Spectrum of Bone Tumors in Chiang Mai University Hospital, Thailand According to WHO Classification 2002: A Study of 1,001 Cases

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Objective: *The aim of the present study was to determine the spectrum, frequency and demographics of bone tumors.*
Material and Method: *A retrospective study of the 1,001 bone tumor specimens from the files at the Pathology Department of the Chiang Mai University Hospital, Thailand from 2000 to 2004.*
Results: *From the study, 41 were non-neoplastic mass lesions, and 960 were neoplastic, with 856 (89%) as primary and 104 (11%) as metastatic tumors. In the primary tumor group, 654 (76%) cases were of hematologic origin, and 202 (24%) were non-hematologic. The most common benign bone tumors were giant cell tumor (n = 37), osteochondroma (n = 25), and chondroma (n = 15). The most common malignant bone tumors were lymphoma-leukemia (n = 583), metastatic malignancy (n = 104), plasma cell myeloma (n = 71), and osteosarcoma (n = 58).*
Conclusion: *The present study showed a higher frequency of osteosarcoma (68%), lower frequencies of chondrosarcoma (12%) and Ewing sarcoma (4%) among primary non-hematologic malignant bone tumors when compared with similar studies based on Western patients. Whether these differences reflect differences in the ethnic population or in practice patterns remains to be determined.*

Keywords: *Bone tumor, Osteosarcoma, Frequency, Distribution, Location*

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Among the varieties of human neoplasms, bone tumors are relatively uncommon. However, they are diverse in their pathologic features and range in their biologic potential from the innocuous to the rapidly fatal. This diversity makes it critical to accurately diagnose, stage, and treat tumors appropriately, so that the patients can survive and maintain optimal function of the affected body part[1].

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The precise incidence of bone tumors is not known as many benign lesions are not biopsied. In general, bone sarcomas account for only 0.2% of all neoplasms[2]. Despite the low incidence, bone sarcoma accounted for 36% of major limb amputations in the hospital[3]. The frequency of bone tumors in the northern part of Thailand has not been well studied. It was previously reported that bone cancer accounted for 0.7% of all cancer cases in Chiang Mai University Hospital, which is the largest tertiary health care provider in this area[4]. Since this is somewhat higher than the value reported in a series from Western countries, accurate information of the bone tumor distribution

in this part of the world would be of value for identifying any differences in specific tumor types. Hence, the objective of the present study was to obtain accurate data on the spectrum, frequency and demographics of bone tumors in Chiang Mai University hospital, Thailand during a 5-year period.

Material and Method

This was a descriptive retrospective study of all clinical and pathological data from bone tumor specimens including bone marrow biopsies submitted to the Pathology Department of Chiang Mai University Hospital from 2000 to 2004. The parameters studied included pathological diagnosis, age and gender of the patients and location of the tumors. The tumors were classified according to the recent WHO classification of bone tumors[2]. Locations were divided into 8 groups, craniofacial, vertebra including sacrum, scapula, clavicle, rib, sternum, pelvic bone, bones of limbs, and bone marrow biopsy. The data were summarized using Intercooled Stata 8.0. This project was approved by the Research Ethics Committee, Faculty of Medicine, Chiang Mai University (reference number 172/2004).

Results

There were a total of 1,001 tumor specimens (Table 1). Patient ages ranged from 7 months to 88 years with median age of 44.2 years (Table 2). Five hundred and fifty patients were male (54.9%). The majority of the specimens were from bone marrow biopsies (n = 664, 66.3%), followed by bones of limb (n = 222, 22.2%), craniofacial bones (n = 45, 4.5%), vertebra and sacrum (n = 34, 3.4%), pelvic bone (n = 22, 2.2%), scapula (n = 6, 0.6%), clavicle (n = 4, 0.4%), rib (n = 3, 0.3%), and sternum (n=1, 0.1%).

Hematologic neoplasms were the most common group of tumors (n = 654, 65.3%). The other common groups of tumors were miscellaneous tumors (n = 119, 11.9%), osteogenic tumors (n = 76, 7.6%), cartilaginous tumors (n = 57, 5.7%), and giant cell tumors (n = 37, 3.7%) (Table 1). After excluding the non-neoplastic bone lesions (n = 41), the number of malignant bone tumors (n = 854, 89.0%) was eight times of thebenign tumors (n = 106, 11.0%). Excluding metastatic tumors, there were 856 (89.2%) primary tumors including 654 (76.4%) hematologic malignancies and 202 (23.6%) non-hematologic tumors.

