

ORIGINAL ARTICLE

Skeletal metastases and pathological fractures of long bones

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The authors have declared that no competing interests exist

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Summary

Introduction. The most common cause of pathological fractures are skeletal metastases. Ten percent of patients with diagnosed skeletal metastases will sustain a pathological fracture. Skeletal metastases can be treated by non-surgical methods, including analgesics, bisphosphonates, and radiotherapy, with the primary goal of relieving pain and slowing down tumor growth. Surgical treatment is indicated for impending or existing fractures. It includes stabilization with internal fixation using various nails, plates, and screws with or without osteoplasty, and endoprosthetic joint replacement, especially in lesions around major joints – hip, knee, and shoulder.

Material and Methods. The study included patients operatively treated at the Institute of orthopedics “Banjica” and pathohistologically analyzed at the Institute of pathology in Belgrade during the period from February 2021 to January 2022. Inclusion criteria were an existing or impending pathological fracture of long bones, operative treatment with tissue sampling, and the consequent pathohistological diagnosis of metastatic carcinoma. Patients with biopsy-proven processes other than metastatic carcinomas were excluded from the study. The total number of patients included in the study was 69.

Results. The mean age of patients at the pathological fracture occurrence was 67.7 (ranging from 42 to 88). Malignant diseases diagnosed were: breast cancer 36.1%, lung cancer 24.5%, kidney cancer 14.5%, prostate cancer 13.1%, colorectal cancer 2.9%, other cancer (8.9%). The radiological presentation was in the form of lysis in 75.4% and in blastic form in 24.6%. Operative treatment included arthroplasty in 53.6% of patients and stabilization with nail or plate in 46.4%.

Conclusion. Pathological fractures represent the final outcome of tumor activity in a bone and cause significant suffering in patients expressed through severe pain and often immobility, which accelerates all the pathological processes and leads to death. Joint methods of contemporary chemotherapy, radiotherapy, and surgery enabled a significant life quality improvement and extension in these patients.

Keywords. skeletal metastases, pathological fracture, surgical therapy

INTRODUCTION

Pathological fracture is a fracture of bone previously affected by a pathological process. These processes can be of metabolic, hormone, developmental or neoplastic origin. The most common cause are skeletal metastases (SM) of various carcinomas – lung, breast, prostate, kidney, and thyroid gland carcinoma have the highest incidence of bone metastases, although skeletal metastases are found in every other carcinoma. (1) During the course of the disease, 60–75% of carcinoma patients will get SM. (2, 3) Ten percent of patients with SM will sustain a pathological fracture. (3) These fractures have a significant impact on morbidity and mortality. Previous studies suggest a one-year survival rate of 40%. (4, 5) These reasons make pathological fractures an important medical and social issue, and studies are directed towards researching risk factors for their occurrence and methods of prevention and treatment. (6-8)

Pain is the leading symptom of SM, followed by movement difficulty and swelling. Spinal cord compression can cause neurological dysfunction, and bone destruction can lead to hypercalcemia and blood aplasia. (6) Pathological fracture is the outcome of a metastasis presence in a bone. It may occur after several months of complaints or a very short period, sometimes even without any previous problems. (9) Various methods are used in the diagnostic process – X-ray, skeletal scintigraphy, PET scan, MSCT, and MRI. (10, 11) Scintigraphy with ^{99m}Tc has special significance as a highly sensitive method indicating possible SM before their clinical occurrence. X-ray shows a lesion in its' later stage but is essential for presenting the exact location, the type of bone reaction (lytic or blastic), the degree of bone destruction, and an existing or impending pathological fracture. (10)

SM are treated by non-surgical and surgical methods. Non-surgical treatment includes analgesics, bisphosphonates, and radiotherapy. For pain control, non-steroid anti-inflammatory drugs are used, but most commonly, opioid analgesics are needed. Bisphosphonates are used to decrease bone resorption. Radiotherapy is performed in a single dose 8Gy regimen or a multiple fractionated treatment 16-30Gy. The main goal of this therapy is pain relief, but also slowing down tumor growth and, with this, a decrease in pathological fracture incidence, nerve decompression, and aplasia prevention. (7, 12, 13)

Surgical treatment is indicated in existing or impending fractures and includes internal fixation using various nails, plates, and screws with or without osteoplasty, usually with bone cement. Next to fixation is an endoprosthetic joint replacement, especially in lesions around the hip joint – hemiarthroplasty (HA), total arthroplasty (TA), and megaprosthesis (MP). (14-16)

The aim of this paper is to present a series of patients with pathological fractures of long bones of extremities that occurred on the basis of SM.

