Bone diaphysis metastases from the perspective of an orthopedic surgeon – review

Przerzuty nowotworowe do trzonów kości długich z perspektywy lekarza ortopedy – przegląd literatury

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Abstract

Bone metastases are a great challenge in the practice of an orthopedic surgeon. Due to the development of oncological treatment, the approach to patients with bone metastases is changing. Previously, these patients were treated palliatively, mainly to decrease the pain intensity. However, with appropriate systemic, surgical and orthopedic treatment, patients with bone metastases often live for many years. Therefore, proper diagnosis and appropriate orthopedic treatment can significantly improve patients’ prognosis. On the other hand, poor qualification for surgery and selection of the wrong treatment method contribute to shortening the patients’ survival. Hence, knowledge of the diagnosis and qualification of patients for surgical treatment is essential in the practice of an orthopedist. In the presented review, the authors focused on summarizing the knowledge in the field of diagnostics, qualification for surgical treatment and orthopedic treatment methods for patients with bone diaphysis metastases.

Key words: bone metastases, long bones, orthopedic treatment, qualification for treatment.

Streszczenie


Słowa kluczowe: przerzuty do kości, kości długie, leczenie ortopedyczne, kwalifikacja do leczenia.

Introduction

Oncological diseases are currently one of the main public health problems worldwide. Latest data show a constant raise of oncological patients it is estimated that in 2022 there will be more than 2 million cases in the US alone [1]. Bone metastases may affect up to 70% of oncological patients, 20% of which might require an orthopedic intervention [2,3]. The development of systemic oncological treatment results in prolonged lifespan of oncological patients – therefore in many cases the presence of bone metastases might not indicate a terminal state. The mean survival of patients suffering from breast cancer with bone metastases is 22-55 months [3]. Therefore, the knowledge and means to properly treat a patient with bone metastases can greatly affect the patients’ survival and quality of life.

The bone tissue is the third most common metastatic localization – after the lungs and the liver [4]. Bone metastases appear most often in breast cancer in women (70%) and prostate cancer (85%) in men. Other are lung cancer (40%) and kidney cancer (40%) [5]. Even though long bones are not the most common location for neoplasm metastases, they can be affected in more than 50% of all bone metastases [2]. They can decrease patients’ quality of life by causing chronic pain or pathological fractures [6]. Interestingly, the distribution of bone metastases is most likely due to the presence of bone marrow, which provides a favorable environment for the growth of cancer cells [7].

Bone metastases can be divided into 3 groups: osteolytic, osteoblastic, and mixed [8]. Osteolytic lesions are characterized by bone destruction which may lead to a pathological fracture of the bone [7]. This type of lesion...
is usually caused by kidney and thyroid cancer, myeloma and melanoma [9]. Breast cancer can also present osteolytic metastases, but in 15-20% of cases a mixed lesion occurs [10]. Osteoblastic lesions are characterized by bone remodeling and are usually seen in prostate cancer, Hodgkin lymphoma and carcinoid [4,8].

**Diagnosing bone metastases**

Bone metastases are most often suspected in patients with a diagnosed neoplasm and complains of bone pains. In approximately 30% of patients a metastatic bone tumor might be the first symptom of a neoplasm [11-13]. Being aware of the usual symptoms is crucial to diagnosing bone metastases.

Among the usual symptoms, the most important is bone pain – it is difficult to pinpoint, often occurs during nighttime and does not pass after rest [8]. The most common laboratory finding is hypercalcemia [8,14]. It is mostly caused by osteolytic lesions and causes symptoms like fatigue, polydipsia, polyuria, constipation, renal failure and arrhythmia [8]. Other laboratory irregularities are elevated OB, ALP and low PTHrP [15]. It is also worth emphasizing that hypercalcemia is an unfavorable prognostic factor in relation to patient survival [9]. Pathological fractures are another common problem among patients with bone metastases. They occur in 10-30% of all oncological and patients, and the most frequent fracture location is femur (over half of all cases) [9]. It is worth emphasizing here that long bone fracture is the most common cause of disability in cancer patients [8]. The risk of a pathological fracture increases with the duration of the involvement of bone metastases. The severity of bone pain is not directly related to the risk of fracture, however pain exacerbated by movement appears to be an important factor in predicting an impending fracture [4].

