55%), being located primarily in the vertebral bodies and the epidural fat. Regardless of their histology, ISCM are even more rare accounting for only 0.9–5% of all spinal metastases^{1,2,13,14}. This is particularly striking, since intracerebral metastases account for 55% of all intracranial tumors⁶. ISCM constitutes only 8.5% of all central nervous system (CNS) metastases^{1–3,15,16}. Buchholz¹⁷ first described metastases in the spinal cord parenchyma in 1897. Lung cancer (54%) with breast car-

cinoma (11%) accounted for a majority of ISCM cases¹⁶. Physicians diagnose only 5% of these metastases before death¹⁸ however, with advanced imaging techniques like MRI, there has been recorded a progressive increase in its frequency^{3,8,9,19}. ISCM is found together with leptomeningeal disease (LMD) in 15–55% of the cases^{3,9,20}.

Dissemination

Three different routes for the spread of tumors to the spinal cord have been hypothesized. Haematogeneous spread is believed to account for most cases^{1–5,9,18,21–23}. The common coexistence of pulmonary metastasis and brain metastasis supports the idea of dissemination through the arterial route^{4,13}. Another haematogeneous route is spread through the vertebral venous plexus (Batson's venous plexus), extending from the pelvis to the cranial venous sinuses, and enabling retrograde transportation to the spinal cord^{1,2,13}. The second mechanism is related to leptomeningeal dissemination by the cerebrospinal fluid. Tumor cells originating from carcinomatous meningitis may infiltrate the Virchow-Robin spaces of vessels, penetrating the spinal cord and pial membrane and invading the spinal cord parenchyma^{1,2,13,18}. The third mechanism is direct invasion from contiguous structures. Although the dura protects the cord from invasion by malignant neoplasms¹³, eventual direct extension of a metastatic tumor from the spinal extradural space or CSF or nerve roots, through the dura and into the cord, and spread along perineural space to subarachnoid space and to cord parenchyma have been suggested^{17,18}.

Clinical presentation

In patients with ISCM, weakness was present at time of presentation in 93%, sensory loss in 78% and urinogenital dysfunction in 62% of patients^{3,7,8,9,13,16,24}. Brown-Sequard syndrome, defined as unilateral weakness or spasticity with contralateral loss of pain and temperature sensation was found in 23% (ref.^{3,16}). Radicular pain was seen as a presenting symptom in 24 to 33% of patients^{1,2,4,16,25}. Rapid progression of the symptoms distinguishes ISCM from primary intramedullary tumors, which appear to typically present with a slower progression^{7,9}. The other major differential diagnosis in the group of patients is far more common epidural spinal cord compression due to the extradural spinal metastasis^{9,18,26,27}. ISCM patients are mostly old and neurological findings associated with myelopathy presents more acutely^{5,27,28}. At the time of the diagnosis most ISCM patients have systemic metastases and nearly half of all ISCM cases have brain metastases³. For these reasons, the brain and spinal cord need to be screened by MRI.

Diagnosis

With the widespread use of MRI, ISCM is being encountered with increasing frequency as it was often underdiagnosed or unconfirmed before the advent of MRI⁹.

Gadolinium MRI has a high sensitivity in identifying such lesions. Furthermore, T2-weighted imaging demonstrates the edema related to metastasis with great success^{3,10,11,16,19,20,29}. MRI with gadolinium has proven high sensitivity in the detection of intramedullary and spinal leptomeningeal neoplasms^{29,30}. Other diagnostic tests such as plain radiographs of the spine, myelography, post-myelography computerized tomography (CT) scan, and lumbar puncture with cerebrospinal fluid (CSF) examinations have much less value in the diagnosis of ISCM^{3,26}. Although the CSF is frequently abnormal, with an elevated protein value, it infrequently contains malignant cells^{5,18,23}. Grem et al.⁴ found malignant cells in 4 of the 22 ISCM cases (18%) in their series. If there is a spinal LMD concomitant with ISCM, the percentage of malignant cells present in CSF is between 50% and 75% (ref.^{3,30}).

Several authors have demonstrated that PET/CT particularly with fluorine-18-fluorodeoxyglucose (F¹⁸-FDG) enables examination of the entire spinal cord and thus permits the detection of ISCM, especially those of renal or lung origin^{31–34}.

