Pathological fractures in patients with bone tumours: Imaging, pitfalls and clues to diagnosis

Poster No.: C-2183
Congress: ECR 2010
Type: Educational Exhibit
Topic: Musculoskeletal - Bone
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Keywords: Pathological fractures, Bone tumours, Diagnostic Imaging
Keywords: Musculoskeletal bone, Musculoskeletal system
DOI: 10.1594/ecr2010/C-2183

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Learning objectives

*The intent of this exhibit is* to offer a comprehensive, illustrated guide to the imaging assessment of pathologic fractures in the cancer patient.
Fig. 0: Pathological fracture just under the intertrochanteric line in patient with lymphoma of the femur, before (A) and after treatment (B)

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Background

The most common cause of fractures is trauma. However, especially in the elderly, broken bones often occur where the bone has been weakened by an underlying process, this is called a "pathologic fracture". A pathologic fracture occurs when a bone breaks in an area that is weakened by another disease process.

A pathologic fracture usually occurs with normal activities; patients may be doing very routine activities when their bone suddenly fractures. The reason is that the underlying disease process weakens the bone to the point where the bone is unable to perform its normal function. For example, a bone cyst may grow to a significant size where the tumour effectively eats away a significant portion of normal bone. This area of bone is now much weaker, and prone to pathologic fracture. Causes of weakened bone include osteoporosis, osteomalacia, Paget disease, osteitis, osteogenesis imperfecta, benign bone tumours, cysts, secondary malignant bone tumours and primary malignant bone tumours.

This exhibit focuses on the evaluation of fractures that occur secondary to bone destruction by metastatic cancer. Breast cancer is the most important source of bone metastasis, and it is responsible for the majority of the skeletal metastases. The risk of pathologic fracture increases with the duration of metastatic disease, because breast carcinoma has a relatively long survival, these patients are more likely to sustain a pathologic fracture. Based on the literature review, breast cancer metastases that are purely lytic are more likely to cause fracture than those blastic or mixed lytic and blastic. However, blastic lesions in high risk areas such as the proximal femur have a high rate of fracture. Prostate cancer, combined with breast cancer, contributes to 80% of all skeletal metastasis. Prostate cancer normally forms blastic metastases which are less susceptible to fracture, but blastic lesions have been shown to decrease the longitudinal stiffness of bone. In addition, some of the treatments that are commonly given for prostate cancer increase the likelihood of pathologic fracture. These include LHRH agonists, orchiectomy, and radiation. In one study, patients receiving LHRH agonists had a 9% incidence of fracture, a rate significantly higher than similar patients not receiving LHRH agonists (Townsend et al. Cancer 1997,). Patients with prostate cancer who have had radiation to bony areas, or who have low bone density due to hormone modification therapies should be considered at increased risk for fracture. Lung cancer has a relatively aggressive course and a short survival after bone metastasis. Thus fewer patients survive long enough to develop pathologic fracture. Metastases are typically lytic and have a correspondingly higher risk of fracture. A small proportion of lung cancer metastasis can occur in bones below the elbow and the knee (acrometastasis). These lesions are frequently painful and require radiation or surgical treatment due to the pain rather than for risk of fracture as the risk of functionally disabling fracture through an acrometastasis is low. Bone metastasis is diagnosed in 4-13% of patients with thyroid cancer (Marcocci et al, Surgery 1989). The lesions are frequently lytic and their fracture risk depends on
their location. Because patients with thyroid cancer may have prolonged survival they are also at increased overall risk of pathological fracture. Approximately 25-50% of renal cell carcinomas metastasize to bone (Case 1 on page 7), (Case 2 on page 7).

*Renal cell metastases to bone* can be unusually expansive and destructive, which creates an increased risk of pathologic fracture.

Bone metastases from epithelial ovarian carcinoma are rare, usually discovered post-mortem. The survival of these patients is poor. Furthermore, only two cases of endometrioid ovarian carcinoma with metastasis to the skeletal structures have been described in the literature. We report our case of tibia metastasis from uterine carcinoma (Case 3 on page 8).

*One difficult area of clinical decision* making is deciding when to fix impending fractures (Case 4 on page 9). In 1989, Mirels developed a scoring system designed to predict the risk of pathologic fracture due to bone metastases in the extremities. It is based on the degree of pain, lesion size, lytic vs. blastic nature, and anatomic location as shown in following table. Mirels recommended prophylactic fixation for a total score 9. This is currently the most helpful scoring system, although it has limitations. The variability in quality of surrounding bone, behavior of metastases from different tumor types, response of these metastases to treatment including radiation, and patient activity level can also have an effect on the probability of fracture.