Radiological imaging is a key asset in the diagnostic process in patients with metastases to the bones. Among all radiological methods, due to its accessibility, low cost and safety, classical radiography remains the gold standard. It allows us to distinguish between osteolytic and osteoblastic lesions. We must remember, that despite a high level of specificity, the sensitivity of finding metastatic lesions is not high (ca. 40-55%). Therefore, some of the early-stage bone metastases might not be discovered with the use of X-Ray [8]. It is worth mentioning that a lesion in the compact bone can be discovered earlier than a lesion in the medullary cavity.

The next examination used in the diagnostic process is bone scintigraphy, which compared to an X-Ray has a higher sensitivity (62-89%) but a lower specificity [8]. This type of imaging is useful in assessing the number of metastatic lesions, which then affects the prognosis and determines the choice of treatment.

Computed Tomography (CT) is especially useful in cases where bone scintigraphy shows the presence of a tumor but an X-Ray is unable to assess its characteristic. All types of bone metastases are fairly easy to visualize in the CT – which results in sensitivity of 70-100% [8,13]. Moreover, a CT scan allows to assess the risk of a pathological fracture using the Mirels criteria [16]. Magnetic Resonance Imaging (MRI) is used mostly in diagnosing metastases in the spine and in cases with soft tissue involvement [8]. PET-CT is used in patients with unknown primary origin, in assessing the response to treatment and to search for metastases in tissues other than the bones [8,17]. It has a higher success rate in finding metastatic lesions than bone scintigraphy – especially when the primary neoplasm origins from the lung and the breast [11,18] (Tab. 1).

Performing a biopsy of a metastatic bone tumor is advised mostly in neoplasms of unknown primary origin (it helps discriminate between primary bone tumors, metastatic and locally malignant lesions) [19]. It means that in patients with a diagnosed neoplasm (both active and in remission) when a bone lesion is found, performing a biopsy is advised. In some cases, when a neoplasm is diagnosed and there are unambiguous radiological findings confirming a metastatic lesion, a biopsy can be omitted [20,21]. The biopsy method varies between oncological centers – but an open (surgical) biopsy and core-needle biopsy is usually performed [19,22]. It is worth noting here that it

<table>
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<tr>
<th>Imaging method</th>
<th>Advantages</th>
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<tr>
<td>X-Ray</td>
<td>– low costs and high availability</td>
<td>– low sensibility</td>
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<td></td>
<td>– differentiating between osteolytic and osteoblastic lesions</td>
<td>– don't detect early-stage bone metastases</td>
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<td></td>
<td>– high level of specificity</td>
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<tr>
<td>Bone scintigraphy</td>
<td>– highly sensitive</td>
<td>– low specificity</td>
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<td></td>
<td>– assessing the number of metastatic lesions</td>
<td>– no differentiation of the osteoblastic process in the bone</td>
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<td>(neoplastic, traumatic or inflammatory)</td>
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<td>Computed Tomography</td>
<td>– hight sensibility</td>
<td>– radiation dose</td>
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<td>– good soft tissue and contrast resolution</td>
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<td></td>
<td>– allows to assess the risk of a pathological fracture</td>
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<td>PET-CT</td>
<td>– hight success rate in finding metastatic lesions in bone and other tissues</td>
<td>– lower accuracy in bone metastasis which are slow growing (renal and prostate cancer)</td>
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<td>– allow to assess the response to treatment</td>
<td>– hight costs</td>
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is recommended that the biopsy and treatment of patients with bone tumors, including metastases, should take place in referred center [23].