Treatment

Three treatment modalities are available for ISCM: radiotherapy, chemotherapy, and surgery. The gold standard remains radiotherapy, with or without steroids to reduce edema^{1,2,4,23,35,36}. There are some reports of long-lasting remission after irradiation, but these are limited to patients in whom a very early diagnosis was made and/or who had highly radiosensitive tumors such as small-cell carcinoma or lymphoma^{4,23,35–38}. Treatment with steroids offered no additional survival benefit when combined with radiation therapy⁴.

Studies on the efficacy of chemotherapy are limited but failed to show any survival advantage³⁶. Holoye et al.³⁶ have described tumor ablation (lung small-cell carcinoma of the lung) with cyclophosphamide, methotrexate, and lomustine, but neurological deficits and survival remained unchanged. Weissman and Grossmann recommended treatment with both intrathecal chemotherapy and radiotherapy in patients with ISCM or meningeal small-cell carcinomatosis³⁹.

Surgery has become an alternative option in an increasing number of cases because of the increased speed and accuracy of diagnostic imaging and advances in microsurgical techniques^{5,17,27}. Surgical resection can be performed in selected cases only and several factors are important when considering surgery^{5,10,11,16,22,27,38,40}. Patient age and performance status affect the candidacy for surgical treatment. The location and severity of the primary neoplasm, as well as other metastases, weigh heavily in evaluating the prognosis, as well as anesthesia and surgical risks. Biological characteristics of the tumor itself should also be considered. Tumors that are known to be highly radioresistant should be preferentially indicated for surgical intervention. Technically, ISCM without leptomeningeal involvement is ideally suited for surgery. ISCM can be removed safely in many cases, since most ISCM are well encapsulated and some are cystic. Cystic tumors often lend themselves to surgical extirpation because the cystic component often reaches the surface of the cord and can therefore be more easily removed without disruption to normal structures¹⁷. In case of leptomeningeal involvement, radical excision is impossible. The preferred option is to limit removal to the well-defined portion of the tumor³⁴. Dam-Hieu et al.³⁴ reported one case of successful surgical treatment of leptomeningeal infiltration of medullary conus and cauda equina and this review reports a second case. This case suggests the possibility of neurological improvement after surgical release of agglutinated (by leptomeningeal infiltration) nerve roots of cauda equina.

Based on surgical findings, the surgeon has to find a balance between radicality and risk for functional deterioration. Complete surgical removal of ISCM should be reserved for those cases where a clear plane of cleavage allows unproblematic microsurgical dissection of the lesion⁶. Histology also influences surgical radicality. All poorly differentiated carcinomas and all sarcomas are difficult to dissect due to the lack of a clear plain of cleavage⁶.

It is only within the last few years, since the development of MRI, that surgical treatment of ISCM has become a realistic treatment option. Up to January 2009 we were able to find an additional 42 references of 87 surgically treated cases of ISCM through a biomedical database search – Table 1 (ref.^{3,5,6,7,8,10,11,16,17,22,23,26,27,28,34,38,40–65}).

We found 13 references to 27 cases with diagnosed and treated ISCM of breast carcinoma in the literature – Table 2 (ref.^{3,11,12,17,27,34,40,42,47,55,60,66,67}). We did not review autopsy diagnosed cases. In only 9 cases of spinal cord metastases of breast cancer was surgical resection of ISCM done (10% of all surgically treated ISCM).

Table 1. Review of publications about surgically treated cases of ISCM.

