



Clinicopathological guide to malignant bone tumours: A retrospective analysis of the cancer registry at Kilimanjaro Christian Medical Centre in northern Tanzania

Pamela T.K. Samoyo*¹, Gilbert Z. Nkya², Fred G. Minja³, Rogers J. Temu¹

¹Department of Orthopaedic Surgery, Kilimanjaro Christian Medical University College, Moshi, Tanzania

²Department of Pathology, Kilimanjaro Christian Medical Centre, Moshi, Tanzania

³Department of General Surgery, Arusha Lutheran Medical Centre, Arusha, Tanzania

*Correspondence: pinx405@gmail.com

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Abstract

Background: Primary neoplasms of the skeleton are rare. This study aimed at determining the spectrum of different malignant bone tumours at a tertiary hospital cancer registry in the Northern Zone of Tanzania, along with related symptoms, clinical presentations, and clinical diagnosis accuracy (using histology as the standard).

Methods: This retrospective study reviewed bone specimen records in the cancer registry at Kilimanjaro Christian Medical Centre (KCMC) in Tanzania, for the period from 1 January 1998-31 December 2012. Patient information for corresponding cancer registry records was traced from hospital files and x-ray reports. Data were analysed using a mixed quantitative and qualitative approach.

Results: Two hundred twenty-five malignant bone tumours were recorded at KCMC Cancer Registry over a period of 14 years. Seventy-five with adequate records were analysed. Forty-seven patients (62.7%) were male. Mean age was 34.1 (standard deviation 20) years. The femur was affected in 26 cases (34.7%). Osteosarcoma (22 cases; 29.3%) was the most common malignant bone tumour. Clinicians correctly preliminarily diagnosed multiple myeloma, osteosarcoma, and ameloblastoma, but had inexperience with carcinomas and other types of sarcomas. Chronic osteomyelitis and metastatic lesions were mentioned frequently by radiologists as the diagnosis of some malignant bone tumours that turned out to be carcinomas or sarcomas on histology.

Conclusions: Clinician and radiologist training of other types of malignant bone tumours other than multiple myeloma, osteosarcoma, and ameloblastoma is required. An Orthopaedic Biopsy Form (OBF) was developed to address high loss to follow-up (66.7%).

Keywords: malignant bone tumours, cancer registry, KCMC

Introduction

Cancer is a worldwide public health problem.¹ In 2008, an estimated 12.7 million new cancer cases and 7.6 million cancer deaths occurred worldwide, with 56% of new cancer cases and 63% of the cancer deaths occurring in developing countries.² Primary neoplasms of the skeleton are rare, amounting to only 0.2% of the overall human tumour burden.³ In countries where there is a high burden of HIV/AIDS (among other infectious diseases), an increasing burden of chronic noncommunicable diseases, along with malnutrition and women dying in childbirth, patients with bone tumours are not seen as a policy or resource-distribution priority but contribute to the mortality rate. In regions where population-based cancer registries are not in existence, hospital-

based cancer registries (HBCRs) are beneficial for policy and planning.⁴ Research done based on HBCRs can be used to update cancer registries and assist the building up of a complete evidence-based cancer register.

The diagnosis of bone tumours requires complex investigations, consisting of computed tomography (CT) scans, bone scans, magnetic resonance imaging (MRI), pathology laboratories, with other new techniques, which include reverse-transcriptase polymerase chain reaction (rt-PCR), molecular genetics, and immununochemistry assays, all of which are not readily available in hospitals in developing countries. At Kilimanjaro Christian Medical Centre (KCMC), for instance, at the time that work described in this report was carried out, there was no MRI machine, the CT machine had not been working for several years, and the hospital relied on short-term visiting histopathologists for many years. It is therefore important that clinicians and radiologists in such hospital environments are competent in clinically diagnosing bone tumours so as to offer correct medical advice, early treatment interventions, and priority referrals to cancer institutes.

