Spinal pain in cancer patients: differential diagnosis

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Learning objectives

The purpose of this educational presentation is to:

- understand the different causes of vertebral pain with an anatomical recall and to present the various physiological assumptions
- illustrate the various aspects of metastatic infiltration of the spine and to make the differential diagnosis
- learn how to differentiate benign from malignant vertebral body compression fractures
- emphasize the importance of an accurate diagnosis to avoid misleading therapy

Background

Many conditions may lead to spinal pain, including spinal and extra spinal lesions. Up to 75% of cancer patients will experience pain caused either by the tumor or the treatment, but pain may be unrelated to cancer. Pain related to cancer presents as neuropathic, visceral and nociceptive syndromes. Pain related to treatment is caused by chemotherapy as well as radiation therapy and surgery [1].

Bone metastases occur in many cancers, especially at advanced stages of the disease as seen on autopsy series, although its prevalence depends on the primary tumor [2, 3]. Several publications found bone metastasis to be the leading cause of cancer-related pain. Spine is a very common location of tumorigenic bone-related pain [3].

Bone-metastasing cancer cells alter the bone remodeling process, which mainly enhances the osteoclastic activity. In those cases tumoral cell factors stimulate the immune system which releases osteoclastic factors, such as as tumor necrosis factor, interleukin 1, protaglandins. However some cancers, such as prostate cancer, stimulate osteoblastic activity [3].

Bone innervation is located in the periosteum and along the blood vessels entering the bone. Pain mechanisms involve (micro) fractures, stretching of the periosteum, bony mechanical stress, and nerve entrapment (3). Experimental models suggest that tumorigenic pain is mediated by different transmitters rather than inflammatory pain and neuropathic pain. Cytokines activate pain receptors. Disproportion exists between bone involvement and tumorigenic bone-related pain [4].
Back pain is also associated to spinal instability and is mechanical in that case (patient with pain relief when lying still). A surgical stabilization is then required increasing morbidity and mortality [2].

**Findings and procedure details**

In our institution, we have retrospectively analyzed different causes of spinal pain in cancer patients, from 2008 to 2014, on MR and CT.

Most causes of back pain were associated to metastatic conditions. Nevertheless, cancer patients may develop pain due to other pathologies, both common and uncommon.

A. Metastatic causes

1. **Cortical involvement** causes non positional and permanent pain and does not respond to classical painkiller medication.

   Case 1: neoplasm of the uterus with lumbar pain. Abdominal CT demonstrates a paravertebral metastatic mass involving the cortical and the lateral part of a lumbar vertebral body. Fig. 1

2. **Intraosseous infiltration** may be painful depending on the importance of the metastatic infiltration and/or of the cortical extent.

   Case 2: 55 year old patient with breast cancer, asymptomatic but positive on PET. MRI also suggests metastases, confirmed later. Fig. 2, 3, 4.

3. **Epidural extension**: any epidural invasion may be responsible for pain due to a rich local innervation. Rapid diagnosis is important considering the risk of spinal cord compression and as an early treatment is recommended.

   Case 3A: osteolytic metastasis involving posterior wall and bulging into the spinal canal. Fig. 5

   Case 3B: large lytic metastasis of the right vertebral pedicle, extending to the posterior arch and the vertebral body but also the epidural space and the right vertebral foramen. The epidural invasion is clearly visible due to the disappearance of the epidural normal fat laterally and anteriorly. Fig. 6
Case 4: osteoblastic metastatic prostatic adenocarcinoma with epidural infiltration. **Fig. 7**

4. **Vertebral compression fracture**: responsible for acute back pain and often associated with a trauma, even minor. The loss of vertebral trabeculae due to a lytic or a mixed metastasis is the main factor leading to a vertebral compression.