**Qualification for a surgical treatment**

The treatment option should always be discussed and decided by an interdisciplinary team. Most of the patients with bone metastases will benefit from conservative treatment such as chemo- or radiotherapy. In this article we would like to focus on the surgical treatment options. Ca. 20% of patients are eligible for a surgical treatment [3,24]. Determining which factors to assess while qualifying the patient for a surgery is crucial. The most important factors are: the pain level, functional assessment, expected survival, the presence of a pathological fracture, the osteoblastic/osteolytic character of the lesion, the histological type of the tumor, the number of metastases, the time between the discovery of the neoplasm and the discovery of bone metastases[2-4,10].

It is worth mentioning that the conservative treatment options are usually ineffective in easing the pain related to the biomechanical insufficiency and instability caused by the pathological fractures. Therefore, in such cases a surgical treatment is advised [25].

The surgical treatment should be planned individually and adjusted to the needs and clinical state of the patient. The expected survival is a crucial factor. Usually, surgeons tend to be overly optimistic when estimating the patients’ survival [26]. An inadequate estimation of patients survival and therefore choosing a wrong treatment effects in lower treatment response, lower patients satisfaction and a higher risk of complications and recurrence [27]. Using objective, specific scales can help the surgeon choose the right option for each patient. While estimating the patients survival, using a PATHFx online tool (validated by the International Bone Metastasis Registry in 2019) and the tool proposed by Willeumier JJ et al., can be helpful [28,29]. In the latter, the patients are divided into 4 groups: (A) >12 months; (B) 6-12 months; (C) 3-6 months and (D) <3 months of expected survival. While assessing the risk of a pathological fracture the Mirels criteria can be useful [30]. Some of the included factors are the localization of the lesion, the pain level, the character and the size of the tumor. The maximum score is 12 points, but a prophylactic stabilization of the affected bone is recommended at the score of eight [30]. Another tool used while dealing with pathological fractures is the Harrington criteria, which suggests stabilizing the bone when the size of the lesion is >25 mm, >50% of the compact bone is affected and the pain does not succumb despite administering radiotherapy [31] (Tab. 2). In most metastatic lesions, the presence of a pathological fracture is a negative prognostic factor [6,32]. Moreover, its presence reduces patients’ quality of life and generates additional costs for the health system [33]. Surgical treatment of pathological fractures is connected to a higher rate of complications and lower functional outcome [32]. Therefore, when the risk of a pathological fracture is high (‘impending fracture’), a prophylactic stabilization should be performed.

| Table 2. The table presents scales for the assessment of the survival time of patients with bone metastases and for the assessment of the risk of pathological fracture. |
|-------------------------------------|-------------------|-------------------|
| Patients survival                   | PATHFx v3.0       | Anderson AB et al. [28] |
| Model for Survival Estimation for Patients with Symptomatic Long Bone Metastases | Willeumier JJ et al. [29] |
| Risk of a pathological fracture     | Mirels criteria   | Mirels H. [30] |
| Harrington criteria                | Harrington KD. [31] |

**Surgical treatment**

Choosing the right surgical method is crucial to achieving a good post-operational result and high patients’ satisfaction. The goals of surgical treatment are: good functionality, the ability to resume daily activities, durability of the fixation (adjusted to patients’ expected survival), pain reduction, and eliminating the risk of recurrence [10,25]. Current scientific strategy is clear – the longer the expected survival the more radical surgical approach [25]. When dealing with bone metastases there are several surgical methods widely used: internal fixation with the help of intramedullary nails, plates and/or screws or implanting a modular endoprosthesis [10,16,25,34]. Each of the mentioned methods has its specific indications and should be individually considered for each patient. Now we will proceed to discuss the use of the listed methods.

The most popular system of choosing the right surgical treatment of bone metastases is the Capann and Campanacci system. It includes 4 classes of cases [10]. The analyzed factors are: expected survival, histological type of the primary neoplasm, stage of the disease, presence of extraosseous metastases, patients general condition and function, time between diagnosing the neoplasm and the bone metastases, chemo- and radiosensitivity of the tumor. The authors recommend a surgical treatment in the first 3 classes – moreover, in the 1 class they suggest a treatment similar to the one used in primary bone neoplasms.