References	Date of ref.	Surgery of ISCM	Primary site of tumors (or histology)
Silva YJ et al. ⁴¹	1967	1	colon
Mercier P et al. ⁴²	1984	2	breast 1, lung 1
Dunne JW et al. ⁸	1986	2	melanoma 1, lung 1
Foster OJ et al. ⁴³	1987	1	colon
Decker RE et al. ²⁷	1987	1	breast
Findlay JM et al. ⁵	1987	2	lung 2
Winkelman MD et al. ³⁸	1987	1	thyroid gland
Tognetti F et al. ²³	1988	4	lung 4
Pelissou-Guyotat I et al. ⁴⁴	1989	1	lung
Koelman JHTM et al. ⁴⁵	1989	1	lung
Raco A et al. ⁴⁶	1992	1	unknown
Stranjalis G et al. ¹¹	1993	1	breast
Bizzozzero L et al. ⁴⁷	1994	1	breast
Fischer G et al. ⁴⁸	1994	4	melanoma 2, lung 2
Honma Y et al. ⁴⁹	1996	1	thyroid gland
Schiff D et al. ³	1996	5	n.a.
Conolly ES Jr et al. ⁷	1996	3	lung 3
Sutter B et al. ¹⁷	1998	3	breast 1, lung 2
Amin R ²⁶	1999	1	cervix
Taniura S et al. ⁵⁰	2000	1	stomach
Isla A et al. ⁴⁰	2000	1	breast
Li Y et al. ⁵¹	2000	1	unknown
Ateaque A et al. ⁵²	2000	1	kidney
Mathur S et al. ⁵³	2000	1	lymfoma
Schijns OEMG et al. ¹⁰	2000	1	kidney
Fakih M et al. ⁵⁴	2001	2	kidney 2
Gasser TG et al. ⁵⁵	2001	2	breast 1, unknown (sarcoma) 1
Ogino M et al. ²²	2002	1	colon
Kaya RA et al. ⁵⁶	2003	2	colon 1, kidney 1
Kalayci M et al. ¹⁶	2004	1	lung
Aryan HE et al. ²⁸	2004	1	lung
Gasser T et al. ⁶	2005	13	n.a. (AdenoCa 6, poorly diff Ca 3, sarcoma 3, small-cell Ca 1)
De Almeida Holanda MM et al. ⁵⁷	2006	1	thyroid gland
Donovan DJ et al. ⁵⁸	2006	1	kidney
Gazzeri R et al. ⁵⁹	2006	1	stomach
Watanabe M et al. ⁶⁰	2006	2	lung 2
Guppy KH et al. ⁶¹	2006	1	lung
Sivan M et al. ⁶²	2006	1	pituitary gland
Grasso G et al. ⁶³	2007	1	colon
Marquart C et al. ⁶⁴	2007	1	lung
Hrabálek L et al. ⁶⁵	2008	1	colon
Dam-Hieu P et al. ³⁴	2009	13	lung 8, breast 2, oesophagus 1, thyroid 1, colon 1
Hrabálek L	2010	1	breast

Date of ref.: Date of reference (year), Surgery of ISCM: Number of patients with spinal cord surgery, n.a.: not available.

Developments in imaging now allow reliable diagnosis, and advances in surgical microscopy have brought these tumors into the domain of neurosurgical care. Early suspicion of ISCM and treatment before the development of paralysis is required to improve neurologic deficit and survival of patients diagnosed with ISCM¹². Radical resec-

tion of an ISCM is indicated in all patients who presents with rapid progressive neurological deficits¹⁶.

Survival and functional outcome

Kalayci et al.¹⁶ reported, that improvement was seen in 66%, no change in 25%, and deterioration in 9% of

Table 2. Review of publications about ISCM of breast carcinoma.

References	Date of ref.	Age (years)	Location	Surgery	RT	ChT	Outcome	Survival (months)
Mercier P et al. ⁴²	1984	51	T	yes	yes	no	no improvement	2
Decker RE et al. ²⁷	1987	42	C	yes	yes	yes	improvement	alive at 15
Stranjalis G et al. ¹¹	1993	47	C	yes	yes	no	improvement	24
Bizzozzero L et al. ⁴⁷	1994	52	T	yes	no	no	improvement	alive at 6
Schiff D et al. ³	1996	n.a.	n.a.	n.a.	n.a.	no	n.a.	median 13 (2–27)
		n.a.	n.a.	n.a.	n.a.	no	n.a.	
		n.a.	n.a.	n.a.	n.a.	no	n.a.	
		n.a.	n.a.	n.a.	n.a.	no	n.a.	
		n.a.	n.a.	n.a.	n.a.	no	n.a.	
Sutter B et al. ¹⁷	1998	40	T	yes	yes	yes	improvement	13
Isla A et al. ⁴⁰	2000	54	conus	yes	yes	no	improvement	5
Gasser TG et al. ⁵⁵	2001	45	T	yes	yes	no	improvement	alive at 6
Villegas AE et al. ⁶⁶	2004	50	T	no	yes	no	improvement	4
Kosmas C et al. ⁶⁷	2005	57	T	no	yes	no	no improvement	1
		51	T	no	yes	yes	no improvement	5
		42	C, T	no	yes	no	no improvement	6
		47	C	no	yes	no	improvement	2
Watanabe M et al. ⁶⁰	2006	46	conus	no	yes	no	n.a.	n.a.
Lee SS et al. ¹²	2007	57	n.a.	no	yes	no	no improvement	3
		50	n.a.	no	yes	no	no improvement	5
		49	n.a.	no	yes	no	no improvement	9
		62	n.a.	no	yes	no	no improvement	alive at 5
		32	n.a.	no	yes	no	no improvement	3
		59	n.a.	no	yes	no	no improvement	4
Dam-Hieu P et al. ³⁴	2009	39	T	yes	no	no	worsening	2
		63	conus	yes	yes	yes	improvement	alive at 24
		35	conus	no	no	yes	no improvement	alive at 6
Hrabálek L	2010	48	conus, c.e.	yes	yes	no	improvement	4

