Malignant bone tumours of the foot

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ABSTRACT

INTRODUCTION Malignant osseous foot tumours are uncommon. Their oncological outcomes have been poorly documented in the literature so far. The aim of this study was to establish the incidence and to evaluate the oncological outcomes of such patients.

METHODS Our large orthopaedic oncology database was used to review 70 malignant osseous foot tumour patients.

RESULTS The age at diagnosis of malignant osseous foot tumours demonstrated a bimodal distribution peaking in the second and eighth decades of life. Overall, 55 primary malignant bone tumours of the foot (79%) were identified. The median duration from onset of symptoms to diagnosis was 52 weeks (interquartile range [IQR]: 17–104). Eight primary tumours (15%) underwent an accidental excision (ie intralesional excision of a malignant bone tumour where some of the tumour has been left behind, also known as a ‘whoops procedure’) prior to referral to our unit. Forty-six patients (84%) underwent surgery overall and thirteen of these developed recurrence or metastases. Seven of eight patients with a previous accidental excision underwent amputation.

Fifteen osseous metastatic foot lesions were identified. The median length of foot symptoms to diagnosis was 24 weeks (IQR: 20–36 weeks). The median time to death following diagnosis of osseous foot metastases was 20.1 months (IQR: 11.3–27.8 months).

CONCLUSIONS A high index of suspicion and awareness of clinical features of malignant osseous foot tumours are both essential to avoid diagnostic delays. Amputation is associated with a respectable outcome for patients who have undergone previous accidental excisions.

KEYWORDS

Bone tumour – Foot – Malignancy – Primary – Metastasis

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Bone tumours of the foot are uncommon, constituting less than 4% of all neoplasms.^{1,2} Only 15–25% of bony foot lesions are malignant,³ making it easy for clinicians to underestimate the malignant potential of an abnormality of the foot. Delays in diagnosis of malignant bony foot tumours may worsen the prognosis and late presentation potentially modifies treatment strategies towards amputation rather than limb salvage.^{4,5}

There have been few reports of large series documenting malignant foot tumours in the literature so their incidence and clinical outcomes remain poorly established. Most studies published so far have focused on soft tissue sarcomas of the foot rather than osseous malignancies.^{6–8}

The present study reviewed our experience with malignant bone tumours of the foot seen at our supraregional sarcoma unit over a 30-year period. The primary objective was to establish the presenting features and incidence as well as evaluating the clinical course and oncological outcomes of malignant osseous foot tumours.

Methods

Our unit maintains a prospective tumour database containing over 40,000 patients, including 4,000 patients with a

bone sarcoma. Using this database, a retrospective search of a 30-year period (1985–2015) was conducted to identify patients with a malignant tumour of the foot. Patients with metastatic lesions to the feet were also included in the study. All haematological malignancies were excluded. Patients' age and sex were recorded, alongside anatomical location, histology, treatment modality, treatment response, complications, previous accidental excisions (ie intralesional excision of a malignant bone tumour where some of the tumour has been left behind, also known as a ‘whoops procedure’), disease recurrence and length of survival.

Overall survival was determined as the interval in months from diagnosis to death or to the date of the last clinic visit. It was assessed using the Kaplan–Meier method. Statistical interpretation was performed for categorical data using the chi-squared test. An alpha value of 0.05 was considered statistically significant.

Results

A total of 239 patients with foot malignancy were diagnosed and treated at our unit over the 30-year study period. There was an equal distribution of male and female patients. Of the 70 patients (29%) who had a malignant tumour involving

bones of the foot, 55 (79%) had primary malignant lesions and 15 (21%) had metastatic lesions. The remaining 169 patients had a soft tissue sarcoma affecting the foot. Our institution serves a population of 15 million. This implies that the overall incidence of primary osseous foot malignancy was 0.12 cases per year per million people.

The age at diagnosis of malignant bone tumours demonstrated a bimodal distribution peaking in the second and eighth decades of life (Fig 1). The median age of presentation for primary bone tumours was 37 years (interquartile range [IQR]: 16–57 years). Ewing’s sarcoma most commonly affected young patients, with a median age at diagnosis of 15 years (IQR: 12–26 years). Comparatively, chondrosarcomas, osteosarcomas and bone metastases affecting the foot were diagnosed later in life (Table 1).

