An Original Study

Characterization and Surgical Management of Metastatic Disease of the Tibia

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Abstract

Osseous metastases are common in advanced cancer stages. The tibia is the appendicular skeleton bone affected third most often. However, tibial metastases are not well described.

We conducted a retrospective descriptive single-institution study of patients with evidence of tibial metastatic disease in order to better characterize tibial metastases in their anatomical distribution and histology, and to describe their clinical presentation and surgical management. Using proprietary research software, we searched pathology and radiology reports and cross-referenced results with *Current Procedural Terminology* procedure codes to identify patients with metastatic lesions of the tibia. We then reviewed these patients' medical records and reviewed and verified all available imaging.

We reviewed the medical records of 36 patients (20 females, 16 males) with 43 affected tibiae. Mean age was 63.5 years. Of 12 different primary neoplasms, the most common were prostate, breast, and lung cancers. The proximal tibia was the region most commonly affected, followed by the diaphysis. Of 6 impending fractures, 3 were treated with intramedullary nail, 2 with total knee megaprosthesis, and 1 with total knee arthroplasty. Of 2 pathologic fractures, 1 was treated with intramedullary nail and 1 with periarticular locking plate. Almost all identified patients (88.9%) had other metastatic lesions. Almost half (47.2%) of patients presented with symptomatic tibia lesions. Mean time from diagnosis of malignancy to tibial metastasis was 1282 days (range, 0-3708 days).

Metastases to the tibia are uncommon but often require surgical intervention. Fixation technique should be selected on a case-by-case basis, and patients should be treated by a multidisciplinary team. Patients with known malignancy and tibial pain should undergo a work-up for tibia lesions.

Metastatic dissemination to bones is common in advanced cancer stages and affects the axial and appendicular skeleton.[1-4] The appendicular skeleton bones most often involved are the proximal femur and the proximal humerus.[5,6] The tibia is involved third most often but is comparatively rarely affected.[4-6] Metastatic involvement distal to the knee or elbow is more typical of advanced disease.[1,3] Distal appendicular lesions are called *acral metastases,* but the term is inconsistently used and may refer to lesions either distal to the knee and elbow or distal to the ankle and wrist. Regardless of terminology, tibia lesions are uncommon and not well described.[1,4,7,8]

The tibia is the primary weight-bearing leg bone. Metastatic tibia lesions may cause pain and instability and impair mobility. Although distal skeletal dissemination often presents late in advanced disease in patients with relatively poor prognoses, in some cases early surgical intervention is indicated for pain relief, increased mobility, and improved quality of life.[4,8-10]

Materials and Methods

Our Institutional Review Board approved this single-institution retrospective study. We used proprietary research software (Clinical Looking Glass) to identify eligible patients treated between 2000 and 2013. The software was used to search all radiology and pathology reports for the term *tibia* or any variation (eg, *tibial*) and *metastasis* or any variation (eg, *metastatic*). The software was then used to search by *Current Procedural Terminology* code for any patients treated with intramedullary nail (IMN)

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Take-Home Points

- Metastatic disease of the tibia is a rare but significant event in a subset of patients.
- Cancer histologies with historically "acral" spread may not apply to tibial disease.
- Patients with leg pain and any cancer diagnosis should be worked up for tibial metastases.
- Tibial disease is probably a late manifestation, and early detection may indicate late diagnosis of malignancy.
- The ultimate surgical plan for these patients should be a patient-centered multidisciplinary decision making process.

or another tibial fixation method. This list was cross-referenced with the list of patients originally identified to help ensure that all eligible patients were identified.

Inclusion criteria were known malignancy and imaging or biopsy evidence of a metastatic tibia lesion. Treatment strategies for patients with metastatic disease and patients with multiple myeloma are sometimes considered together because of similar goals and methodologies. We specifically excluded patients with multiple myeloma in order to more accurately characterize the natural history of metastatic disease and the timing of metastatic development and to report on a more homogeneous population. Patients were excluded if their electronic medical records were inadequate in establishing a diagnosis.

