

Chapter 43

Neoplastic Epidural Spinal Cord Compression



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Abstract Spinal metastasis is the most common type of neoplasia, where in autopsy investigations it has been shown that up to 70% of cancer patients present it (Klimo P Jr, Schmidt MH: *Oncologist* 9(2):188–196, 2004; Chamberlain MC: *Hematol Oncol Clin North Am* 26(4):917–931, 2012). Compression of the spinal cord, an extremely devastating scenario, and mainly caused by spinal metastases with extension to the epidural space, directly affects the quality of life of cancer patients, reaching 5–10% of patients with metastatic cancer (Helweg-Larsen S, Sorensen PS, Kreiner S: *Int J Radiat Oncol Biol Phys* 46:1163–1169, 2000). The thoracic and lumbar spine are the most commonly affected (Klimo P Jr, Schmidt MH: *Oncologist* 9(2):188–196, 2004).

Keywords Spinal cord compression · Oncologic emergency · Pain control

43.1 Introduction

Spinal metastasis is the most common type of neoplasia, where in autopsy investigations it has been shown that up to 70% of cancer patients present it [1, 2]. Compression of the spinal cord, an extremely devastating scenario, and mainly

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caused by spinal metastases with extension to the epidural space, directly affects the quality of life of cancer patients, reaching 5–10% of patients with metastatic cancer [3]. The thoracic and lumbar spine are the most commonly affected [1]. Pain is the most common initial symptom, and as the spinal cord injury progresses, the central nervous system (CNS) is compromised, and if left untreated the spinal cord injury becomes irreversible [4]. The management of neoplastic disease of the spine has changed significantly during the last decades. Advances include improvements in radiotherapy and chemotherapy therapies, and research has been improving our understanding of tumor biomechanics in the spine. Increasingly, the need for a surgical approach is diminishing, but in the scenario of tumor instability it is still the main therapy [5].

43.2 Epidemiology

More than 1.4 million new cases of cancer are diagnosed annually in the United States [6, 7]. Neoplastic Epidural Spinal Cord Compression (NESCC) affects on average 10–15% of patients diagnosed with spinal metastases [8]. The majority of patients with NESCC are over 50 years of age, however, cumulative incidence decreases over the years [4, 9]. The mean interval between cancer diagnosis and NESCC manifestation ranges from 6 to 12.5 months [4].

The most common sources of NESCC are breast cancer (20%), lung cancer (13%), lymphoma (11%) and prostate cancer (9%) [2, 10]. Fifteen percent of all NESCC is located in the cervical spine, 68% occurs in the thoracic spine and 16% in the lumbar spine [2]. The over-representation of the thoracic involvement reflects the large thoracic spine size, as well as the comparatively small diameter of the thoracic spinal canal. Breast and lung carcinomas tend to metastasize to the cervical and thoracic vertebrae, tumors of the prostate, colon, and pelvic areas have a predilection for the lumbar spine and sacral region [7, 8].

NESCC as a primary manifestation of a malignant neoplasm is more common in non-Hodgkin's lymphoma, myeloma, and lung cancer (especially the small cell variant), and such a characteristic is rarely seen in breast cancer, which tends to be later [11]. In the pediatric population, NESCC occurs, as an initial manifestation, more frequently than in adults, and includes neuroblastoma and sarcomas, followed by germ cell tumors and lymphoma [4, 12].

43.3 Pathophysiology

Figure 43.1 shows the anatomy of the spinal cord, associated structures and the location of metastatic lesions in these areas. These lesions usually first invade the epidural space, most often as direct extension of metastatic disease from the vertebral body.