Primary malignant bone tumours of the foot

Primary malignant tumours were found in 27 female and 28 male patients. Eight patients were referred to our unit following an accidental excision at their referring hospitals. Overall, 20 primary tumours (36%) were Ewing’s sarcomas, 25 (46%) were chondrosarcomas (6 low grade, 17 intermediate grade, 1 high grade, 1 dedifferentiated) and 10 (18%) were osteosarcomas (2 low grade central, 4 parosteal, 4 high grade). Grouped according to regions of the foot, 15 primary bone tumours (27%) were located in the hallux, 22 (40%) in the metatarsals, 4 (7%) in the midfoot and 14 (25%) in the hindfoot (Table 2). The forefoot was affected statistically more significantly than the mid or hindfoot ($p=0.04$).

The predominant symptoms of primary osseous foot tumours were non-mechanical pain. Some patients had associated swelling, irrespective of tumour site or histology. The median interval between onset of symptoms and diagnosis of primary malignant bone tumours of the foot was 52 weeks (IQR: 17–104 weeks). Chondrosarcomas presented with the longest duration of symptoms prior to diagnosis (median: 104 weeks, IQR: 52–156 weeks), followed by osteosarcomas (median: 44 weeks, IQR: 28–78 weeks) and Ewing’s sarcomas (median: 26 weeks, IQR: 12–30 weeks).

Four (20%) of twenty cases of Ewing’s sarcoma presented with metastases at diagnosis (2 to lungs, 1 to lung and other bones, 1 to multiple sites). Only one case of osteosarcoma was metastatic at diagnosis. No chondrosarcomas presented with metastases.

The management of all primary malignant tumours of the foot was decided following multidisciplinary discussion. Neoadjuvant and adjuvant chemotherapy as well as

Figure 1 Age at diagnosis of malignant bone tumours.

radiotherapy were administered according to standard protocols for Ewing’s sarcoma and osteosarcoma. Overall, 46 patients (84%) underwent surgery. This was combined with chemotherapy in nine cases (20%). Eighteen patients had hallux amputations, eighteen had below-knee amputations, five had ray amputations, two underwent resections with biological reconstruction and three underwent intralesional curettage for low grade tumours. Subsequently, six patients (4 Ewing’s sarcomas, 1 chondrosarcoma, 1 osteosarcoma) developed local recurrence and a further seven patients (13%) developed metastases. Overall, 8 of these 13 patients with disease recurrence died.

Of the patients who developed local recurrence, three had primary lesions in the metatarsals, one in the cuboid and two in the calcaneus. Interestingly, two (33%) of these patients underwent ray amputations with wide margins before developing recurrence and one had a below-knee amputation. Of the seven patients who developed metastases, two had primary lesions in the hallux, one in the navicular, two in the talus and three in the calcaneus. Three of these patients initially underwent below-knee amputations for their primary lesions, two had hallux amputations and the remaining patients received chemotherapy only.

Of the eight patients who initially underwent an accidental excision, three had ray amputations, three had below-knee amputations, one had a toe amputation and one received only chemotherapy owing to being too frail for surgery. The latter patient subsequently developed local recurrence and another patient who had a ray amputation developed metastasis. These 2 patients (25%) eventually

Table 1 Average age at presentation, duration from onset of symptoms to diagnosis and survival rates by tumour type			
Tumour type	Median age at presentation	Median duration of symptoms	Survival rates
Ewing’s sarcoma	15 yrs (range: 1–45 yrs)	26 wks	58% at 5 and 10 yrs
Chondrosarcoma	56 yrs (range: 19–89 yrs)	104 wks	74% at 5 yrs, 64% at 10 yrs
Osteosarcoma	50 yrs (range: 14–70 yrs)	44 wks	68% at 5 and 10 yrs
Metastases	67 yrs (range: 14–83 yrs)	48 wks	N/A

Table 2 Frequency of tumours by tumour type and region of the foot				
Site	Ewing's sarcoma (n=20)	Chondrosarcoma (n=25)	Osteosarcoma (n=10)	Metastases (n=15)
Hallux (n=15)	3	10	2	0
Rays (n=25)	8	9	5	3
Midfoot (n=12)	2	1	1	8
Hindfoot (n=18)	6	5	3	4

died at 38 months and 55 months respectively following diagnosis but the remaining 6 patients have survived at least 5 years following amputation.