Date of ref.: Date of reference (year), RT: Radiotherapy, ChT: Chemotherapy, Outcome: neurological status, n.a.: not available, Location: level of ISCM, C: Cervical, T: Thoracic, conus: medullary conus, c.e.: cauda equina.

all cases ISCM after treatment. In patients treated with a conservative regiment, 50% improved, 28% showed no change, and 22% deteriorated. In patients with surgical resection improvement was seen in 77%, and no change was seen in 23% of cases. Deterioration was not reported in his group¹⁶. The survey is nearly twice longer in surgical resection group compared to conservatively treated patients¹⁶. Histological type and grade of the tumor represented a major determinant of patient survival. Patients with intramedullary poorly differentiated carcinomas survived shortest, patients with adenocarcinomas longest^{68,69,70}. Patients with lung cancer showed worse prognosis than those with breast cancer, with median survival 1.0 month vs. 5.5 months¹². Interestingly, survival time was independent of CSF findings. Thus, carcinomatous meningitis is not always negative predictive factor for survival⁶.

Despite of recent improvements, ISCM has an poor prognosis. After the appearance of the first symptom, mortality rate in 3–4 months is 80% of cases^{4,10,16,47,71}.

CONCLUSIONS

Three treatment modalities are available for ISCM: radiotherapy, chemotherapy, and surgery. The gold standard remains radiotherapy.

Microsurgical resection of a focal intramedullary mass appears to be feasible and should be considered in selected cases. Patients who have no evidence of widespread organ metastases or multiple intramedullary lesions and who have a life expectancy of at least a few months with tumours of non-lymphoma histology should be considered for tumor resection.

In conclusion, ISCM are difficult to treat lesions, but early diagnosis, careful surgical management and maintenance therapy may substantially contribute to a satisfactory functional outcome and prolonged survival.