Case presentation 1

A 10-year-old boy presented with complaints of a swelling on his left leg for 1 year. The swelling was associated with no other symptoms except night pain and had been gradually growing. He could walk with no difficulties, could still play football with his friends and was attending school, where he walked a long distance to and fro. This boy had normal vital signs, was otherwise healthy for his age and active. X-rays revealed a huge cystic bone tumour on the proximal fibula. The soap bubble appearance on x-ray would suggest an aneurysmal bone cyst. That this boy had normal vital signs, was not clinically wasted or toxic, could still play football and carry out normal daily living activities would suggest a benign bone tumour regardless of size.



Figure 1: A 10-year-old boy with a bone tumour on the left leg (left). Anteroposterior and lateral x-rays of the patient are shown on the right.

Case presentation 2

A 26-year-old male patient presented with a swelling on his left leg for 3 months. The swelling was associated with fast growth, constant pain, skin hyperpigmentation over the swelling, and (at times) ulceration. The patient was weak, sick looking, wasted, with a cough accompanied by haemoptysis. The patient also had a low haemoglobin level. X-rays revealed a sunburst appearance, Codman triangle, and soft tissue bone formation. The fast growth of tumour and general condition of the patient suggests an aggressive bone or soft tissue tumour. The classical x-ray picture diagnoses osteosarcoma.



Figure 2: A 26-year-old male patient with a bone tumour on the left leg (left) and lateral x-ray of the patient (right).

Methods

After ethical clearance (certificate number 646), the KCMC Cancer Registry records (for the years 1998-2012) were reviewed during the period between 13 September 2013 and 13 September 2014. Using a data extraction sheet, information on age at biopsy, sex, residence, hospital file number, date of incidence, date of interview at the registry, clinicians' preliminary diagnosis, and histological diagnosis were extracted. Patient hospital files were traced in the medical records department, and further collection of information was done. Hospital files enabled collection of information such as main complaints, duration of complaints, other associated complaints, clinical findings of clinicians (including their descriptions of patient presentation), and haemoglobin levels. X-rays were then traced in the radiology department and the radiologists' reports were analysed for descriptions of x-rays and preliminary diagnoses.

After gathering information from the 3 different departments (using qualitative comparisons), symptoms, symptom durations, presentations, and clinical findings were grouped and accessed in relation to histological diagnoses. Quantitative analysis was done for age, sex, residence, time duration for patients to reach the cancer registry, type of malignant bone tumours, location of tumours, and histopathological types.



Results

Two hundred twenty-five malignant bone tumours were recorded in the cancer registry for the period 1 January 1998-31 December 2012. A very few benign bone tumours had been biopsied; these were excluded from the 225 malignant bone tumour cases. Out of the 225 malignant bone tumours, 75 had traceable hospital files and x-ray film records and therefore were included in the (qualitative and quantitative) analysis.

Out of 75 cases, 47 patients (62.7%) were male, with a male-to-female ratio of 1.9:1. The age range was 2 to 75 years, with a mean of 34.1 (standard deviation [SD] 20) years. There were 15 paediatric patients (0-17 years of age), accounting for 20% of the cases. The time it took patients to reach the cancer registry for interviews (from the time at which complaints of the malignant bone tumour began) ranged between 6 and 248 days (excluding 2 outliers of 366 and 389 days), with a mean time difference of 62.9 (SD 52.8) days. Fifty-one of the 75 patients (68%) were residing in the Kilimanjaro Region.

The most common bone tumour location was the femur (n = 26; 34.7%), followed by the mandible (n = 12; 16%), and then the tibia (n = 5; 6.7%). Twenty-two bone tumours (29.3%) had a histological diagnosis of osteosarcoma, followed by 18 other types of sarcomas (24%) (3 chondrosarcomas, 1 cystic sarcoma, 2 Ewing's sarcomas, 3 fibrosarcomas, 1 Kaposi's sarcoma, 1 pleomorphic sarcoma, 2 synovial sarcomas, 1 malignant mesenchymal sarcoma, 1 rhabdomyosarcoma, 2 low-grade sarcomas, and 1 high-grade malignant sarcoma), and 9 carcinomas (12%) (3 adenocarcinomas, 2 metastatic carcinomas, 2 poorly differentiated carcinomas, and 2 squamous cell carcinomas).