MATERIAL AND METHODS

The study included patients operatively treated at the Institute of orthopedics “Banjica” and pathohistologically analyzed at the Institute of pathology in Belgrade for one year (February 2021 – January 2022). Inclusion criteria were as follows: an existing or impending pathological fracture of long bones of extremities according to Mirels classification (17), an operative treatment with biopsy, and pathohistologically proven metastatic carcinoma tissue at the fracture site. Patients excluded from the study were those with biopsy-proven processes other than metastatic carcinomas (lymphoma, myeloma, primary tumor, solitary bone cysts, brown tumor). The total number of patients included in the study was 69.

This retrospective, observational study presented clinical, radiological, and pathohistological features: age, previous knowledge of the malignant disease, localization, radiographic presentation (lytic/blastic), and pathohistological diagnosis. A series of various operative methods are also presented.

Statistical analyses were performed using SPSS v.28.0 software (SPSS Inc., Chicago, IL, USA). All data were categorical. Descriptive data were expressed as a percentage of a group for discrete measures.

The study was approved by the Ethical committee of the Faculty of Medicine, University of Belgrade (1322V-3) and the research was carried out in compliance with the Declaration of Helsinki.

RESULTS

The mean age of patients at the pathological fracture occurrence was 67.7, with the youngest patient being 42 years old and the oldest 88 years old. Distribution was: <50 y. 5 pts, 51-60 y. 6 pts, 61-70 y. 28 pts, 71-80 y. 18 pts, and >81 y. 6 pts. Male were 34 (49.3%) and female 35 (50.7%).

Twenty-four (34.8%) patients did not know they had a malignant disease, and skeletal-related events (pain and pathological fracture, both simultaneously or separately) were the first manifestation. Other 45 (65.2%) knew they had a tumor, and pathohistological analysis of tumor tissue from the bone confirmed SM. Malignant diseases diagnosed were: breast cancer in 25 pts. (36.1%), lung cancer in 17 pts. (24.5%), kidney cancer in 10 pts. (14.5%), prostate cancer in 9 pts. (13.1%), colorectal cancer in 2 pts. (2.9%), esophagus cancer in 1 pt. (1.5%), stomach cancer in 1 pt, laryngeal cancer in 1 pt, urinary bladder cancer in 1 pt, squamous cell skin cancer in 1 pt, and skin melanoma in 1 pt.

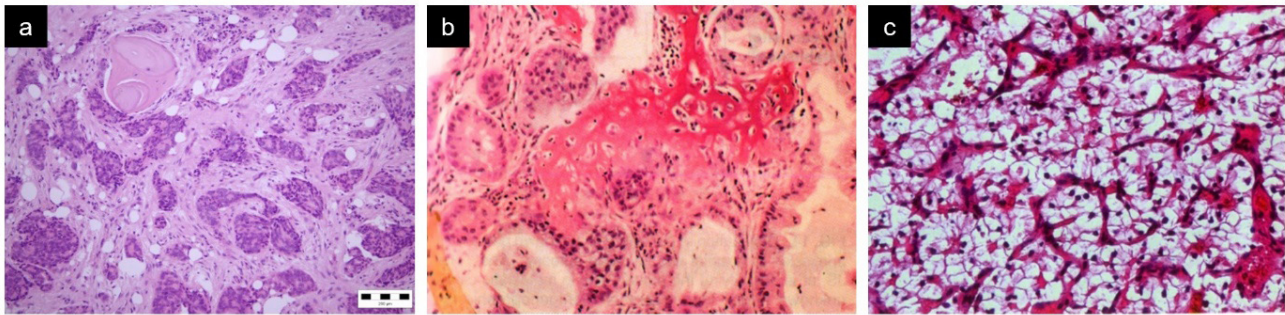


Figure 1. Microphotographs showing a variety of metastatic cancers in bone: a) Clusters of atypical cells with basophilic cytoplasm and nuclear hyperchromasia. Cancellous bone spherule also present - breast cancer SM (HE staining, 200x); b) Adenoid structures in bone tissue. Hypercellular bone with signs of remodeling – lung cancer SM (HE staining, 200x); c) Large cells with light cytoplasm and small excentric nuclei. Characteristic fields of haemorrhage in bone - renal cell carcinoma SM (HE stain, 200x)

The radiological presentation was in the form of lysis in 52 (75.4%) cases and in mixed blastic-lytic form in 17 (24.6%). Blastic-lytic lesions were present in some cases of breast cancer SM, and pure blastic forms were present in all the cases of prostate cancer. All other cancers' SM were lytic.

