

# Differential diagnosis of primary malignant bone tumors in the spine and sacrum. The radiological and clinical spectrum

## Minireview

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### Received

Although primary malignant tumors of the spine and sacrum are described in all orthopedic textbooks, it is still remarkable how little attention is paid to differential diagnosis of persisting lower back pain and how to detect in special the underlying tumor disease. Chordoma, osteosarcoma, chondrosarcoma, plasmacytoma, lymphoma and Ewing's sarcoma, their radiological manifestation, age distribution and preferred location in the spine and sacrum are reviewed and discussed.

**Keywords:** primary malignant bone tumors, chordoma, osteosarcoma, chondrosarcoma, plasmacytoma, lymphoma, Ewing's sarcoma

Primary malignant tumors of the spine are relatively rare and occur 40 times less than skeletal metastases. The most common primary malignant tumors of the spine and sacrum are chordoma, osteosarcoma, plasmacytoma, multiple myeloma, lymphoma and Ewing's sarcoma. Because of the wide variety of primary malignant lesions occurring in the spine they can pose diagnostic and therapeutic challenges. Malignant bone tumors of the spine, similar to tumors of other locations, show typical manifestation sites and age distribution. Whereas the region of the body affected by the tumor stayed the same, age distribution shifted to earlier decades in many diseases. Physicians should be aware of the characteristics of primary malignant bone tumors and include them in their differential diagnosis.

**Clinical presentation.** Most patients with malignant lesions of the cervical and lumbar spine complain of local or radicular pain of the affected area [1], and 4% of patients with malignant tumors of the spine are misdiagnosed and mistreated with disc herniation or similar diagnoses [2]. Especially in children the diagnosis of disc herniation should arouse suspicion as children rarely suffer from this condition [3].

Neurological deficits arise from pressure on the spinal cord or nerve roots by the tumor or compression of the bone due to pathological fractures [4]. Scoliosis caused by bone destruction and muscular tension can be seen in malignant bone lesions and typically shows no rotation or wedging of the vertebra.

In malignant tumors of the spine especially in lymphoma, myeloma and Ewing's sarcoma, systemic signs such as weight loss, fever, fatigue, anorexia, cachexia and constipation may be present. Chordoma of the sacrum can lead to constipation caused by a local mass.

### Diagnosis

**Radiological Findings.** Most tumors of the spine express characteristic features on imaging studies. Therefore plain radiographs of high quality in two planes in a standing position are essential.

The osteolytic or osteoblastic appearance, location within the vertebra, presence and pattern of calcification and involvement of adjacent intervertebral discs are all important criteria to narrow down the differential diagnoses.

Malignant lesions often destroy the architecture of the vertebral bodies with loss of vertebral body height. Slow growing malignant and benign tumors can cause cortical scalloping ex-

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pansion rather than complete destruction. Especially in the cervical spine, tumors located in the anterior part of the vertebral body are more likely to be malignant than lesions involving the posterior region. Tumors arising in the posterior vertebral body are osteochondroma, osteoid osteoma and osteoblastoma. As the exception proves the rule malignant tumors such as chondrosarcoma can occur posteriorly as well [5,6].

**Magnetic Resonance Imaging (MRI), Computed Tomography (CT).** The MRI shows the extent and nature of the tumor and MRI has a high soft tissue resolution giving an impression of the extraosseous extent of the tumor [7]. More recently, MRI has become accepted to be the standard imaging modality in diagnosing tumors of the spine. It provides the advantage of viewing the images in axial, sagittal, coronal and oblique planes, which can be advantageous for surgical planning.

A disadvantage of MRI is the difficulty of distinguishing osteoporotic fracture from pathological fracture caused by destruction of the bone by malignant tumor. In both cases hematoma and edema of the bone marrow are seen, so that compression of the osteoporotic bone can simulate tumor. Advanced MR-techniques such as diffusion-weighted imaging (DWI) help to distinguish between benign and pathological fractures. Another handicap of MRI is the so-called "flare phenomena" which was found studying osteoblastoma, osteoid osteoma and eosinophilic granuloma; the inflammatory response of the surrounding soft tissue simulates a more aggressive tumor than actually exists [8].