**Table 1. Mirel's criteria**

<table>
<thead>
<tr>
<th>Score</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain</td>
<td>Mild</td>
<td>Moderate</td>
<td>Mechanical pain</td>
</tr>
<tr>
<td>Lesional size/ diameter of bone involved</td>
<td>&lt;1/3</td>
<td>1/3 - 2/3</td>
<td>&gt;2/3</td>
</tr>
<tr>
<td>Lesion type (blastic vs lytic)</td>
<td>Blastic</td>
<td>Mixed</td>
<td>Lytic</td>
</tr>
<tr>
<td>Anatomic site</td>
<td>Upper limb</td>
<td>Lower limb</td>
<td>Peritrochanteric (proximal femur)</td>
</tr>
</tbody>
</table>
Fig. 0: Pathological fracture of metastasis from renal cell carcinoma treated with intramedullary nail and cementum within the cavity

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**Fig. 0**: Endomedullar nail of the humerus in a patient undergone surgery for renal carcinoma metastasis

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Fig. 0: Pathological fracture of a tibia metastasis from uterine carcinoma treated with intramedullary nail

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**Fig. 0:** Impending fracture: treated with cement (A) and intramedullary nail (Rush) (B,C)

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We have to suspect a pathological fracture when the fracture happens after a minor injury or during daily activities (walking, standing up, etc.). Usually, the patients with this kind of fractures have in the affected limb an old history of worsening pain especially in the night and under load. Make diagnosis of pathological fractures is important because the prognosis and therapy can be different from case to case.

Clinical examination can be difficult for the pain. Pain is an important but controversial criterion for evaluation of pathologic fractures. In metastatic disease, pain may arise from enlargement of the tumor, perilesional edema, increased intraosseous pressure, or weakness from bone loss. The direct pressure exerted by the tumor on the bone has been shown to stimulate the release of various pain mediators including prostaglandins, bradykinins, and histamine. In addition, tumor invasion of bone can lead to activation of mechanoreceptor and nociceptors which leads to the development of pain. The controversy lies in whether or not pain can be used as a sign of impending fracture. Fidler stated that pain could not be considered a reliable sign of an impending fracture because only half of the patients in his study complained of pain. Keene et al. found that most patients with metastatic bone cancer did develop bone pain, but only 11% of them actually had fractures; therefore, he concluded that pain was not an accurate indication of impending fracture.

Imaging Techniques

Conventional radiography (CR) is the most important technique for fracture diagnosis. The standard radiography must be performed in two projections, antero-posterior and lateral, as only one projection cannot show the characteristics dislocation, the discontinuity or misalignment of the fracture from overlap or from broken bone shadow.

When it is not possible to establish an exact diagnosis based on the standard projection (e.g. in the spiral fractures minimally decomposed), can be used the oblique projection. The fracture can be identified with difficulty if it is studied only a small area. For example, hip fractures can cause pain with irradiation at thigh and knee and it cannot be recognized if we don't study the whole femur. It is also important to study the contralateral portion especially for the pelvic or femoral fractures, because it is possible to have a concomitant trauma. Usually the pathological fractures caused by malignant neoplasm shows multiple osteolytic lesions, visible as radiolucent areas. The conventional radiography is not useful to differentiate disease with reduced bone density (osteopenia), like osteoporotic, osteomalacia, hyperparathyroidism and myeloma. If a fracture is caused by an osteopenia are indispensable laboratory exams for identify the primitive disease. We report our cases identified with CR (Case 5 on page 15), (Case
Computed Tomography (CT), although not necessary for routine, can be useful to complete the exam after CR. CT can show the occult fracture in areas that are difficult to identify with CR due to the other overlying bone structures (e.g. cervical spine). The CT is also useful to establish the Intra-articular fractures. These fractures can damage the articular cartilage and subchondral bone and lead to articular incongruity, step-off and instability. CT can identify the extension of the destruction of bone tissue and the relationship with soft tissue especially with Multi Planar Reformation (MPR) techniques (Case 19 on page 18), (Case 20 on page 19), (Case 21 on page 20), (Case 22 on page 21).

Magnetic Resonance Imaging (MRI) shows without difficulty the soft tissues and differentiates the adipose tissue from water. Within 24h MRI can demonstrate the edema that rapidly is accumulate into the fracture regions during the first inflammatory phase and allows the early diagnosis of occult fractures. The MRI is useful for evaluates the pathological fractures and in the diagnosis of osteonecrosis and osteomyelitis, that can mime the fractures. However the MRI cannot directly shows the bone calcification or mineralization, so it is less sensible then CT or CR. We show the utility of MRI before surgical treatment (Case 23 on page 22).

Although sonography is not the method of choice for the detection of bone fractures, it may be worthwhile to examine the bone contour for a fracture when a painful swelling adjacent to bone is present and is useful to assess the bone regeneration (Case 24 on page 23), (Case 25 on page 24). The method may be particularly rewarding in children due to its rapid non-invasive nature and to the small tissue thickness that has to be penetrated.