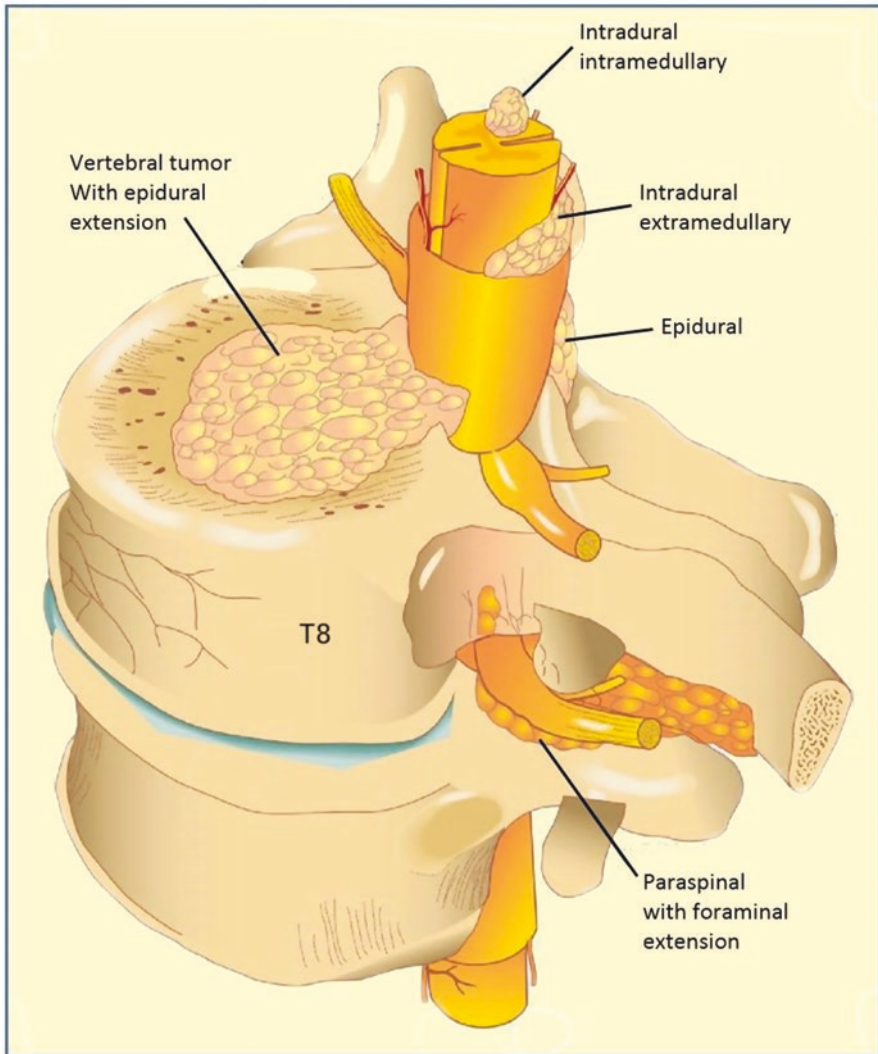


Fig. 43.1 Locations of metastatic lesions of the spine

Several factors contribute to the high incidence of metastatic deposition and growth in the vertebrae. These include the presence of the Batson epidural venous plexus with bidirectional flow and direct communication with the thoracic and pelvic venous system. In addition, the vertebrae contain vascular marrow (red marrow) unlike the bones of the peripheral skeleton [2]. RANKL (the main stimulator of bone resorption and formation / activation of osteoclasts) is overexpressed in bone metastases, whereas osteoprotegerin (OPG) serum levels (negatively regulate bone resorption by inhibition of osteoclasts) are decreased in patients with metastases bone [2, 13].

Pathologically, 3 stages of the ESCC are observed. Initially, axonal and white cord edema of the medullary cord is observed with preservation of the medullary vascular flow. Then mechanical compression of the marrow is increased due to worsening white matter edema and initial changes in vascular flow are seen. At the later stage, hemorrhages and necrosis of white matter are observed [14].

NESCC can be produced by direct mechanical compression of the medullary canal or root of the nerve by the tumor itself; by disruption of the vascular supply to the spinal cord by the tumor; or by direct vertebral compression or collapse due to pathological fracture (spine instability) [15, 16].