CT scan is used to get information about the destruction of bone and the loss of stability.

**Scintigraphic findings.** When plain radiographs are normal, technetium bone scan can be helpful in revealing an osseous lesion [9]. It is non-specific but highly sensitive method that enables evaluation of the entire skeleton. However, differentiation between benign and malignant tumors is often not possible. Wherever new bone is being formed a positive uptake is seen, so that the differential diagnosis of a positive scan should include infection, fracture and inflammation. In solitary plasmacytoma, multiple myeloma, metastases of hypernephroma, and, occasionally in chordoma false negative, "cold", technetium bone scans are reported [10].

**Biopsy techniques.** As in tumors of other locations one has to be careful not to contaminate by surrounding tissue when taking biopsies. There are two different types of biopsies, needle and open biopsy [11,12,13]. The access of the needle biopsy should be planned according to the subsequent resection of the tumor and the most direct access should be used. It is important to obtain a sufficient tissue sample. Whenever needle biopsy is not possible, open biopsy has to be performed.

**Treatment.** Radical resection is the surgery of choice [14] in most of the malignant tumors in combination with (neo-) adjuvant chemotherapy. Adjuvant radiotherapy may be also useful in many cases [15,16,17].

**Characteristics of malignant tumors of the spine.** In table 1, described tumor types with typical location in the spine, age distribution and radiological appearance are summarized.



**Fig. 1. Chordoma. (MRT T1-weighted) reveals an intermediate signal intensity with lobulation with a peripheral fibrous pseudocapsule.**

**Chordoma.** Chordoma (Fig.1) is a rare malignant tumor, which arise from the remnants of embryonic notochord. These tumors are slow growing lesions that affect males more likely than females (2:1). There are two age peaks, the first at the age of 10 to 20 years, the second between the fifth and seventh decade. About 50 % are found in the sacrococcygeal region, 30% in the clivus. The remaining 20% are spread all over the cervical, thoracic and lumbar vertebrae and few other ectopic sites [18]. Chordomas are locally aggressive but they are slow to metastasize. The incidence of metastases varies from 5% to 40%. They are found as early as 1 year and as late as 10 years after diagnosing the pri-

**Table 1. Malignant tumors of the spine and sacrum**

Tumor; Age (yrs) ratio; Incidence male/ female; Typical location; Radiological appearance

1. **Chordoma** 10-20; 50-70; 2:1 50% sacrococcygeal Osteolytic lesions in multiple segments
  1. 30% Clivus, little tumor calcification
  2. 20% entire spine, large anterior mass
2. **Osteosarcoma** 10-20 1:1 anterior vertebral osteoblastic or osteolytic lesions or a mixture of both; 50+ body, pedicles, posterior elements or a mixture of both
3. **Chondrosarcoma** 50-60 1.5- 2:1 posterior elements, scalloping of vertebral cortex, cortical extension, calcification
4. **Plasmacytoma** <50 2-3:1; **Multiple Myeloma** 50-75 3:2 initially in the pedicles, osteolytic lesion, vertebra plana, later on in the anterior column
5. **Lymphoma** 40-60 1:1 anterior column osteolytic lesion, vertebra plana
6. **Ewing's sarcoma** 10-40 1.4:1 vertebral body osteolytic vertebral lesion, surrounded by sclerosis. MRI reveals a soft tissue mass.



**Fig. 2 Typical spinal Osteosarcoma T1-weighted MRI: After iv-contrast medium administration a strong enhancement of this lesion can be seen. The dense lesion arises within the vertebral body eccentrically and extends not into the pedicle.**

mary lesion. Metastases usually occur in lymph nodes, lung or liver and, less often, in the brain, bone and other rather unusual sites including skin or the heart. Spinal chordomas metastasize more likely than sacrococcygeal chordomas.