In a recent study (Paik et al. AJR 2005) high-resolution sonography seemed to be useful in the detection of rib fractures. Sonography can detect a fracture in six times as many patients as radiography and will detect 10 times more fractures than radiography. On sonography, the patient indicates the site of pain and the examiner obtains a cross-sectional image of the region in two planes, with the image closely following the course of the ribs. Some typical sonography findings of rib fracture are gap, step, dislocation, hematoma, and minimal concomitant pleural effusion or even pneumothorax. Wischhofer et al. detected a fracture on sonography in 16 of 21 subjects with suspected rib fracture and normal findings on chest radiography.
If bone scintigraphy showed an increased uptake in the rib cage and sonographic findings for the rib were negative, traumatic fracture could be ruled out. This suggests metastasis, which requires further evaluation. When metastatic lesion involves only bone marrow, bone cortex can be intact and sonography cannot transmit through intact bony cortex. In conclusion, high-resolution sonography of the rib is a useful method in detecting and characterizing rib lesions in those patients who have hot-uptake lesions revealed on bone scintigraphy.

Another study (Wang et al. JCU 1999) describe the detection of occult fractures in the foot and ankle. On sonography, the occult fractures appeared as a discontinuity of cortex echogenicity. Sonography a readily available, noninvasive imaging technique-can provide important information about soft tissue injuries and cortical discontinuities in the foot and ankle area. Using this procedure, occult fractures can be identified and delineated, and costly procedures such as MRI can be avoided.

Other Diagnostic Modalities

The bone scintigraphy, with 99 technetium-marked pyrophosphate or other with analogy of radioactivity, can shows focal lesion of any origin and it is very sensitive in the detection of osseous metastases and is recommended as the first imaging study in patients who are asymptomatic (Case 26 on page 25). The uptake happens where are present areas of new bone tissue (e.g. bone answer at an infection, osteoarthritis, tumours or fracture). The occult fractures that are not shown with CR often can be identified at bone scintigraphy from 3 to 5 days after the trauma. When there is the suspect of a pathological fracture, is indispensable to do a bone scintigraphy to search bone metastases and metabolic lesion in other regions.

Bone is the most common site to which breast cancer metastasizes. Imaging by skeletal scintigraphy, plain radiography, computed tomography, or magnetic resonance imaging is an essential part, and positron emission tomography or single-photon emission computed tomography have a potential of evaluating bone metastases, but no consensus exists as to the best modality for diagnosing the lesion and for assessing its response to treatment. Imaging bone metastases is problematic because the lesions can be osteolytic, osteoblastic, or mixed, and imaging modalities are based on either direct anatomic visualization of the bone or tumour or indirect measurements of bone or tumour metabolism.

Laboratory data

The hematocrit level is the main laboratory analysis to evaluate the blood loss caused by fractures. The fractures, especially of the hip, often are correlated with an important blood loss of the soft tissues, needing transfusion.
The plasmatic alkaline phosphatase level is the only routine laboratory test available that is directly correlated to fracture healing. The plasmatic alkaline phosphatase level increase when increase the bone turnover, during the normal fracture healing, during the muscle growth (childhood), or during skeletal involvement in same neoplastic or metabolic disease (e.g. Paget's disease). Oppositely, the normal calcium plasmatic level does not change during the normal healing of the fractures. The normal calcium plasmatic level can increase during same endocrine diseases (e.g. hyperparathyroidism) or metastatic diseases, especially breast cancer and when there is a rapidly bone resorption during the Paget disease.
Fig. 0: Pathological fracture of humeral head and neck

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Fig. 0: Pathological fracture of the femur just below the intertrochanteric line in patient with multiple myeloma

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**Fig. 0:** Metastatic pathological fracture of the medium third of the humerus

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**Fig. 0:** Pathological fracture just under the intertrochanteric line in patient with lymphoma of the femur, before (A) and after treatment (B)

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**Fig. 0:** Pathological fracture of a clavicular metastasis from HCC

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Fig. 0: Sternal pathological fracture from plasmocytoma

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**Fig. 0:** Pathological fracture of the humeral head and neck

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**Fig. 0:** Pathological fracture of a femur metastasis from breast cancer

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**Fig. 0:** Vertebral metastasis with marked fragment dislocation treated with posterior fixation

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Fig. 0: Pathological fracture of the humerus from breast cancer. Interruption of the cortical profile

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Fig. 0: Rib fracture with bone callus
**Fig. 0:** Pathological fracture of the femoral neck. CR (A,B), CT (C), and PET-CT (D)

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Conclusion

*Pathological fractures have* peculiar clinical and radiological features, which should be known to the radiologist, to properly recognizing the underlying abnormality and to allow an appropriate treatment.
Fig. 0: Metastatic vertebral collapse (A,B) treated with posterior fixation (C)

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Fig. 0

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