REFERENCES

- Edelson RN, Deck MD, Posner JB. Intramedullary spinal cord metastases. Clinical and radiographic findings in nine cases. *Neurology* 1972; 22:1222-1231.
- Jellinger K, Kothbauer P, Sunder-Plassmann E, Weiss R. Intramedullary spinal cord metastases. *J Neurol* 1979; 220:31-41.
- Schiff D, O'Neill BP. Intramedullary spinal cord metastases: clinical features and treatment outcome. *Neurology* 1996; 47:906-912.
- Grem JL, Burgess J, Trump DL. Clinical features and natural history of intramedullary spinal cord metastasis. *Cancer* 1985; 56:2305-2314.
- Findlay JM, Bernstein M, Vanderlinden RG, Resch L. Microsurgical resection of solitary intramedullary spinal cord metastases. *Neurosurgery* 1987; 21:911-915.
- Gasser T, Sandalcioğlu IE, El Hamalawi B, van de Nes JA, Stolke D, Wiedemayer H. Surgical treatment of intramedullary spinal cord metastases of systemic cancer: functional outcome and prognosis. *J Neuro-Oncology* 2005; 73:163-168.
- Connolly ES Jr, Winfree CHJ, McCormick PC, Cruz M, Stein BM. Intramedullary spinal cord metastasis: report of three cases and review of the literature. *Surg Neurol* 1996; 46:329-338.
- Dunne JW, Harper CG, Pamphlett R. Intramedullary spinal cord metastases: a clinical and pathological study of nine cases. *Q J Med* 1986; 61:1003-1020.
- Potti A, Abdel-Raheem M, Levitt R, Schell DA, Mehdi SA. Intramedullary spinal cord metastases (ISCM) and non-small cell lung carcinoma (NSCLC): clinical patterns diagnosis and therapeutic considerations. *Lung Cancer* 2001; 31:319-323.
- Schijns OEMG, Kurt E, Wessels P, Luijckx GJ, Beuls EAM. Intramedullary spinal cord metastasis as a first manifestation of a renal cell carcinoma: report of a case and review of the literature. *Clin Neurol Neurosurg* 2000; 120:249-254.
- Stranjalis G, Torrens MJ. Successful removal of intramedullary spinal cord metastasis: case report. *Br J Neurosurg* 1993; 7:193-195.
- Lee SS, Kim MK, Sym SJ, Kim SW, Kim WK, Kim S-B, Ahn J-H. Intramedullary spinal cord metastases: a single-institution experience. *J Neurooncol* 2007; 84:85-89.
- Okamoto H, Shinkai T, Matsuno Y, Saijo N. Intradural parenchymal involvement in the spinal subarachnoid space associated with primary lung cancer. *Cancer* 1993; 72:2583-2588.
- Smaltino F, Bernini FP, Santoro S. Computerized tomography in the diagnosis of intramedullary metastases. *Acta Neurochir* 1980; 52:299-303.
- Hashizume Y, Hirano A. Intramedullary spinal cord metastasis. Pathologic findings in five autopsy cases. *Acta Neuropathol (Berl)* 1983; 64:214-218.
- Kalayci M, Cagavi F, Gül S, Yenidünya S, Acikgöz B. Intramedullary spinal cord metastases: diagnosis and treatment - an illustrated review. *Acta Neurochir (Wien)* 2004; 146:1347-1354.
- Sutter B, Arthur A, Laurent J, Chadduck J, Friehs G, Clarici G, Pendl G. Treatment options and time course for intramedullary spinal cord metastasis. Report of three cases and review of the literature. *Neurosurgical Focus* 1998; 4(5):e3.
- Costigan DA, Winkelman MD. Intramedullary spinal cord metastasis, a clinicopathological study of 13 cases. *J Neurosurg* 1985; 62:227-233.
- Fredericks RK, Elster A, Walker FO. Gadolinium-enhanced MRI: A superior technique for the diagnosis of intraspinal metastases. *Neurology* 1989; 39:734-736.
- Crasto S, Duca S, Davini O, Rizzo L, Pavanello IG, Avataneo T, Cirillo S, Regge D, Soffietti R. MRI diagnosis of intramedullary metastases from extra-CNS tumors. *Eur Radiol* 1997; 7:732-736.
- Chason J, Walker F, Landers J. Metastatic carcinoma in the central nervous system and dorsal root ganglia. *Cancer* 1963; 16:781-787.
- Ogino M, Ueda R, Nakatsukasa M, Murase I. Successful removal of solitary intramedullary spinal cord metastasis from colon cancer. *Clin Neurol Neurosurg* 2002; 104:152-156.
- Tognetti F, Lanzino G, Calbucci F. Metastases of the spinal cord from remote neoplasms. *Surg Neurol* 1988; 30:220-227.