43.4 Clinical Evaluation

The most common presenting symptom in patients with metastases involving the axial skeleton is the back pain [4, 7, 17, 18]. This symptom is usually neglected due to high incidence of musculoskeletal pain not a carcinogen in common society. However, any back pain in a patient with cancer known to frequently seed to spine or epidural space should be considered of metastatic origin until proven otherwise.

Pain ensues when the richly innervated periosteum is involved (periosteal stretching and/or a local inflammatory process stimulates the pain fibers within the spinal periosteum). Three classic pain syndromes affect patients with spinal metastases: local, mechanical, and radicular pain [7]. Local pain is usually described by patients as a persistent. Mechanical pain is exacerbated by movement, activity, or the Valsalva maneuver. Radicular pain in the thoracic region is usually bilateral, whereas cervical and lumbar radiculopathies are unilateral [19]. Referred pain may mimic a radiculopathy. Especially with intraneural tumor spread, neuropathic features (allodynia, hyperpathia, hyperalgesia) may predominate [4].

Motor dysfunction is the second most common presenting complaint of patients with vertebral metastases. Occurs before sensory disturbance [20]. Typical early complaints are difficulty raising your legs, climbing stairs or getting up from a chair, by sensation of “heavy” legs [17, 18]. Due to the majority of the NESCC begin in the thoracic spine, most patients present with a paraparesis. Epidural progression of metastases to the upper lumbar spine results in conus medullaris syndrome with distal lower extremity weakness, saddle paresthesia, and bladder or bower dysfunction (autonomic symptoms).

Thoracic pain is less common than is pain originating from the cervical and lumbar regions, where degenerative disease is the more common precipitating cause of pain; thus pain in the thoracic region should raise a level of suspicion for to be oncologic.

Sensory disturbances typically occur in correlation with motor dysfunction both in location and time of onset. The level of hypesthesia is usually two to three segments below the metastatic lesion [18]. It is important to carry out a thorough questioning of patients with spinal metastases due to the neglect of early symptoms such as nocturia, pollakisuria, urinary loss, mild limb paresthesia or in band.

The table below (Table 43.1) summarizes the spinal cord syndromes according to their topography and symptoms.

Table 43.1 Topographic spinal cord syndromes

Clinical features	Spinal cord (above the conus medullaris)	Conus medullaris	Cauda equina (below the conus medullaris)
Evolution	Variable	Hyperacute	Subacute
Motor	Upper motor neuron	Upper and lower motor neuron disorder	Lower motor neuron
Sensory	Segmental with sacral sparing	Saddle	Dermatomal
Deep tendon reflexes	Increased	Increased or decreased depending on caudal extension of the lesion	Decreased
Incontinence	Late	Early	Late

Adapted from: Chamberlain MC. (2015) Neoplastic myelopathies. *Continuum (Minneapolis)*. 21: 132–145

43.5 Diagnosis

A recent study indicates that 62% of patients are ambulatory at the time of diagnosis [21, 22]. The mean time between the onset of symptoms and the definitive diagnosis is 3 months [18]. Neurologic examination must be the first step performed in this patient.

The presentation of a new symptom of back pain and/or neurological disorder in a cancer patient or in case of atypical pain in a non-oncological patient requires a more complex investigation, with more elaborate imaging exams than X-ray films [4].

Magnetic resonance imaging (MRI) is the most sensitive and the preferred method for early detection of NESCC [4, 7, 23, 24]. MRI provides a clear relationship between soft tissue and bone tissue, yielding accurate anatomic detail of bony compression or invasion of neural and paraspinal structures [24]. Therefore, accurately identifies and guides the physician about the exact location of the treatment performed on the patient, and furthermore, metastases can be distinguished from other pathologic processes (bacterial abscess, leptomeningeal carcinomatosis, intradural extramedullary tumors, inflammatory myelitis) [4, 25].

In patient who need a choice to MRI, one option is computed tomographic myelography. Computed tomography (CT) evaluates of the bone anatomy and the extent of the lesion within the bone. In this scenario, the benefit is greater if it is used

in conjunction with myelography in order to accurately determine the cord involvement, and being able to distinguish if caused by pathological fracture or tumor expansion [4, 7].