Case 5: patient with lung cancer and acute dorsal pain. On MR, T1 sagittal sequence demonstrates a dorsal vertebral fracture. CT is more accurate in detecting lytic component and in confirming pathological compression fracture. **Fig. 8, 9, 10**

Case 6: patient with cancer and a unique lesion on L1. The compression fracture is associated to vertebral body heterogeneity and to heterogeneous enhancement after IV gadolinium injection. These criteria are typically metastatic. **Fig. 11, 12**

Case 7: diffuse or multifocal metastatic infiltration associated to vertebral compression is not a differential diagnosis problem. **Fig. 13, 14, 15**

Case 8: importance for differential diagnosis to get a T1 pre-contrast sequence on MR as metastases can be difficult to detect only after a T1 post-contrast sequence. **Fig. 16, 17**

5. **Meningeal carcinomatosis**: provoke back pain with weakness and, in more advanced stages, headache, confusion, paresthesias and/or paresias. Most frequent cancers associated with meningeal carcinomatosis originate from breast, lung and melanoma.

Case 9: patient with breast cancer and sciatica. MRI reveals no bone metastasis but multiple leptomeningeal nodular and linear enhancements on T1 with IV contrast. **Fig. 18, 19, 20**

6. **Intradural intramedullary metastasis**: back pain, walking disorders especially when conus medullaris is affected. Breast, lung cancers and melanoma are also the main originators.
Case 10: patient with breast cancer and known bone metastasis associated to a chronic back pain, developing walking disorders. The conal lesion is not visualized on T1 sagittal sequence without IV contrast injection. **Fig. 21, 22, 23, 24, 25**

7. **Extraspinal soft tissue mass**: often presented as a clinical palpable mass with or without pain but occasionally associated only with discomfort or pain (essentially in the lumbosacral area associated with fat importance).

Case 11: patient after 8 years of breast neoplasm with low back pain. MRI demonstrating a soft tissue retrosacral mass on T1 and T2. Biopsy revealed a first metastasis of breast cancer. **Fig. 26, 27**

B. Non metastatic causes: differential diagnosis

1. Case 12: acute pain in a cancer patient without known metastasis. On MRI, L2 is moderately compressed and diffusely infiltrated. A metastatic involvement was suspected but enhancement appears homogeneous and there a few older vertebral compression are visible. Moreover, the spine has a diffuse hyperintense signal on T1. These signs are typically associated to osteoporosis. CT confirmed absence of lytic or blastic lesion. **Fig. 28, 29, 30**

Case 13: patient suspected to have bone metastases according multifocal spine hotspots on bone scintigraphy. MRI revealed multiple vertebral dorsal compression fractures with a band alteration signal beneath the superior vertebral endplate. This band enhances strongly after IV injection contrast. These MRI signs are also typical of recent post-traumatic compression fractures which were also confirmed by the patient. **Fig. 31, 32, 33, 34.**

**Vertebral compression fracture and osteoporosis** are frequent in cancer patients mainly due to age, menopause, diet, endocrine disorders,... or medication and, more particularly, corticosteroids but also drugs used in cancer treatment like aromatase inhibitors, methotrexate,... or radiotherapy. Of course, trauma can responsible for vertebral fracture, therefore importance of anamnesis.

An inaccurate diagnosis can have dramatic consequences as unnecessary irradiating therapy or a heavier medical treatment increases patient discomfort.

Case 14: acute dorsal pain in a male patient treated for a breast cancer. A diagnosis of metastatic compression fracture associated to a carcinomatous epiduritis had been
given based on the MRI. This was an incorrect diagnosis for at least two reasons: homogeneous enhancement of the vertebral compressed body, except for an irregular band like after IV gadolinium contrast injection, diffuse hyperintense signal of dorsal and lumbar vertebrae demonstrating an important fatty component. All these signs are typically in favour of a fracture associated to osteoporotic changes due to corticosteroid therapy. Unfortunately, the patient received radiotherapy. A few months later, a spine MRI control demonstrated an increase of the signal intensity on T1 of the vertebrae included in the irradiated field. Furthermore, an accentuation of the previous compressed vertebral body and the appearance of new vertebral compression fractures in the irradiated zone caused deterioration in the patient’s condition. **Fig. 35, 36, 37**