- Schiff D, Shaw EG, Cascino TL. Outcome after spinal irradiation for malignant epidural spinal cord compression. *Ann Neurol* 1995; 37:583-589.
- Thomas AW, Simon SR, Ewans C. Intramedullary spinal cord metastases from epithelial ovarian carcinoma. *Gynecol Oncol* 1992; 44:195-197.
- Amin R. Intramedullary spinal metastasis from carcinoma of the cervix. *Br J Radiol* 1999; 72:89-91.
- Decker RE, Sundrani S, Citron ML, Herrschaft DS. Intramedullary spinal cord metastases. Treated by complete resection of tumor prior to radiotherapy and chemotherapy. *Spine* 1987; 12:393-395.
- Aryan HE, Farin A, Nakaji P, Imbesi SG, Abshire BB. Intramedullary spinal cord metastasis of lung adenocarcinoma presenting as Brown-Sequard syndrome. *Surg Neurol* 2004; 61:72-76.
- Kamholtz R, Sze G. Current imaging in spinal metastatic disease. *Semin Oncol* 1991; 18:158-169.
- Schuknecht B, Huber P, Bulle B, Nadjmi M. Spinal leptomeningeal neoplastic disease. *Eur Neurol* 1992; 32:11-16.
- Jayasundera MV, Thompson JF, Fulham MJ. Intramedullary spinal cord metastases from carcinoma of the lung: detection by positron emission tomography. *Eur J Cancer* 1997; 33:508-509.
- Komori T, Delbeke D. Leptomeningeal carcinomatosis and intramedullary spinal cord metastases from lung cancer: Detection with FDG positron emission tomography. *Clin Nucl Med* 2001; 26:905-907.
- Poggi MM, Patronas N, Buttman J, Hewitt S, Fuller B. Intramedullary spinal cord metastasis from renal cell carcinoma: Detection by positron emission tomography. *Clin Nucl Med* 2001; 26:837-839.
- Dam-Hieu P, Seizeur R, Mineo JF, Metges JP, Meriot P, Simon H. Retrospective study of 19 patients with intramedullary spinal cord metastasis. *Clin Neurol Neurosurg* 2009; 111(1):10-17.
- Choucair AK. Myelopathies in the cancer patient: incidence, presentation, diagnosis and management. *Oncology* 1991; 5:25-31.
- Holoye P, Libnoch J, Cox J, Kun L, Byharhdt R, Almaoro U, McClelland S, Chintapali K. Spinal cord metastasis in small cell carcinoma of the lung. *Radiat Oncol Biol Phys* 1984; 10:349-356.
- Murphy KC, Feld R, Evans WK, Shepherd FA, Perrin R, Sima AA, Poon PY. Intramedullary spinal cord metastases from small cell carcinoma of the lung. *J Clin Oncol* 1983; 1:99-103.
- Winkelman MD, Adelstein DJ, Karlins NL. Intramedullary spinal cord metastasis. Diagnostic and therapeutic considerations. *Arch Neurol* 1987; 44:526-531.
- Weissman DE, Grossmann SA. Simultaneous leptomeningeal and intramedullary spinal metastases in small cell lung carcinoma. *Med Pediatr Oncol* 1986; 14:54-56.
- Isla A, Paz JM, Sansivirini F, Zamora P, García Grande A, Fernandez A. Intramedullary spinal cord metastasis. A case report. *J Neurosurg Sci* 2000; 44:99-101.
- Silva YJ, McSwain B. Intramedullary spinal cord metastasis: the sole clinical manifestation of an adenocarcinoma of the colon. *Can J Surg* 1967; 10:341-344.
- Mercier P, Vialle M, George B, Fardoun R, Guy G. Les metastases rachidiennes intradurales des cancers viscéraux. A propos de quatre cas. *Neurochirurgie* 1984; 30:177-181.
- Foster OJ, Crockard HA. Cervical syrinx associated with an intramedullary metastasis: case report. *J Neurol Neurosurg Psychiatry* 1987; 50:637-639.
- Pelissou-Guyotat I, Guyotat J, Szapiro J, Ravon R, Moreau JJ, Vidal J. Métastases spinales intradurales de néoplasies viscérales. A propos de quatre cas. *Revue de la littérature. Neurochirurgie* 1989; 35:236-241.
- Koelman JHTM, Visser MDE, Kuster JAM, Dreissen JJR, Valk J, Koster PA. Intramedullary spinal cord metastasis following a slowly progressive course. *J Neurol Neurosurg Psychiatry* 1989; 52:1451-1452.
- Raco A, Delfini R, Salvami M, Innocenzi G, Ciappetta P. Intramedullary metastasis of unknown origin: case report. *Neurosurg Rev* 1992; 15:135-138.
- Bizzozzero L, Ferrari M, Villa F, Fontana R, Brusamolina R, Collice M. Intramedullary spinal cord metastasis. Case report. *J Neurosurg Sci* 1994; 38:193-195.