Bone scintigraphy is insufficient to assess the level of cord involvement. PET-CT cannot substitute for more detailed anatomic imaging techniques [4].

43.6 Treatment Guidelines

The primary goal of treatment is pain management and functional improvement. The expected practical outcome after therapy is largely dependent on pretreatment neurologic status. The three traditional mainstays of therapy have been corticosteroids, radiation therapy, and surgery.

Corticosteroids are the initial treatment in patients with suspected spinal cord compression, not only facilitate pain management but also reduce vasogenic cord edema and may prevent additional damage to the spinal cord from decreased perfusion. However, opioids are also usually required.

This treatment may require high doses of corticosteroids (dexamethasone – 4 mg every 6 h), which can lead to undesirable side effects [4, 26]. The intravenous application is made available to those who can not swallow. There are protocols with higher doses in the initial days of the symptoms (bolus of 100 mg followed by 96 mg divided into four doses for 3 days), but it remains unclear if their use leads to an improvement in neurologic recovery or preservation of motor function [27, 28].

The treatment options for patients with stable spinal disease include decompressive surgery, radiotherapy (RT), or both. In cases of instability of the spine, radiotherapy will not resolve the complication, and must be treated surgically with fixation or with percutaneous vertebroplasty (if there is no epidural disease) followed by RT. However, it is necessary to evaluate the stability of the spine using the SINS score (Fig. 43.2) [29]. Should be interpreted and conducted as follows: Score 13–18, spine unstable, patients should be nursed horizontally in bed, and a surgical approach considered; score 7–12, an indeterminate classification, possible impending instability, warrants surgical consultation; and score 0–6, stable spine.

The role of chemotherapy in this context should be used in very chemosensitive tumours and with presenting with stability of the spine. Solitary metastasis with indolent disease, may be candidates for attempted cure with en bloc resection (total spondylectomy) [30]. Radiotherapy alone if the tumour is very radiosensitive. But in most cases of stable spinal cord compression, the combination of decompression surgery followed by radiotherapy is preferable. Results in maintained ambulation in 94% treated with surgery and RT versus 74% for RT alone are observed in these patients [31].

The radiotherapy protocols consist of 5–10 applications of 3–4 Gy (total dose 30 Gy). There are some places that choose to perform higher daily doses (5 Gy) during a 3 days induction phase followed by daily fractions of 3 Gy over 5 days for consolidation [32]. Better local control and similar functional outcome, was

SINS Component	Score
Location	
Junctional (occiput-C2, C7-T2, T11-L1, L5-S1)	3
Mobile spine (C3-C6, L2-L4)	2
Semirigid (T3-T10)	1
Rigid (S2-S5)	0
Pain*	
Yes	3
Occasional pain but not mechanical	1
Pain-free lesion	0
Bone lesion	
Lytic	2
Mixed (lytic/blastic)	1
Blastic	0
Radiographic spinal alignment	
Subluxation/translation present	4
De novo deformity (kyphosis/scoliosis)	2
Normal alignment	0
Vertebral body collapse	
> 50% collapse	3
< 50% collapse	2
No collapse with > 50% body involved	1
None of the above	0
Posterolateral involvement of spinal elements†	
Bilateral	3
Unilateral	1
None of the above	0

Fig. 43.2 Classification system for spinal instability in neoplasia disease. SINS, spinal instability neoplastic score. *Pain improvement with recumbency and/or pain with movement/loading of spine. †Facet, pedicle, or costovertebral joint fracture or replacement with tumor. Adapted from: Fourny DR, Frangou EM, Ryken TC et al. Spinal Instability Neoplastic Score: an analysis of reliability and validity from the spine oncology study group. *Journal of Clinical Oncology* 2011; 29(22): 3072)

observed in long-course RT and it is generally reserved for those patients with better life expectancy.

Stereotactic radiosurgical may be an option for conventional RT, provides a higher radiation dose without exceeding the tolerance of the spinal cord, and is a good alternative for those who have progressed after RT or as adjuvant therapy after surgery [4].

