Vol.: 6, No: 1, Feb, 2020, P 1-7
DOI, 10.15562/tcp.82

CANCER PRESS
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Mini Review

Diagnostic Imaging Modalities for Skeletal Metastasis in Soft Tissue Sarcoma

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Submitted: 06.08.2019
Accepted: 25.09.2019
Published : 02.02.2020

Keywords: soft tissue sarcoma, bone metastasis, Imaging Modalities

Abstract

Soft tissue sarcomas (STS) are usually highly malignant. Bone metastasis is less common in STS but it significantly affects patients` quality of life and also is indicator of poor prognosis. Different types of imaging modalities are available for diagnosis and follow-up of STS. Bone scintigraphy is a sensitive and cost effective method for screening bone metastases however it`s poor specificity must be covered by other imaging methods like computed tomography. More sophisticated methods are available including whole body magnetic resonance imaging (MRI) and positron emission tomography (PET). Equipment limitations and high costs are the main problems with ofthese methods.

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Introduction

Soft tissue sarcomas (STS) are groupof heterogeneous neoplasms, accounting for less than 1% of all human malignancies. STS have tendency to spread via bloodstream.Half of STS patients develop metastatic disease[1]. The lungs are the most common sites of the metastasis [2]. In a study conducted by Yoshikawa*et al.,*the incidence of skeletal metastasis in STS patients was 10%[3]. Additionally Skeletal involvement was different in subtypes of STS. Alveolar soft-part sarcoma, dedifferentiatedliposarcoma, angiosarcoma and rhabdomyosarcomashowed a higher incidenceof skeletal metastases[3, 4].

Skeletal metastasis leads to skeletal related events (SREs). "The term SRE is used to encompass common complications of bone metastases such as pathologic fracture secondary to a bone metastasis, spinal cord compression or the need for surgery or radiotherapy to bone"[5]. SREs can have significant adverse effects on patients' quality of life;accordingly, clinicians must consider management of the SREs in STS patients, even if survival is limited. Additionally, with the recent advances, overall survival in STS patients has increased and new imaging techniques have improved the diagnosis of bone metastasis[4].

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Selecting the appropriateimaging modalitiesis an important issue. A diagnostic imaging modality must be cost-effective and accurate for medical interventions. Scintigraphy, positron emission tomography (PET) and whole body MRI are the main diagnostic modalities. Other imaging techniques such asradiography, computed tomography (CT) andMRIcan be used to confirm the diagnosis and evaluate the extent of metastasis and its characteristics [6].

In this brief review, we will discuss the available imaging modalities for diagnosis of skeletal metastasis in STS patients.

Association of symptoms with bone metastases

The most common signs of bone metastases are pain, fracture, spinal cord compression, and hypercalcemia.Bone pain is often the first symptom of bone involvement. Most patients (75%) diagnosed with bone metastases experience severe bone pain [7, 8].The pain in patients with bone metastases can be due to various causes including, tumor-induced osteolysis, direct infiltration of nerves, production of endothelins and nerve growth factors from local tissue, stimulation of ion channels and production of growth factors and cytokines from the tumor[9, 10]. Also, bone metastases can weaken bones and lead to pathological fractures. Subsequently, these fractures often cause severe pain [3, 8]. Meijer *et al.* found a correlation between the location of bone metastasisand bone pain[7]

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Spinal cord compression, which is another sign of bone metastases can lead to pain in the neck, back and lower limbs with or without neurological complication and mechanical instability [10].

Patients may experience different symptoms as a result of diffuse bone marrow infiltration which usually happens in those who have received radiotherapy or chemotherapy. Patients whose red blood cells are affected, experience anemia, fatigue, and weakness. decreased white blood cell count increases the risk of infection. A low platelet count may lead to coagulation defects [8, 9]. In some patients, swelling is reported as a symptom of bone metastases [3].

Hypercalcemia is a nonspecific symptom and leads to constipation, nausea, and anorexia, however, it is a significant complication in the treatment of the STS and indicates a worse prognosis [6].

Chow *et al.* studied five hundred eighteen cancer patients with bone metastasis and identified three symptoms clusters: 1) the most common symptoms including fatigue, pain, drowsiness and poor sense of well-being, 2) depression and anxiety, which was more prevalent in women, and 3) the rare symptoms including shortness of breath, nausea, and anorexia [11].

The best diagnostic modality

Imaging techniqueshave significant roles in detection, follow-up, monitoring and planning treatment of bone metastases[12]. The most common imaging modalitiesfor finding bone metastasisin soft tissue sarcoma patients are radiography, bone scintigraphy, computed tomography (CT) scanning, radioisotope scanning's like PET, and magnetic resonance imaging (MRI).

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Radiography is a cheap and fast imaging technique. It is usually used to confirm the findings of other methods, however because of poor sensitivity it is not recommended as a screening method for bone metastases [13, 14].

Computed tomography (CT) can evaluate metastases within bone marrow before bone destruction has occurred. This technique can be usedfor detecting metastasis in axial bones.In addition, it can give us information about the size and structure of the metastasis, which is important in selection of an orthopedic implant. CT does not have screening role for bone metastases because it is time-consuming and it imposes high amount of radiation[13, 15-18].

Bone scintigraphy is more sensitive than radiography and CT for detection of metastases in bone marrow, but it has poor specificity.Because some trauma and degenerative diseases can increase tracer uptake which canmimic skeletal metastases [19, 20]. Nevertheless, it is the most cost-effective whole body screening technique of bone metastases[6, 21]. A study conducted by Barai*et al.* showed that routine scintigraphy in STS has a relatively low yield. This study suggests preforming scintigraphy only for patients with bone pain, however in this case asymptomatic patients may be missed[19].

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Positron emission tomography (PET) especially with 18F-fluorodeoxyglucose (FDG) has an important role in the detection of bone metastases [22]. PET is expensive and takes longer time compared to other imaging modalities[23, 24].

Today, whole body magnetic resonance imaging (MRI) and FDG-PET may improve detection of bone metastasis. MRI is a fast and simple modality for evaluating the axial skeleton. In MRI, most false negative detections were located in small and flat bones such as the skull, the ribs, and the carpal bone[13, 18, 20].

Daldrup-Link *et al.* compared the diagnostic accuracy of whole-body magnetic resonance imaging (MRI), FDG-PET and bone scintigraphy for identifying bone metastasis. In this study, FDG-PET showed the highest sensitivity (86%) compared to MRI (82%) and bone scintigraphy (71%)[20]. Currently, it seems that the best diagnostic modality of bone metastases in patients with soft tissue sarcoma is utilizing a combination of imaging techniques. Generally, the first choice of screening is bone scintigraphy because of its high sensitivity and cost-effectiveness . However, bone scintigraphy needs to be followed by other methods for an accurate diagnosis. Bone scintigraphy and FDG-PET are useful to detect bone metastases in asymptomatic patients [7, 25]

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The most important limitation of accurate methods like FDG-PET and whole-body MRI is their high cost.

Conflicts of Interest:

The authors declare no conflict of interest.

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