Demographic and pathology data were collected directly from the institutional electronic medical records system. Dr. Geller and Dr. Greenbaum used Centricity software (General Electric Healthcare) to review all imaging on medical diagnostic display monitors. If their interpretation differed from that in the radiology report, or if clarification was needed, the study was sent to Dr. Thornhill, the institution's director of musculoskeletal radiology, for review and interpretation. Investigated radiographic characteristics included location, cortical breakthrough, presence of fracture, and size (if advanced imaging was available). Surgical interventions were recorded from reviews of operative reports and postoperative imaging studies.

Time to metastasis was defined as number of days from diagnosis of malignancy to diagnosis of tibial osseous spread. Date of diagnosis of malignancy was the date that a biopsy or other confirmatory test was performed. In cases in which that date was unavailable, an imaging study consistent with disease or a clinical note documenting the known diagnosis date was used instead. When only month and year (ie, not an exact date) of diagnosis were available, the 15th of the month was used as an estimate. Of the 36 patients, 4 had records insufficient for establishing date of diagnosis. The first date of any imaging study confirming (or suggestive of) a metastatic lesion of the tibia was used as the date of tibial metastasis.

Many patients had osseous lesions at sites other than the tibiae. These lesions were noted on review of imaging studies, screening examinations, and physicians' clinical notes. Widespread disease was defined as including both axial and appendicular lesions, and lesions of the tibiae.

Tibia lesion presentation was recorded as either *symptomatic* or *incidental*. If the tibiae were imaged for pain, including posttraumatic pain, the presentation was symptomatic. If a lesion was identified on staging examination (eg, bone or positron emission tomography scan), or if the tibiae were imaged for another reason, the presentation was incidental.

Results

Demographics

Thirty-six patients had 43 affected tibiae. Sixteen male patients (44.4% of the total) had 19 (44.2%) of the affected tibiae, and 20 female patients (55.6%) had the other 24 affected tibiae (55.8%). Mean age was 63.5 years for all patients (range, 6-95 years), 68.1 years for males, and 59.8 years for females. Of the 36 patients, 32 (88.9%) were over age 40 years (**Table**). All patients had radiographic evidence of ≥1 tibia lesion, and 6 (16.7%) also had biopsy-proven metastatic disease of the tibia.

Tumor Characteristics

There were 12 different primary neoplasms (Table). The most common were prostate cancer (7 patients, 19.4%; 10 tibiae, 23.3%), breast cancer (7 patients, 19.4%; 9 tibiae, 20.9%), and lung cancer (7 patients, 19.4%; 7 tibiae, 16.3%). For males, the most common diagnoses were prostate cancer (7 cases, 43.8% of males) and diffuse large B-cell lymphoma and lung cancer (3 cases and 18.8% of males each). For females, the most common diagnoses were breast cancer (7 cases, 35.0% of females) and lung cancer (4 cases, 20.0% of females).

Most of the lesions were proximal (31 tibiae, 72.1%), followed by diaphyseal (7, 16.3%) and distal (2, 4.7%) (Table). Three tibiae (7.0%) were entirely involved, but 1 of these was more affected at the distal end. One tibia had 2 lesions, 1 proximal and 1 distal.

Time to Metastasis, Other Osseous Disease

Mean time from diagnosis of malignancy to diagnosis of osseous disease of the tibia was 1282 days (range, 0-3708 days) (Table). Of the 36 patients, 32 (88.9%) had other metastatic lesions, 3