Operative treatment included arthroplasty in 37 (53.6%) patients and stabilization with nail or plate in 32 (46.4%) patients. Hip hemiarthroplasty and total arthroplasty were used in cases of a femoral neck fracture, and resection megaprosthesis was used in trochanteric region fractures, as in cases of neck fracture where a significant part of the trochanteric region was affected.

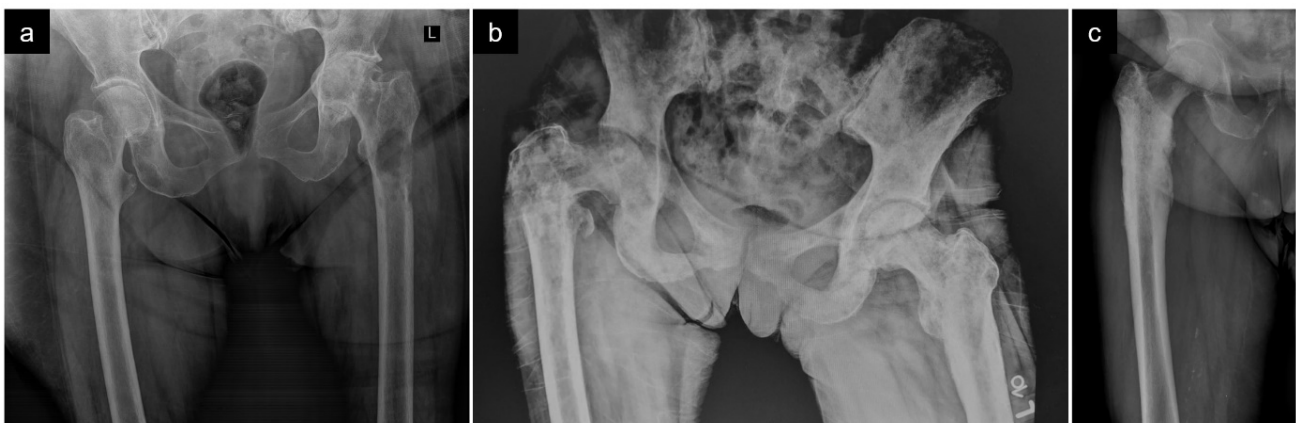


Figure 2. X-ray presentation of bone metastases: a) Lytic lesion in proximal femur – lung cancer SM; b) Mixed lesion with pathological fracture of trochanteric region – breast cancer SM; c) Blastic lesion involving trochanteric region and proximal diaphysis – prostate cancer SM

Table 1. Distribution of bone metastases and type of operative treatment

Bones		Operation				
		RA	IMS	P&S		
Humerus	Proximal	2	/	/		
	Diaphysis	10	9	1		
Radius	Diaphysis	P&S				
		1	1			
Femur	Neck	HA	TA	RA	IMS	
		13	4	2	/	
		7	7	22	7	
Diaphysis	7	7	7	19		
	P&S					
Tibia	Proximal	1	1			
	Distal	1	1			

RA – Resection Arthroplasty, IMS – Intramedullary Nailing Stabilisation, HA – Hip Hemiarthroplasty, TA – Hip Total Arthroplasty, P&S – Plates and Screws Stabilisation

DISCUSSION

The mean age of the patients in this study was 67.7 years. Previous studies showed different ages, most similar to our results (16, 18) and, in rare cases, younger. The mean age of 53.1 years in patients with triple-negative metastatic breast cancer was reported. (19) Most patients in this study were above 50, a significant number even above 70, which is related to bone atrophy (osteopenia/osteoporosis) that can be an important factor in pathological fracture development. (20)

The malignant diseases diagnosed in this study align with earlier findings. (1, 6) Most patients (36.5%) had breast cancer, followed by lung cancer (24.5%) and this incidence matches the familiar data that breast cancer is the most frequent in female population and lung cancer in male population. (21) Colorectal cancer is also widespread in the general population, but it is known that it more often gives visceral metastases than SM, which might be the reason for the low incidence of pathological fractures when it comes to this tumor. (22)

The femur stands out as the most common localization of pathological fractures, with 78.2% of all long bone fractures. As a lower extremity bone, it bears the weight of the entire body, which is especially true of the neck and the trochanteric region of the femur that are exposed to forces unevenly deployed through the bone cortices, making them particularly vulnerable; so even a small loss of the bone tissue in the critical zone can result in a fracture. (23, 34)

Radiological presentation of SM is usually in the form of lysis, although breast cancer SM are present in a blas-

tic form in 20-40% of cases, and prostate cancer SM are always blastic. (9, 25). An earlier standpoint was that lysis represented a higher risk for fracture (17), but recent studies showed that blastic SM also carried a high risk, especially in the proximal femur. (23, 24) The results of this study confirm these findings.