The most common complaint is pain due to local pressure. In the sacrococcygeal region chordoma may produce lower back pain or sacral pain radiating into the buttocks, perineum or legs. Because of their slow growing nature and the relatively large space available for expansion they can reach considerable size before provoking clinical signs. In 20 % of patients bowel or bladder dysfunction leads to diagnosis.

In spinal chordomas spinal stenosis is the most false diagnosis in the elderly population. Pathological fracture of the vertebrae can occur. Several vertebral bodies can be involved; the intervertebral discs are always spared.

Lesions in the cervicothoracic spine can cause myelopathic symptoms. Lumbar and lumbosacral lesions often compress nerve roots leading to sensory and motor changes, therefore patients often are misdiagnosed.

Chordomas situated at the clivus mostly are associated with increased intracranial pressure causing head ache, impaired vision, dysphagia and cranial nerve palsies [19,20]. Generally, patients with a chordoma of the clivus are younger than those with a chordoma of the sacrococcygeum [21,22].

Radiographic findings vary with tumor location. Sacral chordomas mostly appear as lytic lesions involving multiple

segments with little, mainly peripheral tumor calcification. Usually an extensive anterior mass can be seen. Spinal chordomas involve the vertebral body, the posterior elements of the vertebral column are spared in most cases, but exceptions are known [23,24].

MRI precisely demonstrates the extension of the soft tissue mass in multiplanar views. In T2-weighted images, the tumor has a strongly increased signal compared to surrounding soft tissue [25]. On one hand these informations are useful for planning surgical resection and in determining the possible need for colostomy and rectal resection, on the other hand it also provides valuable information on follow-ups regarding possible recurrence.

Compared to other therapies, primary surgical resection has proven to be the most effective therapy in chordomas [26]. Whenever possible, a wide extralesional resection should be performed. In most chordomas a marginal resection is not always satisfactory.

Radiation is used only as an adjuvant or palliative therapy [27,28,29], although total recovery has been accomplished in the clivus because higher doses of radiation are being tolerated at this site [30,31,32].

In chordomas involving the spine, spondylectomy should be performed. Due to high rates of recurrence postoperative radiation is strongly recommended.

The 5-year metastasis rate is reported to be 5%. Neither incidence of metastases nor local recurrence correlates with the presence of tumor at the margin of resection. Over all, sacrococcygeal chordomas seem to be less aggressive with better survival rates compared to those of the spine. Survival rate of patients suffering from chordoma is limited with only few patients surviving for 10 years after initial diagnosis [33]. Efforts to improve prognosis include more aggressive surgical resection and improved (neo-) adjuvant therapy.

**Osteosarcoma.** Osteosarcoma (Fig.2) is the second most common malignant bone tumor mostly affecting the long bones. 3 % of all osteosarcomas are seen in the spine and sacrum, representing about 5 % of all primary malignant tumors of the spine. The tumors most often occur in the second or fourth to fifth decade. Patients with osteosarcoma of the spine seem to be slightly older than patients with osteosarcoma of the long bones. Male to female ratio of patients with spinal osteosarcoma is 1:1, in contrast to the male predominance in long bone osteosarcoma.

Patients present with pain localized to the affected area. About 60% of patients develop concurrent neurological deficits, especially when the cervical spine is involved [34].

In spinal osteosarcoma typical radiological features of osteosarcoma like Codman's triangle and periosteal lifting are not present. The lesions can either be primarily osteolytic or osteoblastic or, most commonly, a mixture of both. Most tumors affect the anterior portion of the vertebral body but the posterior parts and the pedicles can also be involved. One should be attentive in osteosarcoma limited to the posterior elements. This is less common and is often mistaken for



**Fig. 3 Chondrosarcoma CT of D12 (Fig. 3a):** osteolytic – expansile destruction of the spinal process with characteristic chondroid bone-matrix mineralization with rings and arcs-like appearance is visible in most of this tumors. The T2-weighted image (Fig 3b) exhibits a very high signal.

osteoblastoma [35,36]. MRI is helpful in evaluating soft tissue components of the tumor and the tumor invasion of surrounding vital structures.