Table. **Patient Data**

Pt	Primary Malignancy	Age, y	Sex	Tibiae Involved, n	Other Osseous Disease	Days to Metastasis	Clinical Presentation	Cortical Breakthrough	Fracture	Tibial Location	Hardware
1	Neuroblastoma	6	F	2	Bilateral femora	1667	Incidental	No	No	Proximal	N/A
2	Hodgkin lymphoma, nodular sclerosing	20	F	1	Femur	63	Incidental	No	No	Proximal	N/A
3	Spindle cell sarcoma	24	M	1	Femur	231	Incidental	No	No	Proximal	N/A
4	Neuroblastoma	37	F	2	Bilateral femora	133	Pain	No	No	Proximal	N/A
5	Lung	41	F	1	Femur	?	?	Yes	No	Proximal	Total knee arthroplasty, cemented
6	Breast	42	F	1	Widespread	3474	Incidental	No	No	Distal	N/A
7	Colon	46	M	1	Ipsilateral femur, fibula	?	Pain	No	No	Proximal	N/A
8	Lung (NSCLC)	51	M	1	Ipsilateral foot	1014	Pain	Yes	No	Proximal	N/A
9	Lung	53	F	1	Bilateral femora	0	Pain	Yes	No	Diaphyseal	Intramedullary nail
10	Breast	54	F	2	Widespread	3189	Incidental	No	No	Proximal	N/A
11	Breast	57	F	2	Widespread	272	Incidental	No	No	Entire tibia	N/A
12	Diffuse large B-cell lymphoma	57	M	1	Axial	0	Incidental	No	No	Proximal	N/A
13	Breast	59	F	1	Bilateral femora	3708	Incidental	No	No	Proximal	N/A
14	Endometrial	60	F	1	Femur	176	Incidental	Yes	No	Proximal	Total knee megaprosthesis, cemented
15	Lung (NSCLC)	61	F	1	None	0	Mass	No	No	Diaphyseal	N/A
16	Colon	61	M	1	None	275	Pain	Yes	No	Proximal	Total knee megaprosthesis, cemented
17	Lung (NSCLC)	62	M	1	None	22	Pain	Yes	No	Proximal	Intramedullary nail, screw-plate construct, cement
18	Melanoma	65	F	1	Femur	372	Pain	No	No	Diaphyseal	N/A
19	Prostate	67	M	1	?	?	Pain (trauma)	No	No	Proximal	N/A
20	Prostate	70	M	2	Widespread	2507	Incidental	No	No	Proximal	N/A
21	Breast	72	F	1	Widespread	2417	Incidental	No	No	Proximal	N/A
22	Lung (NSCLC)	73	F	1	Widespread	0	Pain (trauma)	Yes	Yes	Proximal	Periarticular locking plate, cement
23	Prostate	74	M	1	Widespread	1110	Incidental	No	No	Proximal	N/A
24	Rectal	76	F	1	Ipsilateral foot	1596	Pain	Yes	No	Entire tibia	N/A
25	Diffuse large B-cell lymphoma	76	M	1	Ipsilateral foot, fibula	2081	Pain	No	No	Diaphyseal	N/A
26	Diffuse large B-cell lymphoma	76	M	1	Widespread	1948	Pain	No	No	Proximal	N/A
27	Uterine	78	F	1	Ipsilateral foot	599	Pain	Yes	No	Distal	Intramedullary nail, cement
28	Prostate	79	M	1	Widespread	2969	Incidental	No	No	Proximal	N/A
29	Prostate	80	M	1	Axial	28	Pain	No	No	Diaphyseal	N/A
30	Carcinoid	80	F	1	Ipsilateral femur	2262	Pain	No	No	Proximal	N/A
31	Breast	81	F	1	Widespread	?	Pain (trauma)	No	No	Diaphyseal	N/A
32	Prostate	84	M	2	Widespread	1048	Incidental	No	No	Proximal	N/A
33	Prostate	87	M	2	Widespread	849	Incidental	No	No	Proximal	N/A
34	Urothelial	88	F	1	Ipsilateral scapula	2563	Pain	Yes	Yes	Diaphyseal	Intramedullary nail
35	Breast	93	F	1	Widespread	1885	Incidental	No	No	Proximal	N/A
36	Lung (NSCLC)	95	M	1	Widespread	2575	Incidental	No	No	Proximal	N/A

Abbreviations: N/A, not applicable; NSCLC, non-small cell lung cancer; ?, data unavailable.