**Table 1:** differential diagnosis between osteoporotic and metastatic vertebral compression fracture.

<table>
<thead>
<tr>
<th>Osteoporosis</th>
<th>Metastasis</th>
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<tr>
<td>Typical signs:</td>
<td>- presence of other metastatic lesions</td>
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<tr>
<td>- homogeneous enhancement on T1 after IV contrast injection</td>
<td>- diffuse heterogeneous signal on T1 and/or on T2</td>
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<tr>
<td>- band like image hypointense on T1 and hyperintense on T2</td>
<td>- heterogeneous enhancement</td>
</tr>
<tr>
<td>- hyperintense signal on T1 of the adjacent vertebral bodies</td>
<td>- lytic component visible on CT</td>
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<td>Atypical but orienting signs:</td>
<td>- infiltration of the posterior arch</td>
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<tr>
<td>- absence of infiltration of the posterior arch</td>
<td>- nodular infiltration of soft tissues</td>
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<tr>
<td>- diffuse and homogeneous infiltration of soft tissues</td>
<td>- asymmetric aspect of the vertebral compression in frontal plane</td>
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<tr>
<td>- symmetric aspect of the vertebral compression in frontal plane</td>
<td></td>
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<tr>
<td>- gas formation inside the vertebral compression</td>
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A non posttraumatic vertebral compression fracture of the cervical spine is always pathological and is never due to osteoporosis.

2. **Case 15:** patient referred to radiotherapist for acute cervical pain due to cervical spine metastasis. He underwent surgery for cancer of the pharynx and has a local paraoesophageal recurrence treated by chemotherapy. On MR, there is an infiltration
of a vertebral body. CT shows a heterogeneous vertebral body but multiplanar reconstructions demonstrate that two vertebral bodies were involved as well as the intervertebral disc. These images oriented diagnosis for a spondylodiscitis. Patient avoided radiotherapy, received antibiotherapy and evolved favorably. \textbf{Fig. 38, 39, 40}

\textbf{Spondylodiscitis} may occur in cancer patient due to their weakness and to their immunodeficiency according to different tumors and/or treatment. A rapid diagnosis is important for an adequate support.

3. Case 16: patient with breast carcinoma referred for acute pain irradiating in a lower limb. On MR, there were few nodular metastases but overall, an intracanalar mass at L3-L4 level corresponding to a large extruded herniated disc. \textbf{Fig. 41}.

\textbf{Disc herniation} is a common spinal problem that can also occur in a cancer patient. Symptoms are acute and, most of the time, circumstances of occurrence are evocative but can be difficult to diagnose sometimes in a patient with chronic pain.

4. Case 17: 59 year old patient with breast cancer complaining of chronic low back pain. On a CT, bilateral isthmolysis of L5 was found and concluded to be the reason for the pain. Nevertheless, an MRI was performed that demonstrated an anterolisthesis of L5 due to the bilateral isthmolysis of L5 but also metastatic infiltration of L2, L5, S1 and S2. \textbf{Fig. 42, 43}.

\textbf{Isthmolysis and anterolisthesis} are responsible for chronic lower back pain. Generally, these are found in much younger patients. When a patient with cancer and chronic pain notices a change and an abnormal increase of pain, even when there is an obvious cause on CT or on plain radiography, it is necessary to investigate with an MRI for a more accurate for diagnosis of diffuse metastatic infiltration.

\textbf{Degenerative spine} is also responsible for chronic pain (see also case 2). Generally, the patient and his doctor are aware of this condition. An imaging is necessary, only if symptoms change rapidly with presence of constant pain which does not reduce by inflammatory treatment and/or broken sleep and/or development of paresthesia or muscular weakness. The development of an arthrosynovial cyst from a degenerative interapophyseal posterior joint can increase a chronic low back pain.

5. Case 18: patient with a prostatic cancer who received radiotherapy due to diagnosis of a metastasis, complaining about lower back pain. MRI demonstrated a vertebral compression fracture of L5 with heterogeneous signal on T1 and T2 sequences and a persisting heterogeneous signal after IV contrast injection of the vertebral body L5 and
of the sacrum. A review of this case proved that the presumed metastatic infiltrations of the sacrum and the iliac wings were in fact stress fractures. The radiotherapy resulted in osteonecrosis of the sacrum and of L5 and precluded healing of the sacral fractures. Follow up confirmed osteonecrosis. Fig. 44, 45, 46, 47

Stress fractures occur frequently in the pelvis and especially in the sacrum and the iliac wings due to osteopenia caused by different anticancer treatments or radiotherapy. Diagnosis is easy to do by using multiplanar reconstructions on CT, showing a band like appearance surrounded or not by sclerosis. Rest and a adequate medical treatment are sufficient for recovery. Radiotherapy blocks fracture’s healing and increases the risk of osteonecrosis.