Treatment of osteosarcoma of the spine is similar to osteosarcoma of the long bones. The golden standard includes neoadjuvant chemotherapy followed by radical surgical resection and postoperative chemotherapy [37].

Prognosis of patients suffering from osteosarcoma of the spine still remains poor with mean survival rates ranging from 6 to 10 months. Long term survival has not been reported.

**Chondrosarcoma.** Chondrosarcoma (Fig.3) usually develop in the pelvis, femur and scapula. Approximately 6% affect the spine whereas they more often occur in the thoracic and



**Fig. 4 Multiple Myeloma with multiple pathological fractures and fish vertebrae.** T2-weighted MRI after iv.-administration of contrast medium revealed a patchy – inhomogeneous appearance of the infiltrated bone marrow

lumbar spine and the sacrum than in the cervical spine [38,39]. Male to female ratio of chondrosarcomas of the spine ranges from 1.5:1 to 2:1<sup>10</sup>. The tumor can be seen in all age groups, the fifth and sixth decade is to be the most common [41].

Infrequently the tumor affects the posterior vertebral portion and may be mistaken for aggressive osteoblastoma. Approximately 85 % of chondrosarcoma are found to be primary lesions, 15% result from secondary malignant degeneration of a preexisting osteochondroma or enchondroma.

Signs and symptoms are similar to those of other tumors of the spine.

Low grade chondrosarcoma generally cause scalloping of the vertebral cortex and cortical expansion, calcification usually is present as well. The higher the malignancy grade of the tumor, the more bone destruction can be seen.

Therapy of choice is complete surgical resection. Chondrosarcomas are radioresistant and in most cases patients do not benefit from chemotherapy. In palliative care radiation therapy can be attempted [42].

**Plasmacytoma/ Multiple myeloma (Fig.4).** The spine is involved in 25-50% of the cases with preference of the thoracic

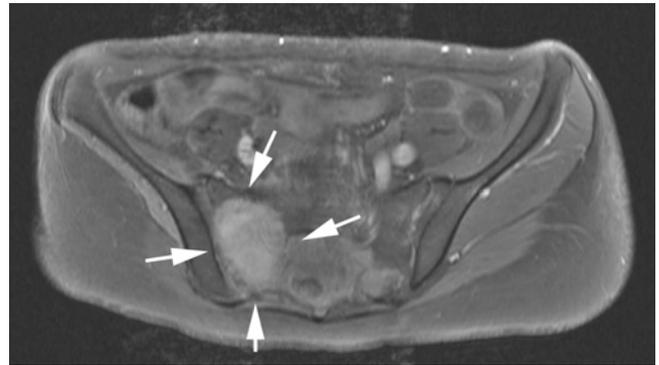


**Fig. 5. B-cell-Lymphoma:** Diffuse infiltration of a vertebral body and expansion into the spinal cord. T2-weighted image shows inhomogeneous high signal intensity.

spine. Male to female ratio is 2 to 3:1. In general, patients are older than 50 years, but plasmacytoma has also occurred in adolescent. The commonest symptom is local pain in the region of the affected spine or radicular pain, but neurological complications have been reported as well. Usually, plasmacytoma is diagnosed with a delay of about 6 months, because clinical signs are mistaken for degenerative disease. Signs of spinal cord and nerve root compression have been reported in 1/3 of patients.

Lesions often start growing in the pedicles; later on the anterior column is involved as well. For plasmacytoma of the sacrum CT or MRI may be necessary to detect the tumor. Technetium bone scan is normal, and only shows an uptake in case of a pathological fracture.

Treatment of choice is chemotherapy and/or radiotherapy. Surgery is performed for decompression and stabilization of the spine in case of pathological fracture, kyphosis, neurological deficit or pain caused by instability. An anterior decompression and stabilization is necessary, an additional dorsal procedure is only requested in case of posterior element involvement [43]. In solitary plasmacytoma 5-year survival rate is about 70%. A poorer prognosis is to be ex-



**Fig. 6. Ewing-sarcoma:** 17 y old girl with a mass in the pelvis, originated from the os sacrum. T1-weighted MRI with after administration of contrast-medium reveals a penetrating bone tumor with a huge soft tissue mass without calcifications.

pected in older age groups, affection of the spine and persisting production of paraproteines after treatment [44].