(8.3%) had isolated tibia lesions, and 1 (2.8%) had a medical record insufficient for establishing lesion status (isolated or not). Of the 32 patients with known other osseous metastases, 14 (43.8%) had widespread (axial and additional appendicular) disease, and 3 (9.4%) had additional lesions only distal to the identified tibial metastases.

Clinical Presentation

Of the 36 lesions, 18 (50%) were asymptomatic and were found on screening examinations, 17 (47.2%) presented with pain, and 1 (2.8%) had a presentation that could not be determined from the medical record (Table). Of the 17 painful lesions, 3 (17.6%) were found after a trauma brought attention to the site, and the other 14 (82.4%) were atraumatic in origin.

Of the 10 patients with cortical breakthrough, 8 (80%) had painful lesions, 1 (10%) had a lesion that was found on screening examination, and 1 (10%) had a medical record insufficient for establishing clinical presentation. Of the 8 patients who underwent surgical stabilization, 6 (75%) had painful lesions. Only 1 patient with an asymptomatic tibia lesion underwent surgical intervention (total knee arthroplasty).

Surgical Intervention

Two patients (5.6%) with affected tibiae (4.8%) had pathologic fractures. One fracture (non-small cell lung cancer) was treated with open reduction and internal fixation (periarticular locking plate with cement augmentation), and the other (urothelial cancer) was treated with IMN fixation.

Ten patients (27.8%) with affected tibiae (23.8%) had radiographs that showed cortical breakthrough (Table). Two of the 10 cases were managed nonoperatively, and the patients died before surgical stabilization could be attempted. Of the 8 surgically managed cases, 3 were prophylactically stabilized with IMN (2 of these were augmented with cement, and the third with a screw-plate construct), 2 were treated with periarticular resection and reconstruction (total knee megaprosthesis), 1 was treated with an approach undertaken to address a concomitant distal femoral pathologic fracture, and 1 was treated with total knee arthroplasty undertaken to address lesions at the proximal end of the tibia and the distal end of the femur.

Discussion

We have described a retrospective descriptive study conducted to characterize tibial metastases, their histologies, and the circumstances surrounding diagnosis and surgical management. In all cases, general findings confirmed advanced metastatic disease. In only 3 cases, the tibia lesion was an isolated metastatic lesion.

Sex predilection of tibial metastases remains controversial. One study found males had up to twice as many hand and foot metastases as women,[11] but this contrasts with the relatively equal sex ratio found in other studies[8,10] and in the present study. We found metastatic disease of the tibia was unsurprisingly concentrated in patients over age 40 years, in whom the vast majority of all cancers develop.[12,13] Our study agrees with those that have found most tibia lesions develop in patients in the 6th decade of life on average.[8,10] Mean age was 8.3 years higher in our male patients than in our female patients.

Tumor Characteristics

The most common primary neoplasms in our cohort were prostate, breast, and lung cancers, which are among the most common cancers in the United States[12,13] and which have a predilection for osseous spread.[2,6,9,14] Renal cell carcinoma has been reported to spread to distal (or "acral") skeletal sites,[2-4,9,11,14] but the present study did not identify any patients with this diagnosis. Of our patients with a primary lung cancer for whom a histologic description was available (5/7), all had non-small cell lung cancer. Three patients had a primary malignancy of colorectal cancer, which occasionally metastasizes to the distal skeleton.[3,8,11] We identified 3 patients with diffuse large B-cell lymphoma, a histology not widely reported to metastasize to distal skeletal sites.

Metastatic disease of the tibia is most common at the proximal end of the bone.[1,10,11,14] Other studies[8,10] have found the proximal tibia is affected much more commonly than the tibial diaphysis, and even fewer cases develop at the distal end. Our findings agree with theirs: Proximal lesions outnumber all other lesions combined (Table).