The spinal cord decompression surgery is still a reason for intense discussions and deserves a more careful analysis. In selected patients, tumor resection has a greater functional benefit than irradiation (onset of neurological symptoms <48 h, younger patients, less radiosensitive tumors, no recent history of cancer, presence of pathological fracture causing compression, spine instability). Surgical morbidity is

considerable. This procedure includes resection of the affected vertebral body and implantation of stabilizing instrumentation [33].

It should be discussed on a case-by-case basis on the use of bisphosphonate in this scenario, since it can reduce skeletal-related events [34, 35].

Questions

1. The most common presenting symptom of spinal cord compression from tumor is:

- (a) Paresthesias.
- (b) Pain.
- (c) Bladder retention.
- (d) Weakness.

1. (b) Pain is the most common, early and consistent symptom in patients with metastatic spine disease.

2. The most effective surgical technique for spinal metastatic pathological fracture (in the correct clinical context) with spinal cord compression is:

- (a) Laminectomy.
- (b) Laminectomy and instrumented fusion.
- (c) Posterior and anterior decompression and stabilization.
- (d) Cement augmentation.

2. (c) When feasible, ventral and dorsal decompression with stabilization is ideal for the treatment of symptomatic pathological fractures, especially if kyphosis exists.

3. Man, 57 years old, presented with severe back pain and bilateral leg weakness for 3 days. Magnetic resonance imaging (MRI) of the spine reveals metastatic lesion in the vertebral body of T10 with significant spinal cord compression. What are the most likely primary tumors?

- (a) Lung cancer and breast cancer
- (b) Lung cancer and lymphoma
- (c) Breast cancer and lymphoma
- (d) Colon cancer and prostate cancer

3. (b) Although most patients with malignant medullary compression have a history of malignancy, about 20% develop this complication in the initial presentation. Breast cancer is the most common cause of this complication, but rarely occurs as an initial manifestation. The most common causes of malignant medullary compression in the presentation are lung cancer, non-hodgkin lymphoma, and multiple myeloma.

4. This patient was diagnosed with non-small cell lung cancer, what should be the initial measure taken for pain control?

- (a) Chemotherapy
- (b) Corticosteroids

- (c) Anti-inflammatory
 - (d) Opioids
4. (b) Corticosteroids act not only to control the pain, but also reduce vasogenic cord edema and may prevent further damage to the cord.
5. **A woman on follow-up for breast cancer, a hormonal receptor positive, using aromatase inhibitor 3 years ago, starts atypical back pain in the thoracic spine without improvement with common analgesics. What is the best exam to apply for in this context?**
- (a) Request column RX
 - (b) Request Bone Cintology
 - (c) Request Computed Tomography
 - (d) Request column MRI
5. (d) Although the other tests have a good sensitivity to investigate bone metastases, the ideal is to request MRI in this context due to a better evaluation of the spinal cord, is the most sensitive and the preferred method for early detection of compression cord medullary.
6. It is known that in the treatment of ESCC the use of corticosteroid is intensively used. It is a complication of prolonged use of corticosteroids:
- (a) Cardiomyopathy
 - (b) Polyneuropathy
 - (c) Gastric ulcer bleeding
 - (d) Renal failure
6. (c) Gastric intolerance is a frequent symptom of the use of corticosteroids, even for those who take short periods of treatment. Patients in use concomitant use of drugs such as non-hormonal anti-inflammatory drugs and anticoagulants, are at increased risk of bleeding digestive, as well as the presence of neoplasia malignant, elderly and previous history of digestive ulcer, being in these cases indicated use of prophylactic drugs.
7. **Patient, 50 years old, with metastatic prostate cancer to the lumbar spine, initiates frame of weakness of lower limbs and symptoms of shocks during sneezing and coughs. Look for medical assistance, which is the best option below the next steps:**
- (a) Thorough evaluation of the lumbar spine and immediate treatment with neurosurgery if the spinal cord compression is confirmed.
 - (b) Thorough evaluation of the lumbar spine and immediate treatment with local radiotherapy if the spinal cord compression is confirmed.
 - (c) Thorough evaluation of the lumbar spine, and outpatient treatment with physiotherapy and corticosteroids if the spinal cord compression is confirmed.
 - (d) Thorough evaluation of the lumbar spine, and treatment with opioids and local radiotherapy if the compression of the spinal cord is confirmed.