Operative methods used for patient treatment in this series are in line with contemporary standards. (26, 27) The question of osteosynthesis or arthroplasty is still open. (28) The method of choice depends on SM localization, the existing or impending fracture, the degree of bone tissue loss, the patient's general condition, and expected survival. (27) Diaphysis fractures are usually treated by stabilization using an intramedullary nail. Depending on the tissue loss, part of the bone affected by SM can be resected and the defect filled with bone cement. Proximal femur fractures (trochanteric and subtrochanteric region) can be treated by intramedullary stabilization in cases where bone destruction is not significant and femoral neck and head are preserved. (28, 29) In cases where meta-epiphysis is affected, particularly in femoral neck fractures, arthroplasty is indicated. Hemiarthroplasty, total arthroplasty or resection, and megaprosthesis implantation are used in these cases. Besides localization and bone loss, general condition and expected survival of the patient are the factors influencing the choice of the operative method – as a less demanding procedure, intramedullary stabilization is used in cases with more significant bone destruction but where the general condition does not allow the extensive surgical procedure. (27, 29, 30)

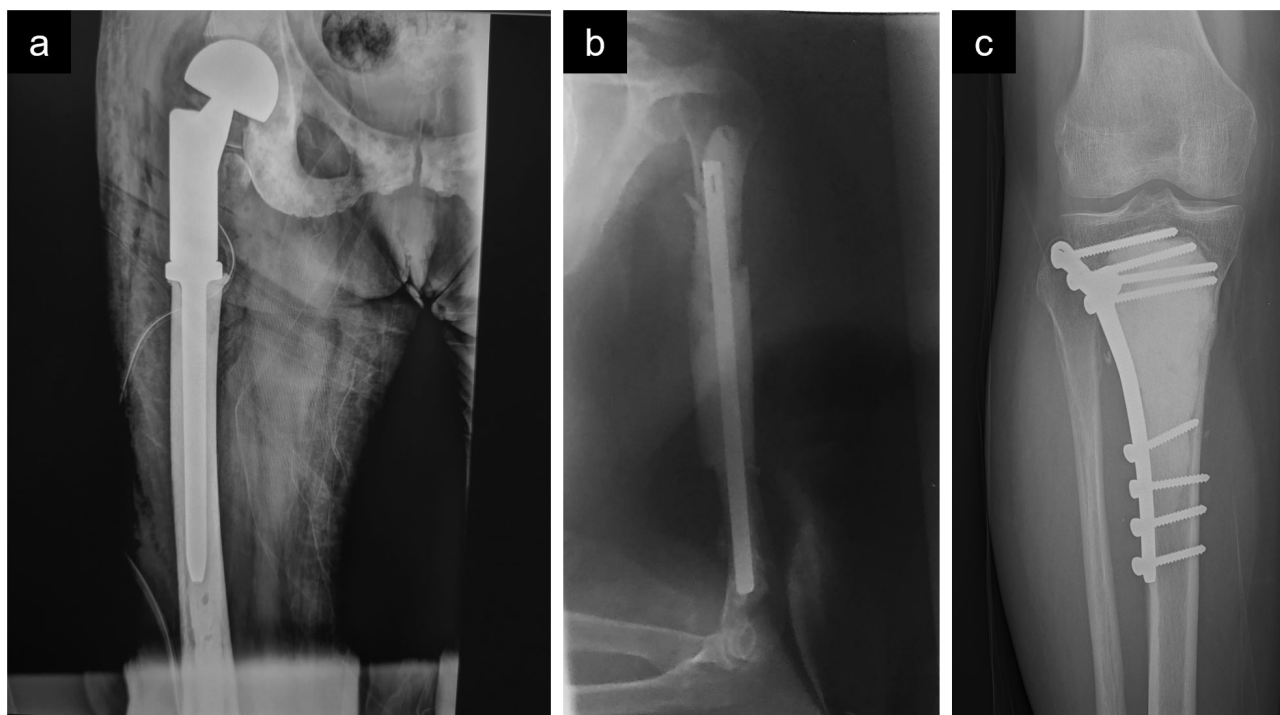


Figure 3. Postoperative X-ray showing different methods of surgical treatment: a) Resection of proximal femur with megaprosthesis arthroplasty – breast cancer SM; b) Intramedullary stabilization with cementing of humerus – lung cancer SM; c) Plate and screws stabilization with cementing of proximal tibia – melanoma SM