Time to Metastasis

Distal metastases are typical of late-stage metastatic disease,[1,3] but quantification of the time from diagnosis of malignancy to presentation of a tibia lesion is not well defined. In our study, time to metastasis was <100 days for some patients (Table). As osseous involvement, especially acral disease, was considered a late-stage manifestation of malignancy, this result was unexpected and most likely

represents undiagnosed and untreated malignancy. Six patients in this group were diagnosed with tibial metastases within 30 days, essentially at the same time the primary neoplasm was diagnosed. These findings suggest that a tibia lesion found at time of patient presentation should raise concern for late-stage undiagnosed metastatic cancer.

Other Osseous Disease

The patients identified in this study had advanced malignancy, and most had widespread bony dissemination. Those with the lowest disease burden had isolated tibia lesions or additional metastases only distal to the tibia lesion in the ipsilateral lower extremity. Most of these patients had undergone surgery or were scheduled for it (Table). Most of the patients with appendicular metastases proximal to the tibia lesion had disease of the femora, the most common long bones affected by osseous metastatic disease.[5,6] In accordance with orthopedic oncology principles, all other osseous disease should be thoroughly identified and staged before any surgical planning for identified tibia lesions. Ipsilateral distal femoral lesions are of particular importance for patients with proximal tibia lesions, as reconstruction with total knee endoprosthesis can potentially provide a functional reconstructive option after resection of both lesions.

Clinical Presentation

Most of the patients who had cortical breakthrough or required surgical stabilization had painful lesions. Although tibial metastasis is rare, its potential occurrence should raise concerns and be investigated in the patient with tibial pain.

Surgical Intervention

General surgical management of metastatic disease of other long bones has been extensively studied,[6,7,9,14] but there are fewer published recommendations regarding specific treatments for metastatic lesions of the tibia. In 2003, Kelly and colleagues[8] described an algorithm based on the anatomical location of the lesion, with either internal fixation or IMN fixation representing the preferred management for lesions in the metaphyseal or diaphyseal regions. For epiphyseal or extensive proximal metaphyseal lesions, modular oncology endoprostheses are described as the procedure of choice. Piccioli and colleagues[10] in 2013 and Beauchamp and Sim[1] in 1988 described a similar operative approach.

It is unknown if the algorithm of Kelly and colleagues[8] was referenced during clinical decision-making, but it appears operative management mirrored these principles. Deviations from this general approach in the operative management of the patients in the present study included modifications such as the addition of a screw-plate construct to an IMN for better stability.

Surgical management depends largely on the anatomical location within the bone and on remaining bone stock. Generally, extensive proximal disease is managed with total knee endoprosthesis reconstruction, diaphyseal disease with IMN, and distal disease with internal fixation. Construct augmentation, such as the addition of cement or use of additional hardware, is decided case by case on the basis of desired stability and surrounding bone stock.

Study Limitations

Despite being a larger series, this single-institution study had a relatively small sample size, and its patient demographics and primary malignancies may reflect institutional recruitment bias. In addition, the study was limited by its retrospective design and some incomplete medical records. Eleven patients had only a bone or positron emission tomography scan depicting metastatic disease, limiting characterization of these lesions. One patient lacked radiologic images, and characterizations were based on written reports. As multiple physicians were involved in diagnosis and treatment, there were many inconsistencies in clinical decision-making across the group.

Conclusion

Metastasis to the tibia is a rare but significant event in a subset of patients over the course of their treatment and surveillance. Patients may present with pain secondary to either pathologic or impending pathologic fractures, and in such instances surgical intervention is often needed. Despite the historical reports of "acral" histologies, tibia lesions are not indicative of histology, and biopsy should be considered, especially if management will depend on histology. Patients with lower leg pain and known malignancy should be evaluated to rule out tibial metastasis, but screening examinations may be prudent for asymptomatic patients as well. Increased vigilance may be indicated for those with prostate, breast, or lung cancer. These lesions should be surgically managed case by case using fundamental tenets of both orthopedic fracture care and orthopedic oncology. Ideally, patients should be treated by

a multidisciplinary team using a patient-centered approach.

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