48. Fischer G, Brotchi J. Intramedullary spinal cord tumors. Report. French Society of Neurosurgery. 45th annual congress. Neurochirurgie 1994; 40 Suppl 1:1–108.
49. Honma Y, Kawakita K, Nagao S. Intramedullary spinal cord and brain metastases from thyroid carcinoma detected 11 years after initial diagnosis – case report. Neurol Med Chir 1996; 36(8):593–597.
50. Taniura S, Tatebayashi K, Watanabe K, Watanabe T. Intramedullary spinal cord metastasis from gastric cancer. J Neurosurg (Spine) 2000; 93:145–147.
51. Li Y, Takayasu M, Takali T, Yoshimoto M, Mitsui Y, Yoshida J. Intramedullary spinal cord metastasis associated with hemorrhage: a case report. No Shinkei Geka 2000; 28:453–457.
52. Ateaque A, Martin JL, O'Brien C. Intramedullary spinal cord metastases from a hypernephroma 11 years following the diagnosis and treatment of the primary lesion. Br J Neurosurg 2000; 14:474–476.
53. Mathur S, Law AJJ, Hung N. Late intramedullary spinal cord metastasis in a patient with lymphoblastic lymphoma: case report. Journal of Clinical Neuroscience 2000; 7:264–268.
54. Fakih M, Schiff D, Erich R, Logan TF. Intramedullary spinal cord metastasis (ISCM) in renal cell carcinoma: a series of six cases. Ann Oncol 2001; 12:1173–1177.
55. Gasser TG, Pospiech J, Stolke D, Schwachheimer K. Spinal intramedullary metastases. Report of two cases and review of the literature. Neurosurg Rev 2001; 24:88–92.
56. Kaya RA, Dalkilic T, Ozer F, Aydin Y. Intramedullary spinal cord metastasis: a rare and devastating complication of cancer. Neurol Med Chir (Tokyo) 2003; 43:612–615.
57. De Almeida Holanda MM, de Andrade EM, da Silva JA. Intramedullary spinal cord metastasis from thyroid carcinoma: case report. Arq Neuropsiquiatr 2006; 64 (2A):338–41.
58. Donovan DJ, Freeman JH. Solitary intramedullary spinal cord tumor presenting as the initial manifestation of metastatic renal cell carcinoma: case report. Spine 2006; 31:E460–463.
59. Gazzeri R, Galarza M, Faiola A, Gazzeri G. Pure intramedullary spinal cord metastasis secondary to gastric cancer. Neurosurg Rev 2006; 29:173–177.
60. Watanabe M, Nomura T, Toh E, Sato M, Mochida J. Intramedullary spinal cord metastasis: a clinical and imaging study of seven patients. J Spinal Disord Tech 2006; 19:43–47.
61. Guppy KH, Wagner F. Metastasis to the conus medullaris: case report. Neurosurgery 2006; 59 (5):E1148.
62. Sivan M, Nandi D, Cudlip S. Intramedullary spinal metastasis (ISCM) from pituitary carcinoma. J Neurooncol 2006; 80:19–20.
63. Grasso G, Meli F, Patti R, Giambardino F, Florena AM, Iacopino DG. Intramedullary spinal cord tumor presenting as the initial manifestation of metastatic colon cancer: case report and review of the literature. Spinal Cord 2007; 45:793–796.
64. Marquart C, Weckesser M, Schueller P, Hasselblatt M, Wassmann H, Schroder J. Intramedullary spinal cord metastasis as initial presentation of a systemic cancer-report of a rare case. Zentralbl Neurochir 2007; 68:214–216.
65. Hrabálek L, Kalita O, Ehrmann J, Srovnal J, Hajdúch M. Spinal cord metastasis of adenocarcinoma – case report. Cesk Slov Neurol N 2008; 71/104(5):583–587.
66. Villegas AE, Guthrie TH. Intramedullary spinal cord metastasis in breast cancer: clinical features, diagnosis, and therapeutic consideration. Breast J 2004; 10:532–535.
67. Kosmas C, Koumpou M, Nikolaou M, Katselis J, Soukoulis G, Markoutsaki N, Kostopoulou V, Gaglia A, Mylonakis N, Karabelis A, Pestasides D. Intramedullary spinal cord metastases in breast cancer: report of four cases and review of the literature. J Neuro-Oncology 2005; 71:67–72.
68. Constantini S, Miller DC, Allen JC, Rorke LB, Freed D, Epstein FJ. Radical excision of intramedullary spinal cord tumors: surgical morbidity and long-term follow-up evaluation in 164 children and young adults. J Neurosurg 2000; 93:183–193.
69. Cooper PR. Outcome after operative treatment of intramedullary spinal cord tumors in adults: intermediate and long-term results in 51 patients. Neurosurgery 1989; 25:855–859.
70. Fornari M, Pluchino F, Solero CL, Giombini S, Luccarelli G, Oliveri G, Lasio G. Microsurgical treatment of intramedullary spinal cord tumors. Acta Neurochir Suppl 1988; 43:3–8.
71. Mut M, Schiff D, Shaffrey ME. Metastasis to nervous system: spinal epidural and intramedullary metastases. J Neuro-Oncology 2005; 75:43–56.