Osteonecrosis is a complication found after radiotherapy or after some medical treatments. It is important to differentiate osteonecrosis from metastasis in order to avoid useless and heavy therapies and to prevent complications. It is difficult to diagnose on CT without a fracture associated. On MRI, a central heterogeneous aspect on T1 and T2 of a vertebral body with a poor enhancement and a persisting heterogeneity after IV contrast injection must call osteonecrosis to mind.

6. Case 19: 77 year old patient with prostate cancer and diffuse osteoblastic bone metastasis was admitted for acute lower back pain radiating to the right leg. He was previously treated for a left sided carcinomatous epiduritis at L3. A lumbar CT with IV contrast injection was performed. It did not demonstrate any epiduritis but revealed a dissected aorto-iliac aneurysm. Patient was rushed to the operating room but died during surgery. Fig. 48, 49.

Aneurysm (with or without dissection), renal colic, pancreatitis may be responsible for acute dorsal, lumbar or pelvic pain. A good clinical examination is necessary before asking for any further examination.

7. Case 20: 77 years old patient with a history of breast cancer considered in complete remission hospitalized for thoracolumbar diffuse pain. On MR, there was a diffuse signal heterogeneity of the spine and a few vertebral compression fractures. MRI aspect and clinical evolution were not typical for metastatic infiltration. Biological tests attested a multiple myelome. Fig. 50, 51

Multiple myelome or other cancers must be suspected in case of discordance in the evolution of the disease and/or when imaging is not typically correlated to the previous disease. In these cases, biology and/or biopsy must be performed to confirm diagnosis.
Benign lesions such hemangioma can be painful when they are large and/or complicated by compression fracture. In elderly patients, moderate pain can be associated with Paget disease.

Images for this section:

Fig. 1: Case 1: Axial CT. Metastatic mass eroding vertebral body.
**Fig. 2:** Case 2: Pet image. Metastasis(arrow)

**Fig. 3:** Case 2: Sagittal T1 sequence. Nodular hypointense signal in L3: metastasis
**Fig. 4:** Case 2: Sagittal T1 sequence after IV injection contrast. Enhancement of the metastasis.
**Fig. 5**: Case 3A: Axial CT. Osteolytic metastasis involving posterior wall and bulging into the spinal canal
Fig. 6: Case 3B: MRI. Axial T1 sequence after IV contrast injection.
Fig. 7: Case 4: Axial CT: osteoblastic metastasis with epidural blastic infiltration
Fig. 8: Case 5: Sagittal T1 sequence. Hypointense signal of the vertebral compression fracture.
**Fig. 9:** Case 5: Sagittal reconstruction CT. Lytic lesion confirming metastatic hypothesis.

**Fig. 10:** Case 5: Axial CT. Lytic component and soft tissue infiltration.
**Fig. 11**: Case 6: Sagittal T1 sequence. Signal heterogeneity of the compressed vertebral fracture of L1.
Fig. 12: Case 6: Sagittal T1 sequence after IV contrast injection. Heterogeneous enhancement of the metastatic vertebral compression fracture.
Fig. 13: Case 7: Sagittal T1 sequence. Multiple metastases and compression fractures.
Fig. 14: Case 7: Sagittal STIR sequence. Multiple metastases and compression fractures.
Fig. 15: Case 7: Sagittal reconstruction CT. Multiple metastases and compression fractures.
**Fig. 16:** Case 8: Sagittal T1 sequence after IV contrast injection.
**Fig. 17:** Case 8: Sagittal T1 sequence without IV contrast injection.
Fig. 18: Case 9: Sagittal STIR sequence.
Fig. 19: Case 9: Sagittal T1 sequence. No evidence of metastasis.
**Fig. 20:** Case 9: Sagittal T1 sequence after IV contrast injection. Multiple foci of meningeal carcinomatosis in the spinal canal.