7. (a) The approach with neurosurgery in this scenario is preferable since it is a young patient with a long life expectancy and the response to local radiotherapy does not overcome local surgical treatment aiming at quality of life.
8. **About malignant spinal cord compression is correct to affirm:**
- (a) The evaluation of the medullary stability is performed only by physical examination and patient complaints, with no need for complementary exam.
 - (b) It is important to evaluate the stable spinal disease according to the SINS score.
 - (c) The use of bisphosphonate is essential in the control of pain and follow-up of these patients.
 - (d) The best treatment for spinal instability is immediate radiotherapy.
8. (b) There is a score for spinal instability neoplastic score (SINS), which should be used for therapeutic decision. Score 13–18, spine unstable, score 7–12, an indeterminate classification, score 0–6, stable spine. In addition to the clinical evaluation, it is necessary to perform spinal imaging tests for this score.
9. **The resection en bloc is the treatment of choice for which of the following tumors in the spine?**
- (a) Lung metastasis
 - (b) Prostate metastasis
 - (c) Lymphoma
 - (d) Sacral chordomas
9. (d) Block resection is advocated for some solitary metastatic lesions in the spine. In this case wide en bloc spondylectomy is the treatment of choice for cases of chordoma or chondrosarcomas.
10. **What is the most frequent location of Epidural Spinal Cord Compression (ESCC)?**
- (a) Sacral spine
 - (b) Cervical spine
 - (c) Thoracic spine
 - (d) Lumbar spine
10. (c) Cervical spine is responsible for 15% of the ESCC presentation, 68% occurs in the thoracic spine and 16% in the lumbar spine. The over-representation of the thoracic involvement reflects the large thoracic spine size, as well as the comparatively small diameter of the thoracic spinal canal.
11. **Is it an option for the surgical treatment of spinal cord decompression when this is not possible?**
- (a) Local radiotherapy at the dose of 30Gy.
 - (b) Stereotactic radiosurgical.

- (c) High doses of corticosteroids
 - (d) A and B are correct.
11. (d) When surgery is not an option for the patient, radiotherapy should be the treatment of choice, and the stereotactic radiosurgical may be an option for conventional RT, provides a higher radiation dose without exceeding the tolerance of the spinal cord, and is a good alternative for those who have progressed after RT or as adjuvant therapy after surgery.
12. **Possible differential diagnoses to malignant medullary compression:**
- (a) Leptomeningeal carcinomatosis
 - (b) Inflammatory myelitis
 - (c) Bacterial abscess
 - (d) All are correct
12. (d) There are many benign causes of back pain and they should be excluded from possible malignancies, metastases can be distinguished from other pathologic processes (bacterial abscess, leptomeningeal carcinomatosis, intradural extramedullary tumors, inflammatory myelitis).
13. **It is not related to the pathophysiology of spinal cord compression:**
- (a) Axonal and white cord edema of the medullary cord is observed in at the onset of symptoms.
 - (b) Presence of the Batson epidural venous plexus in the spine.
 - (c) RANKL is deleted in bone metastases, whereas osteoprotegerin serum levels are overexpressed in patients with metastases bone.
 - (d) Hemorrhages and necrosis of white matter are observed at the later stage.
13. (c) RANKL (the main stimulator of bone resorption and formation / activation of osteoclasts) is overexpressed in bone metastases, whereas osteoprotegerin (OPG) serum levels (negatively regulate bone resorption by inhibition of osteoclasts) are decreased in patients with metastases bone.
14. **On the use of corticosteroids in the treatment of malignant medullary compression, which is the most used dosage of this medication:**
- (a) Dexamethasone – 4 mg every 12 h.
 - (b) Dexamethasone – 4 mg every 6 h.
 - (c) Dexamethasone bolus of 100 mg followed by 96 mg divided into four doses for 3 days.
 - (d) Dexamethasone – 8 mg every 6 h.
14. (b) This treatment may require high doses of corticosteroids (dexamethasone – 4 mg every 6 h), which can lead to undesirable side effects. There are protocols with higher doses but it is not yet clear whether there is a greater functional benefit in its use.