In the case of bone metastases, a surgery is recommended even if the expected survival is 2-6 weeks [25]. In this group a minimally invasive approach – like using an intramedullary nail - is recommended. Additional benefits of this approach are good stabilization of the bone, relatively low blood loss, low cost and rapid recovery to daily activities [35]. In this method it is important to remember to use the maximal available size of the intramedullary nail. Moreover the nail should be blocked in two spots – proxi-
mal and distal (in the case of lower extremity two proximal and two distal screws are used) [25,34]. A simple, closed osteosynthesis (without open curettage) can be considered in patients in bad general condition with expected survival of less than 3 months [25]. This method allows for a radical treatment with excision of the lesion and replacing it with bone cement. If this method is used, a more radical surgical approach is needed. The bone cement is the most popular material for replacing excised bone tissue for several reasons. Among its benefits are: enhanced structural stability, rapid recovery and better local control after curettage due to its thermic characteristic [36,37]. The drawbacks are longer prolonged surgery, a risk of wound healing disorders and local bleeding. Using the bone cement requires the use of PMMA (PolyMethyl MethAcrylate) of low viscosity, applied under minimal pressure. A proper level of patient hydration is also important – it reduces the risk of fat embolisms [37]. Using an intramedullary nail also has its limitations. Its durability in treating bone metastases is estimated to be 12-18 months [10,38]. One of the reasons is the lower healing potential of bone tissue affected with metastases. Healing indications were present in 5-20% of pathological fractures caused by metastases [37,39]. The healing potential in bone metastases from breast cancer is estimated to be 34% – but from lung cancer 0% [40]. Therefore, in patients with expected survival of >12 months a different stabilization method should be considered.

Another method used in osteosynthesis in bone metastases to long bones are plates and screws. The plate should be long enough to withstand the muscular forces affecting the bone. Moreover, the compact bone both proximally and distally of the lesion must be of sufficient durability and quality [25,34,41]. In this method a radical resection with bone cement implantation can also be administered [34]. Due to its limitations, stabilizing the bone with plate and screws is mostly used in lesions localized in the arm and forearm bones [41,42]. Using this method is suggested in patients with good prognosis and expected survival of more than 12 months [10]. The overall implant survival of megaprostheses was 68% and 52% at 5 and 10 years [43]. This method is especially recommended for patients qualified to class I according to Capanna [10]. It is worth noting that a radical surgical treatment, especially in clear cell renal carcinoma achieved by en-bloc resection, results in good patients’ survival [44].

Post-operative care focuses mainly on ensuring a rapid return to daily activities and preventing complications. Especially when using an intramedullary nail to stabilize a bone, a quick mobilization of the patient is recommended. During the surgery and right after it, a prophylactic anti-coagulant and antibiotic treatment is recommended [37]. If radiotherapy is required as an adjuvant treatment, it should be administered after 3-4 weeks after the surgery to allow for a full healing of the wound. The use of RTH reduces the risk of reoperation from 15 to 3% [45].

Summary

Bone metastases are a multidisciplinary problem which requires the cooperation of orthopedic surgeons, radiologists, oncologists and many others healthcare professionals. Even though bone metastases are often an indication of an advanced stage, implementing a proper diagnostic and therapeutic process can greatly benefit the patient. In metastatic lesions in long bones, surgery is especially needed when there is pain that can not be dealt with inoperable treatment, when there is a pathological fracture or high risk of occurrence fracture. Among the methods of surgical treatment of metastases to the bones diaphysis, the most frequently chosen are the intramedullary nail, plates and screws, as well as modular endoprostheses. However, it should be remembered that the method of surgical treatment of patients should always be selected individually.

References


13. Descotte B, Botton E, Le Gal G et al.: Investigations for bone metastasis from lung cancer 0% [40]. Therefore, in patients with expected survival of >12 months a different stabilization method should be considered.

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