In our series, femoral neck fracture was treated by cemented hemiarthroplasty. Cemented total arthroplasty was used in cases of femoral neck fracture with the concomitant degenerative condition or acetabulum damage of any origin. Also, patients with a solitary metastasis in the femoral head or neck in good general condition and with long-expected survival were treated by cemented total arthroplasty. Resection and megaprosthesis implantation were performed in cases where the pathological process was located in meta-epiphysis: head and surgical neck of the humerus and the trochanteric region of the femur. This method was used in cases of femoral neck fracture where pathological processes significantly affected the trochanteric region. Intramedullary stabilization was used in all cases of humerus and femur diaphysis fractures, as well as in some cases of subtrochanteric femoral fracture in patients with the poor general condition and short expected survival. Stabilization using plate and screws with bone defect cementing was used in radius and proximal tibia fractures.

CONCLUSION

Pathological fractures represent the final outcome of tumor activity in a bone. Their occurrence was also the final stage of the disease since patients after these fractures suffered severe pain and were often immobile, which accelerated all the pathological processes and led to death. In the last few decades, joint methods of contemporary chemotherapy, radiotherapy, and surgery enabled significant life quality improvement and extension in these patients.

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Conflict of interest

None to declare.

Contributors

SR was responsible for designing and writing the protocol, conducting the search, collecting surgical data, reviewing other studies in this field, extracting and analyzing data, interpreting results, and writing the report. LM helped in collecting surgical data, reviewing studies, conducting statistical analysis, interpreting the results, and writing the report. LS was responsible for pathologic diagnostics, collecting pathological data, analyzing and interpreting results, and writing the report. GD took part in collecting and analyzing radiological data and analyzing and interpreting results. ZB supervised the collection of surgical data and helped interpret results. JS took part in designing and writing the protocol, supervising pathological data, reviewing previous studies, and analyzing and interpreting results.

Ethical approval

Study was performed with the appropriate participants' informed consent in compliance with the Helsinki Declaration. The Medical Faculty University of Belgrade Research Ethics Committee issued an approval (1322V-3).

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SKELETNE METASTAZE I PATOLOŠKI PRELOMI DUGIH KOSTIJU

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Sažetak

Uvod. Najčešći uzrok patoloških preloma kostiju su metastaze. Deset odsto pacijenata sa dijagnostikovanim metastazama na skeletu će zadobiti patološki prelom. Skeletne metastaze se mogu lečiti nehirurškim metodama, uključujući analgetike, bisfosfonate i radioterapiju, sa primarnim ciljem ublažavanja bolova i usporavanja rasta tumora. Hirurško lečenje je indikovano za postojeće ili preteće prelome. Obuhvata stabilizaciju sa unutrašnjom fiksacijom različitim klinovima, pločama i šrafovim sa ili bez osteoplastike i endoprotetsku zamenu zgloba, posebno kod lezija oko velikih zglobova – kuka, kolena i ramena.

Materijal i metode. Studijom su obuhvaćeni pacijenti operativno lečeni u Institutu za ortopediju „Banjica“ i patohistološki analizirani u Institutu za patologiju u Beogradu u tokom jedne godine, u periodu od februara 2021. do januara 2022. Kriterijumi za uključivanje su bili postojeći ili preteći patološki prelom dugih kostiju, operativno lečenje uz uzimne uzorka i posledičnu patohistološku dijagnozu metastaze nekog karcinoma. Iz

studije su isključeni pacijenti sa patohistološki dokazanim procesima koji nisu metastatski karcinomi. Ukupan broj pacijenata uključenih u studiju bio je 69.

Rezultati. Prosečna starost pacijenata u vreme nastanka patološkog preloma bila je 67,7 godina (u rasponu od 42 do 88 godina). Dijagnostikovane maligne bolesti su: karcinom dojke 36,1%, pluća 24,5%, bubrega 14,5%, prostate 13,1%, kolorektalni 2,9%, „ostali“ (8,9%). Radiološki prikaz je bio u obliku osteolize u 75,4% slučajeva i blastičnom obliku u 24,6%. Operativno lečenje uključivalo je artroplastiku kod 53,6% pacijenata i stabilizaciju klinom ili pločom kod 46,4%.

Zaključak. Patološki prelomi predstavljaju krajnji ishod tumorske aktivnosti u kosti i izazivaju značajnu patnju kod pacijenata izraženu jakim bolom i često nepokretnošću, što ubrzava sve patološke procese i dovodi do smrti. Zajedničke metode savremene hemoterapije, radioterapije i hirurģije omogućile su značajno poboljšanje i produženje kvaliteta života ovih pacijenata.

Ključne reči: skeletne metastaze, patološki prelom, hirurška terapija

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