15. What are the clinical criteria for the best benefit to indicate the surgical treatment of spinal decompression?

- (a) Pathological fracture.
- (b) Poorly radiosensitive tumors (ex: melanoma).
- (c) Paresthesia of limbs in less than 48 h.
- (d) A, B and C are correct.

15. (d) In selected patients, tumor resection has a greater functional benefit than irradiation (onset of neurological symptoms <48 h, younger patients, less radiosensitive tumors, no recent history of cancer, presence of pathological fracture causing compression, spine instability).

Clinical Case

A 28-year-old man, with no pathological history, with clinical neoplasm of the testis. He reported the presence of a nodule in the left testicle, 5 months of evolution, not associated with trauma or fever. Three weeks later, he presented lumbar pain, type of slings, of moderate intensity and not disabling, without irradiation. With no other complaints, including motor or sensory changes.

On clinical examination, ECOG 0. On inspection of the genital tract was scrotal dysmorphism by enlargement of the left scrotal sac, 8 cm in diameter of stone consistency. He did not present palpable adenomegalias or alterations to the neurological examination. In USG scrotal it confirmed the presence of a solid, heterogeneous mass in the left testicle. Serum values of the tumor markers were AFP (4500 ng/ml), β -HCG (310 mUI/ml) and DHL (2030 U/L). Held a computed tomography (CT) thoraco-abdominal-pelvic for staging showed that pulmonary nodular lesions bilateral, abdominal, inguinal and mediastinal adenopathies.

He underwent left radical orchidectomy. The anatomopathological examination confirmed the presence of a germ cell tumor of non-seminomatous mixed pattern.

Three days after surgery was admitted for paresthesia of lower limbs, associated with low back pain with bilateral limb irradiation and abdominal wall, accompanied by urinary retention – less than 24 h of evolution. An MRI of the spinal axis showed changes in signal strength in the vertebral body of T12, of almost normal morphology, and a soft tissue component with space extension antero-lateral epidural, of L2-L4, corresponding to a possible compression of the spinal cord.

Corticosteroid therapy, analgesia and bladder catheter were started. Chemotherapy (QT) was urgently instituted, BEP scheme every 21 days, of which it fulfilled 4 cycles. There was progressive neurological improvement with resumption of ambulation after 2 cycles of chemotherapy and functional recovery of the urethral sphincter to the third cycle. MRI of the vertebral axis, 1 month after the onset of QT, demonstrated the disappearance of soft tissue mass within the medullary canal.

It continued performing motor rehabilitation, with progressive improvement of its functionality. Follows oncological follow-up and at the moment with negative markers.

Comments

The present case report describes a clinical situation with medullary compression, which requires of an emerging intervention. MRI of the vertebral axis (sensitivity 0.44–0.93, specificity 0.90–0.98) constitutes the best examination to clarify the level and cause of the syndrome, according to published systematic reviews (Penas-Prado M et al).

Symptomatic treatment is of great importance for the control of pain, physical rehabilitation and prevention of intercurrents. The etiologic treatment associates the accomplishment of corticoterapia, the chemotherapy, radiotherapy and/or surgery.

In this case, due to tumor chemosensitivity and in the absence of instability the early onset of chemotherapy was essential. Its efficacy in the treatment of spinal cord compression in patients with germ cell tumors has been described in series of cases since 1977; the largest series available (study retrospective; 1984–2009) included 29 patients with compression medullary (Grommes C et al., Cancer, 2011).

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