Malignant bone tumour presenting symptoms

Pain was present in 64 (85.6%) of the malignant bone tumours, with 7 (9.3%) having no mention of presence or absence of pain. However, only 15 malignant bone tumours had a mention of pain duration, with a mean of 7.1 months. Swelling was recorded in 63 (84%) of the malignant bone tumours, with 7 (9.3%) having no mention of whether a swelling was present or absent. The duration of swelling in 55 patients ranged from 1 week to 10 years, with a mean of 20.7 months. Gradual swelling was recorded in 33 (44%) of the malignant bone tumours, while 17 (22.7%) were fast growing. Some malignant bone tumours with pathological fractures had a course without any swelling, but with pain as the main complaint among other associated symptoms. Pathological fractures occurred in 14 of 75 malignant bone tumours (18.7%), where osteosarcoma, giant cell tumour, multiple myeloma, metastatic carcinomas, and high-grade malignant tumours were diagnosed (histologically) to be the cause. Having a cough, difficulty in breathing, haemoptysis, and pleural effusions were recorded in patients who were suspected of having metastasis to the lungs. Chest x-rays of patients who were thought to have lung metastases mentioned micro or macro nodules, at times solitary nodules, and blunt costophrenic angles. Ten patients (13.3 %) had a haemoglobin level less than 7.0 g/dL, and 40 (53.3 %) had levels over 10.0 g/dL.

Clinical presentation of different malignant tumour types

Osteosarcomas

On clinical recordings by clinicians, appearance of osteosarcomas had descriptions such as, "firm"; "tender to touch"; "worsening pain on touch"; "oedema of lower limb"; "shiny skin over



tumour, with visible blood vessels”; “inguinal lymph nodes”; “ulcerated tumour”; and some with a “foul-smelling discharge”. Other than pain and swelling, other symptoms that were associated with osteosarcoma were fever, weight loss, loss of appetite, wasting, tiredness, heart palpitations, headache, itching, bursts of swelling, oedema of legs, and pathological fractures. A swelling duration over 3 months was associated with complaints of fever, cough, difficulties in breathing, vomiting, chest pain and lymph nodes. Some patient files reported rapid tumour growth following open biopsy, to the extent of the tumour fungating outside of the surgical incision (what we call “the bubbling-over phenomenon”). Osteosarcoma on x-rays had the mention of the following terms by radiologists: “bone destruction”, “osteoblastic” or “osteolytic” lesions, “soft tissue bone formation”, “bony speckles in soft tissues”, “Codman triangle”, “periosteal reaction”, “pathological fracture”, “sunray” or “sunburst” appearance, “osteopenia”, “joint osteolysis”, “hair-on-end new bone formation”, and “soft tissue calcifications”.

Multiple myeloma

Multiple myeloma was frequently associated with spinal complaints, such as back pain, lower limb weakness and paraesthesia; as well as constipation and nontraumatic paraplegia. X-rays reported narrowing of intervertebral joint spaces, lytic lesions on vertebrae, pedicle destruction, vertebral compression, punched-out lesions of various sizes on the skull and pelvis, and pathological fractures.

Carcinomas

Other than the already named general symptoms of malignant bone tumours, the most common complaints of patients with carcinomas by histology were loss of function of the affected limb, wasting, pathological fracture, and an HIV diagnosis. For carcinomas that presented on the face (mandible, maxilla, and hard palate, for example), additional symptoms were painful chewing, painful swallowing, headache, fever, insomnia, loose teeth, proptosis, epistaxis, blindness, and ulceration of tumour. Carcinomas in the shoulder, which were radiologically diagnosed as tuberculous arthritis, were reported as having increased density of the glenoid (with or without its deformation) and lytic lesions of the humeral head (with or without joint subluxation) on x-rays. Besides tuberculous arthritis, radiological preliminary diagnoses of carcinomas mentioned conditions such as pyomyositis and chronic infection.