Of all patients who died, the median time to death was 19 months (IQR: 17–25 months) for Ewing's sarcoma, 47 months (IQR: 44–68 months) for chondrosarcoma and 27 months (IQR: 24–31 months) for osteosarcoma. The Kaplan–Meier survival estimate for both five and ten years for Ewing's sarcoma was 57.9% (95% CI: 39.5–85.0%). For chondrosarcoma, the Kaplan–Meier five-year estimate was 74.2% (95% CI: 58.4–94.3%) while the ten-year estimate

was 63.6% (95% CI: 46.1–87.7%). For osteosarcoma, the survival estimate for both five and ten years was 67.5% (95% CI: 43.0–100%). The Kaplan–Meier survival curves are shown in Figure 2.

Metastatic bone tumours of the foot

Of the 15 patients (9 female, 6 male) with osseous metastatic lesions to the foot, 12 had metastases in the mid or hindfoot while the remaining 3 patients had lesions in the forefoot (Table 2). The median duration of foot symptoms to diagnosis was 24 weeks (IQR: 20–36 weeks). The disease free

period from diagnosis of primary malignancy to the detection of bony foot metastases ranged from 7 to 64 months (mean: 19.3 months).

Only four patients (27%) with osseous foot metastases had primary lung carcinoma. Two patients (13%) had primary breast malignancy and nine (60%) had infradiaphragmatic primary lesions (2 in bladder, 2 melanomas, 1 uterine, 1 anal, 1 vaginal, 1 rhabdomyosarcoma). Three patients (20%) with bony foot metastases presented with no history of previous malignancy and the sites of their primary tumours were only determined following biopsy. In 12 patients (80%), foot metastasis was the only metastasis apparent at the time of presentation. Only three patients (20%) were found to have additional metastases in sites other than the feet. Nine patients (60%) underwent palliative radiotherapy to the feet, three (20%) underwent amputation and three (20%) were managed palliatively. The median time to death following diagnosis of osseous foot metastases was 20.1 months (IQR: 11.5–27.8 months).

Discussion

Malignant bone tumours of the foot are rare, and the epidemiology and clinical outcomes have not been extensively studied in the literature. This study reviewed the clinical course of 70 malignant bone tumours of the foot over a period of 30 years in our supraregional sarcoma unit. In our experience, 79% of malignant bone lesions affecting the foot were primary tumours and the remaining 21% were bone metastases. Our institution has a catchment population of 15 million and the incidence of primary bone tumours of the foot is 0.12 cases per year per million people.

All malignant bone tumours of the foot presented with non-mechanical pain and some with associated swelling. Chondrosarcomas were the most frequent primary tumour to affect the foot (46%) and osteosarcomas were the least frequent (18%) at our unit. The majority (67%) of primary tumours were located in the forefoot whereas the majority (80%) of metastases were located in the mid or hindfoot. This highlights that symptoms of non-mechanical pain in any region of the foot could potentially indicate osseous malignancy.

An increasing number of studies have shown that otherwise healthy young individuals are presenting with malignant foot tumours.^{9–11} In our cohort, the age of diagnosis of malignant bone tumours of the foot peaked in the second and eighth decades of life. This was also found in a review by Khan *et al.*⁵ Furthermore, our findings that Ewing's sarcomas commonly present in the second decade of life whereas chondrosarcomas and osteosarcomas usually present between the fourth and sixth decades are supported by those of Bos *et al.*⁴

This age of presentation of osteosarcomas of the foot is contrary to the usual age of presentation in the rest of the appendicular skeleton (second and third decades of life).¹² We cannot explain this observation although Choong *et al* reported similar findings.¹³ It is therefore important to raise the clinical suspicion of foot malignancy in patients of any age in order to reduce the risks of a delayed diagnosis.

Aside from their relatively low prevalence, malignant bone tumours of the foot can also often be misdiagnosed owing to the variety of potential differential diagnoses. Bisaglia *et al* described a series where there was initial misdiagnosis of 6 out of 12 osteosarcoma cases.¹² In addition, a study by Adkins *et al* found that 11 of 16 Ewing's sarcoma patients had initial misdiagnoses.¹⁴ The most common symptoms of malignant bone tumours of the foot include pain or a palpable swelling.^{15,16} However, these are frequently misdiagnosed as a benign condition such as osteoarthritis, rheumatoid arthritis or a benign tumour.¹⁵ Clinical suspicion may only increase if a swelling that has remained dormant for many years suddenly becomes symptomatic or starts growing; this can result in a delayed diagnosis.¹⁷

Our series confirmed that patients with either a primary tumour or metastasis often suffer from protracted symptoms before establishing a correct diagnosis. The overall duration of symptoms prior to diagnosis of malignant bone tumours of the foot ranged from 4 to 780 weeks. The median duration was 52 weeks. Chondrosarcomas are the most slow growing of these tumours⁴ and therefore have the most prolonged duration of symptoms.