*Lymphoma.* Lymphoma (Fig.6) of the spine is a rare disease. Only in 15% of patients suffering from lymphoma the disease involves the bone. The spine is affected in 15% and in about 3% of the patients signs of spinal cord compression are found. In Hodgkin's disease usually no lesions of the bone are seen, whereas in Non-Hodgkin's lymphoma either a solitary lesion or, more commonly, disseminated affection of the bone occurs. Patients are between 40-60-years of age with an even male to female ratio [45].

In most cases, lymphoma involves the anterior vertebral column, whereas posterior involvement is rare. Because spinal lymphoma responds very well to chemotherapy and radiotherapy isolated lesions without bone compression should be treated that way. Radiation dose is limited due to the location adjacent to the spine. Lesions that cause pathological fractures or compression with neurological deficits may require surgical decompression and stabilization using an anterior approach primarily followed by chemotherapy and radiation [46,47]. Improved results are provided when radical surgical resection of the tumor is followed by chemotherapy. If intraoperative tissue margins are positive, subsequent radiation therapy is necessary. Follow-up biopsy of lesions treated by radiation and chemotherapy only is recommended at 6 months after treatment to detect residual disease.

Survival rate of non- Hodgkin's lymphoma involving the bone is 30% at 10 years [48].

*Ewing's sarcoma.* Ewing's sarcoma (Fig.5) is a highly malignant round cell tumor. 8% of the tumors occur in the spine, half of them in the sacrum. Patient's average age is 16.5 years with a range from 10 to 40 years<sup>38</sup>.

Commonest presenting sign of patients suffering from spinal Ewing's sarcoma is pain [50]. Symptoms develop at an average of 8 months before the disease is diagnosed. In 80% of patients neurological deficit or radiculopathy is seen.

On plain radiographs usually a lytic vertebral lesion is seen, surrounded by osteosclerotic areas at the periphery. MRI reveals a generally concomitant soft tissue mass. MRI also helps to evaluate spinal canal stenosis and invasion of surrounding vital structures [51,52]. In staging CT chest and technetium bone scan are used to exclude metastases.

Treatment of choice in spinal Ewing's sarcoma includes a multimodal approach. Best results are provided in radical resection and (neo-) adjuvant chemotherapy combined with radiation therapy [53,54]. Average survival of patients treated aggressively compared to survival of patients without treatment is 33 months to 15 months. Total survival rate is 20% [55].

### Discussion

Primary malignant tumors of the spine and sacrum are very rare and are often underdiagnosed in patients with back pain. Patients whose symptoms progress or fail to respond to conservative therapy after an appropriate period of time should be further evaluated.

1 % of all malignant tumors are bone tumors. The ratio of malignant bone tumors compared to skeletal metastases is 1:40. 10% of all primary malignant tumors of the bone arise in the spine and sacrum. In children 30%, in adults 80% of all tumors of the spine and sacrum are malignant.

Assessment of the tumor must include plain radiographs; MRI with T1-, T2-weighted images and T1-weighted images post gadolinium as well as a 3-phase-bone scintigraphy. The CT scan gives information about stability of bone. Using these imaging studies, in most patients with unspecific pain of the spine, correct diagnosis can be established. In some cases additional biopsy may be necessary.

Unfortunately the basic principles of treating primary malignant tumors of the bones with improved survival rates cannot be applied to malignant tumors of the spine. One possible reason for this is the anatomical complexity of the spine with close proximity to vital structures. For that reason en bloc resection often is not possible and the attempt to resect the affected spinal segment by vertebrectomy may lead to local recurrence.

Complete surgical resection of the tumor followed by spinal instrumentation in cases of deformity or instability is the treatment of choice. This procedure reduces recurrence rate and enables correcting deformity performing bone fusion.

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