Other types of sarcomas

Synovial sarcomas were recorded in small bones, such as tarsals, phalanges, and the fibula. To the general symptoms reported by patients, itching, night pain, and ulceration of skin over swellings were common. X-rays reported lytic lesions of the tarsals or phalanges. When synovial sarcomas were reported on the femur, they behaved like osteosarcomas, with large soft tissue swelling, bone destruction, calcifications, and bone speckles forming in soft tissue. Chondrosarcomas were recorded near joints in the proximal femur and proximal humerus. Chondrosarcomas were recorded as initially being painless and then becoming painful over time.

Clinician and radiologist preliminary diagnoses of malignant bone tumours

Clinicians managed to preliminarily diagnose 4 of 4 of multiple myelomas, 16 of 22 osteosarcomas, 3 of 3 ameloblastomas, 1 of 4 giant cell tumours, but 0 of 9 of carcinomas and 0 of the 18 other types of sarcomas. Overall, clinical (versus histological) diagnosis had 44% (33 out of 75) accuracy. Sarcomas of joints were clinically labelled as septic arthritis, as well as



carcinomas in joints for tuberculous arthritis. Other types of sarcomas, carcinomas, and undifferentiated malignant tumours (20 of 34) were broadly recorded by clinicians as “malignant bone tumour”, “bone tumour”, or simply “tumour” or “mass”, and “pathological fractures” (in those malignant bone tumours that presented as low-energy fractures). Radiologists described what they saw on x-rays; however, not all patients had a radiological preliminary diagnosis. Of the hospital files that had radiological preliminary diagnoses, overall accuracy was 30% (15 out of 50). Radiologists were able to diagnose osteosarcoma and multiple myeloma most correctly; however, other bone tumour types were recorded as “bone tumour”, or simply “tumour”, without any specific mentioning of probable bone tumour types. Chronic osteomyelitis, tuberculous arthritis, pyomyositis, and metastasis or metastatic bone disease were mentioned frequently by radiologists as preliminary diagnoses of some malignant bone tumours that were carcinomas or sarcomas histologically.

Discussion

General distributions of this study agree with already existing data: the male dominance,^{5,6,7} the male-to-female ratio,⁸ age range of 2 to 75 years,⁹ the femur being the leading tumour site,^{5,9} and osteosarcoma being the leading tumour type.^{5,7} The main cardinal signs for malignant tumours in this study were pain (85.6%), swelling (84%), and pathological fractures (18.7%). By comparison, Bhurghi et al. in Pakistan reported pain (32.4%) and pathological fractures (66.2%).⁶

Clinicians and radiologists were experienced in diagnosing multiple myeloma and osteosarcoma. This could be explained by the high frequencies at which multiple myeloma and osteosarcoma are encountered clinically, giving clinicians accuracy acquired through experience. On the other hand, carcinomas and other forms of sarcomas were misdiagnosed as infections, such as tuberculous arthritis and pyogenic arthritis. Clinicians and radiologists should therefore consider carcinomas and other forms of sarcomas as probable diagnoses.

This study had a 66.7% loss to follow-up. This is because the majority of patient hospital files could not be traced, as some biopsy specimens of bone tumours that were read and recorded at KCMC Cancer Registry were from other hospitals and the patients had not attended KCMC physically. This means that bone biopsies were taken in other hospitals and were brought to the regional teaching and referral hospital, KCMC, for reading. It is not possible to request clinicians from other centres within the Kilimanjaro Region to refer bone tumour patients to KCMC for diagnostic investigations, as this would make medical care more expensive to our already struggling communities. However, if cancer registries are to collect adequate quality information, we emphasise and recommend that all referred biopsy specimens be accompanied by a completed Orthopaedic Biopsy Form (OBF) (Appendix 1). There is therefore need to communicate with other medical facilities in the region and to make the suggested OBF readily available.