![Image of Case 9](image)

**Fig. 21:** Case 10: Sagittal STIR sequence. Bone metastases. Abnormal signal in the conus medullaris.
Fig. 22: Case 10: Sagittal T2 sequence. Bone metastases. Abnormal signal in the conus medullaris
**Fig. 23:** Case 10: Sagittal T1 sequence. Bone metastases.
**Fig. 24:** Case 10: Sagittal T1 sequence after IV contrast injection. Nodular enhancement in the conus medullaris due to intramedullary metastasis.
**Fig. 25**: Case 10: Sagittal fat suppressed T1 sequence. Intramedullary metastasis (white arrow)
**Fig. 26:** Case 11: Sagittal T2 sequence. Important hyperintense and heterogeneous signal of a retro-sacral mass
Fig. 27: Case 11: Sagittal T1 sequence. Hypointense signal of the retro-sacral mass.
Fig. 28: Case 12: Sagittal T1 sequence. Hypointense signal of L2 associated to a vertebral compression fracture.
Fig. 29: Case 12: Sagittal T1 sequence after IV contrast injection. Homogeneous enhancement of the vertebral compression fracture of L2.

Fig. 30: Case 12: Axial CT. Recent fracture (arrows)
Fig. 31: Case 13: Sagittal SPECT image. Multiple dorsal spots.
Fig. 32: Case 13: Sagittal STIR sequence. Multiple vertebral compression fractures associated to a band like hyperintense signal under the endplates (arrows)
Fig. 33: Case 13: Sagittal T1 sequence. Multiple vertebral compression fractures associated to a band like hypointense signal under the endplates.
**Fig. 34:** Case 13: Sagittal T1 sequence after IV contrast injection. Multiple vertebral compression fractures associated to a band like enhancement under the endplates.
**Fig. 35:** Case 14: Sagittal T1 sequence. Dorsal vertebral body compression fracture. Diffuse hyperintense signal of the other vertebral bodies.
**Fig. 36:** Case 14: Sagittal T1 sequence after IV contrast injection. Homogeneous enhancement except for an irregular band like image. Typical for osteoporotic fracture.
**Fig. 37:** Case 14: Sagittal T1 sequence. Few months after radiotherapy, the fatty component increased in the irradiated field (between arrows). Appearance of new vertebral compression fractures.

**Fig. 38:** Case 15: Axial CT. Heterogeneous vertebral cervical body suspected to be metastatic.
Fig. 39: Case 15: Coronal T1 sequence. Cervical spine suspect infiltration (thin arrow). Tumor recurrence (large arrow)

Fig. 40: Case 15: Coronal reconstruction CT. Two vertebral bodies are concerned. Disc space appears narrow with irregular and eroded adjacent endplates.
**Fig. 41:** Case 16: Sagittal T1 sequence. Small metastatic lesions (thin arrows) and large extruded disc herniation (large arrow).

**Fig. 42:** Case 17: Axial CT. Bilateral isthmolysis of L5. Absence of visible metastasis.
**Fig. 43:** Case 17: Sagittal STIR sequence. Multiple metastatic infiltrations. Antelishment of L5
**Fig. 44:** Case 18: Sagittal STIR sequence. Abnormal infiltrations of L5 and sacrum with compression fracture of L5.
**Fig. 45:** Case 18: Sagittal T1 sequence. Heterogeneous signal in L5 and sacrum.
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**Fig. 47:** Case 18: Axial CT. Fractures of the sacral wings (red arrows) with heterogeneous aspect of underlying sacral bone.
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**Fig. 50:** Case 20: Sagittal STIR sequence. Diffuse mild heterogeneous signal of all vertebral bodies.
Fig. 51: Case 20: Sagittal T1 sequence. Diffuse mild heterogeneous signal of all vertebral bodies.
Conclusion

In cancer patients, pain is mainly due to the different aspects of the metastatic involvement such as: the epidural invasion, the meningeal carcinomatosis or the intramedullary metastasis which can have dramatic consequences if not rapidly diagnosed and treated.

Acute pain in a patient with known metastatic disease is often due to a vertebral compression fracture.

Nevertheless, we have to keep in mind that cancer patients can develop also other pathologies unrelated to their cancer or indirectly related to their treatments. Anamnesis, good clinical investigation and evolution of the disease are the clues for adequate and rapid support.

Personal information

References

6. Finucane L. Metastatic disease masquerading as mechanical low back pain; atypical symptoms which may raise suspicion. Man Ther. 2013 Dec;18(6):624-7