Worryingly, 15% of the primary bone malignancies in the foot had undergone accidental excision prior to being referred to our unit. Six of the eight patients who received an accidental excision had a chondrosarcoma of the forefoot. This reflects the difficulty in distinguishing between benign and malignant lesions in the foot region based on clinical history and examination alone. Many studies have reported that differentiation of chondrosarcomas from benign cartilage tumours may even prove difficult on histology for an experienced pathologist.^{18–21} Despite this, our study shows that chondrosarcoma patients still have the longest average length of survival compared with those with any other bony foot malignancy.

Surgical amputation was performed in 73% of our cohort of patients with primary malignant bone tumours of the foot, regardless of tumour histology or site. Amputation may be in the form of below-knee amputation for midfoot or hindfoot involvement, or ray amputation for toes or metatarsals. The majority (82%) of patients who underwent amputation had no local recurrence or metastases. The remaining 18% may have had occult metastases that were not detected or removed at the time of surgery.

Amputation is particularly appropriate for Ewing's sarcoma and osteosarcoma as these tumours are less amenable to limb sparing surgery because of poor tumour compartmentalisation in the foot and difficulty in achieving adequate resection margins.^{2,5,15} In our experience, amputation was an appropriate management option for patients with accidental excision. Seven of the eight patients who were referred with initial accidental excision subsequently underwent amputation. This achieved a five-year survival rate of 75% with no local recurrence or metastases.

A third (31%) of our cohort of patients with osseous foot malignancy died within five years of diagnosis. The mean time to death overall was 28.2 months. Local recurrence developed in 10.9% of patients and a further 12.7% developed metastases. Comparatively, 14–25% of patients with

soft tissue sarcomas of the foot die within ten years of diagnosis.^{22–24} The recurrence rate can be up to 12%.²⁴ This reflects a worse prognosis for patients with osseous sarcomas of the foot than for those with soft tissue sarcomas.

Our finding that Ewing's sarcoma has the worst prognosis of malignant osseous foot tumours (despite most frequently affecting the youngest patients) concurs with that of O'Connor and Pritchard.²⁵ Our study reflects that this tumour has the shortest median time to death compared with any other osseous foot malignancy. Patients with Ewing's sarcoma had the highest occurrence of distal metastases at diagnosis (especially to the lungs and bones) compared with other primary foot tumours. Shirley *et al* reported similar findings.²⁶ In our cohort, the local recurrence rate was also highest in Ewing's sarcoma cases.

The reported average time to death for osseous foot metastases is 9.9–14.7 months.²⁷ The overall mean time to death in our series was slightly longer at 20.1 months. Moreover, the duration of symptoms prior to diagnosis of foot metastases (median: 24 weeks) was shorter than that for primary bone tumours (median: 52 weeks). The delayed diagnosis of primary bone tumours relative to diagnosis of metastatic lesions of the foot may be related to the physician not considering primary malignant neoplasm as a possible differential diagnosis. The diagnosis of metastatic lesions could still prove difficult, however, as 80% of our patients had no other metastasis at presentation and 20% did not have a known existing primary malignancy. Consequently, new symptoms (such as pain or swelling) in any part of the foot should be investigated promptly using further imaging as they may be the only indication of a disseminated malignancy.

Conclusions

Our study included the largest number of malignant bone tumours that were categorised to various anatomical areas of the foot. It has demonstrated that patients with osseous foot malignancy often have a protracted length of symptoms. A high index of suspicion as well as an awareness of the epidemiological and clinical features of malignant bony foot lesions are therefore required to avoid diagnostic delays. Surgical amputation achieved respectable survival in patients with primary malignant bone tumours of the foot, including those who had originally undergone accidental excision. Early diagnosis and appropriate management of malignant bone tumours of the foot are key factors in improving oncological outcomes for patients.

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