Another factor that contributed to the 66.7% loss to follow-up could have been that some bone tumour specimens were missed, as descriptions at the KCMC Cancer Registry were broad. For example, if biopsy site is recorded as “thigh”, one might suppose that this referred to a soft tissue tumour, but after reviewing patient hospital files and x-rays, the correct location may have been the femur instead of simply “thigh”. Our developed OBF addresses this issue and we recommend surgeons to fill in section II of the OBF after the biopsy procedure. It might be of importance to mention that the surgeon has to record section II of the OBF if we are to narrow down terminologies and be more specific. This will increase clerical work to the surgeon, but it will improve the quality and completeness of data available in our cancer registry.



The review of the KCMC Cancer Registry for the years 1998 to 2012 was manual, through filled-in registry forms stored in lever arch files. Paper storage in files has a disadvantage of termite manifestations and fading ink. For better efficiency, cancer registries should have computed records preferably with backup.

Study limitations

There is substantial subjective variability among clinicians and radiologists in documented observations within patient hospital files and interpretation of biopsy slides and x-ray films. Inadequate patient files limit our findings to the 75 cases that were discussed in this study; however, the study created a platform to completing data at the cancer registry and future studies.

Conclusions

Clinicians and radiologists are competent in diagnosing bone tumours, especially multiple myeloma, osteosarcoma, and ameloblastoma. However, they require further training in diagnosing other tumours that affect the bone, especially carcinomas (adenocarcinoma, squamous cell carcinoma, metastatic carcinoma) and other forms of sarcomas (Ewing's sarcoma, synovial sarcoma, fibrosarcoma, Kaposi's sarcoma, chondrosarcoma). Clinicians are required to thoroughly examine patients with bone tumours and to document findings appropriately and adequately in patient hospital files. The KCMC Cancer Registry has not been capturing adequate information from referred, local bone biopsy, and orthopaedic specimens. We recommend referred specimens to be accompanied by a completed OBF.

Recommendations

Clinicians and radiologists require training in diagnosing some forms of sarcomas and carcinomas. Inadequate files were a limitation in this study, in terms of the accuracy of study findings. The introduction of the OBF will improve file accuracy and completeness at the cancer registry.

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References

1. Wiredu E, Armah H. Cancer mortality patterns in Ghana: a 10-year review of autopsies and hospital mortality. *BMC Public Health*. 2006;6:159.
2. Ferlay J, Shin HR, Bray F, Forman D, Mathers C and Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008. *Int J Cancer*. 2010;127(12):2893-2917.
3. Fletcher CDM, Unni KK, Mertens F(Eds): World Health Organization Classification of Tumors. Pathology and Genetics of Tumors of Soft Tissue and Bone. IARC Press: Lyon 2002.
4. Jedy-Agba EE, Curado MP, Oga E, Samaila MO, Ezeome ER, Obiorah C et al. . The role of hospital-based cancer registries in low and middle income countries-The Nigerian case study. *Cancer Epidemiology*. 2012;36(5):430-5.
5. Solooki S, Vosoughi AR and Masoomi V. Epidemiology of musculoskeletal tumors in Siraz, south of Iran. *Indian Journal of Medical and Paediatric Oncology*. 2011;32(4): 187-191.
6. Bhurgri Y, Usman A, Bhurgri H, Fardi N, Bashir I, Bhurgri A et al. . Primary Malignancies of Bone and Cartilage in Karachi. *Asian Pacific Journal of Cancer Prevention*. 2009;10: 891-894.
7. Obalum DC, Eyesan SU, Ogo CN and Enweluzo GO. Multicentre study of bone tumours. *The Nigerian Postgraduate Medical journal*. 2010;17(1):23-6.
8. Abdulkareem FB, Eyesan SU, Akinde OR, Ezembakwe ME and Nnodu OE. Pathological study of bone tumours at the National Orthopaedic Hospital, Lagos, Nigeria. *West African Journal of Medicine*. 2007;26 (4):306-11.
9. Ode MB, Msauno MA, Nwadiaro HC, Onche II, Shitta AH and Amupitan I. Pattern and Distribution of Primary Bone Tumors in Jos Nigeria. *IOSR Journal of Dental and Medical Sciences*. 2014;13(12 ver 1):9-12.

Appendix 1: Orthopaedic Biopsy Form (OBF)

SECTION 1: To be filled in by doctor during patient hospital admission

1. First name of patient: _____

2. Middle name/s of patient: _____

3. Last name of patient: _____

4. DOB: _____

Example: 15 December, 2012

5. Age: _____

6. Sex: *Tick only one oval.*

- Male
- Female

7. Residence for the past 6 months: _____

8. Patient's contact phone number: _____

9. Name and contact phone number of first close relative: _____

10. Name and contact phone number of second close relative: _____

11. Date that tumor began: _____

Example: 15 December, 2012

12. Patient's vitals: BP _____

HR _____

RR _____

SO₂ _____

13. On examination: *Tick all that apply.*

- Pale
- Cyanosed
- Jaundiced
- Tachypnic
- Sick-looking
- Weak
- dehydrated

14. Cardinal symptoms: *Tick all that apply including growth type and fill duration in days, weeks, months and years.*

- Pain duration _____
- Swelling duration _____ Fast growth _____ Slow growth _____
- Pathological fracture duration _____
- Cough duration _____
- Hemoptysis duration _____
- Weight loss duration _____
- Wasting
- Fever
- Night sweats
- Other _____

14. Clinician's descriptions of tumor:

Size _____

Mobility _____

Consistency _____

Vascularization _____

Skin pigmentation _____

Ulceration _____

Discharge _____

15. Investigations: FBC: WBC _____

HB _____

Platelet count _____

HIV status: _____

X-ray: Of _____
Radiologist's description _____
Radiologist's diagnosis _____

Ultrasound findings: _____

CT scan report: _____
Diagnosis: _____

MRI report: _____
Diagnosis: _____

Other: _____

16. Admitting/referring clinician's impression: _____

Admitting/referring officer's name in full and qualification: _____

Hospital: _____

Date: _____

SECTION II: To be filled in by surgeon after biopsy taking

Histology requesting surgeon (write full name and qualification): _____

Date of biopsy taking: _____
Example: 15 December, 2012

Location where biopsy was taken from (be specific e.g. distal femur): _____

Specimen taken: *Tick all that apply.*

- Bone
- Muscle
- Synovium
- Other: _____

Surgeon's pre-op clinical diagnosis: _____

Intra-op findings/descriptions (explain visual findings e.g. lysed bone within hematoma).

Please note: In case of amputation, the surgeon is recommended to dissect the tumor post-op and to fill in this section:

Surgeon's post-op clinical diagnosis: _____

SECTION III: To be filled in by pathologist

Histology read by (write full name and qualification): _____

Histological diagnosis: tumor type _____

Histological descriptions (explain visual findings e.g. giant cells):

Histological diagnosis: tumor grade _____

Specimen received by: _____

Date: _____

- * Tumor size- in centimeters
- * Tumor mobility- fixed, partially mobile and/or freely mobile
- * Tumor consistency- soft, firm, fleshy, nodular, rubbery and/or bony
- * Tumor vascularization- normal or hyper
- *Skin pigmentation- normal, hypo, hyper and/or mixed
- *Ulceration- present or absent
- *Discharge- pus, serous, sanguineous and/or sero-sanguineous, then state if the described discharge has a foul smell e.g. foul smelling serous discharge or non-foul smelling serous discharge
- *FBC- full blood count
- *WBC- white blood count
- *HB- haemoglobin
- *HIV status- positive or negative