The three most common bone lesions found in the present study were lymphoma and leukemia (n = 583, 58.2%), metastatic malignancy (n = 104, 10.4%),

Table 1. Frequency of bone tumors

Tumors (% in group)	Total, n (%)
Cartilaginous tumors	57 (5.7)
- Osteochondroma (43.9)	25 (2.5)
- Chondroma (26.3)	15 (1.5)
- Chondroblastoma (10.5)	6 (0.6)
- Chondromyxoid fibroma (1.8)	1 (0.1)
- Chondrosarcoma (17.5)	10 (1.0)
Osteogenic tumors	76 (7.6)
- Osteoma (18.4)	14 (1.4)
- Osteoid osteoma (3.9)	3 (0.3)
- Osteoblastoma (1.3)	1 (0.1)
- Osteosarcoma (76.3)	58 (5.8)
Fibrogenic tumors	1 (0.1)
- Desmoplastic fibroma (100.0)	1 (0.1)
Fibrohistiocytic tumors	6 (0.6)
- Benign fibrous histiocytoma (16.7)	1 (0.1)
- Malignant fibrous histiocytoma (83.3)	5 (0.5)
Ewing sarcoma / peripheral PNET	3 (0.3)
Hematologic neoplasms	654 (65.3)
- Leukemia-lymphoma (89.1)	583 (58.2)
- Plasma cell myeloma (10.9)	71 (7.1)
Giant cell tumor	37 (3.7)
Chordoma	5 (0.5)
Vascular tumors	2 (0.2)
- Hemangioma	2 (0.2)
Miscellaneous tumors	119 (11.9)
- Adamantinoma of jaw bone (8.4)	10 (1)
- Metastatic malignancy (87.4)	104 (10.4)
- Mixed tumor of long bone (0.8)	1 (0.1)
- Sarcoma, not otherwise specified (3.4)	4 (0.4)
Miscellaneous lesions	41 (4.1)
- Aneurysmal bone cyst (7.3)	3 (0.3)
- Simple bone cyst (14.6)	6 (0.6)
- Fibrous dysplasia (24.4)	10 (1.0)
- Osteofibrous dysplasia (12.2)	5 (0.5)
- Non-ossifying fibroma (5.1)	2 (0.2)
- Langerhans cell histiocytosis (9.8)	4 (0.4)
- Bone cysts associated with dental structures (24.4)	10 (1.0)
- Juvenile xanthogranuloma (2.4)	1 (0.1)
Total	1001 (100.0)

Table 2. The distributions of gender, age, and location of bone tumors

Tumors	(M:F ratio)	Age in year Range, median Mean (SD)	Location, n(%)									Total (N)
			Cranio-facial bone	Spine and sacrum	Scapula	Clavicle	Rib	Sternum	Pelvic bone	Bone of limb	Bone marrow biopsy	
Lymphoma-leukemia	(1.4:1)	12-88, 46 46.4 (16.7)	-	-	-	-	-	-	-	2 (0.3)	581 (99.7)	583
Metastatic malignancy	(0.9:1)	1-82, 60 57.3 (14.4)	1 (1.0)	24 (23.1)	-	2 (1.9)	1 (1.0)	-	10 (9.6)	49 (47.1)	17 (16.4)	104
Plasma cell myeloma	(1.4:1)	15-81, 58 56.8 (13.7)	-	-	-	-	-	-	1 (1.4)	4 (5.6)	66 (93.0)	71
Osteosarcoma	(1.2:1)	8-61, 18 20.5 (11.4)	3 (5.2)	-	-	-	-	-	4 (6.9)	51 (87.9)	-	58
Giant cell tumor	(0.9:1)	12-58, 37 35.8 (12.7)	1 (2.7)	-	1 (2.7)	-	-	-	2 (5.4)	33 (89.1)	-	37
Osteochondroma	(1.1:1)	4-51, 16 18 (10.0)	-	-	2 (8.0)	-	-	-	1 (4.0)	22 (88.0)	-	25
Chondroma	(0.4:1)	9-58, 33 31.2 (15.5)	1 (6.7)	-	1 (6.7)	-	-	-	-	13 (86.7)	-	15
Osteoma	(0.2:1)	0.58-67, 41 37.5 (16.3)	12 (85.7)	-	-	1 (7.1)	1 (7.1)	-	-	-	-	14
Chondrosarcoma	(1.5:1)	20-71, 48.5 49.5 (14.9)	-	-	1 (10.0)	-	-	1 (10.0)	1 (10.0)	7 (70.0)	-	10
Adamantinoma of jaw bone	(0.7:1)	6-54, 42.5 38.6 (15.4)	10 (100.0)	-	-	-	-	-	-	-	-	10
Fibrous dysplasia	(1:1)	4-56, 20 25.8 (17.6)	4 (40.0)	-	-	-	1 (10.0)	-	-	5 (50.0)	-	10

Table 2. The distributions of gender, age, and location of bone tumors (cont.)

Tumors	(M:F ratio)	Age in year Range, median Mean (SD)	Location, n(%)									Total (N)
			Cranio-facial bone	Spine and sacrum	Scapula	Clavicle	Rib	Sternum	Pelvic bone	Bone of limb	Bone marrow biopsy	
Bone cyst associated with dental structure	(0.25:1)	6-70, 33 35.4 (22.5)	10 (100.00)	-	-	-	-	-	-	-	-	10
Chondroblastoma	(All male)	14-43,22 23.5 (10.4)		-	-	-	-	-	-	6 (100.0)	-	6
Simple bone cyst	(1:1)	12-31, 24 23.4 (7.7)		1 (16.7)	1 (16.7)	-	-	-	-	1 (16.7)	3 (50.0)	6
Malignant fibrous histiocytoma	(4:1)	47-78, 66 63.6 (12.0)		-	-	-	-	-	1 (20.0)	4 (80.0)	-	5
Chordoma	(1.5:1)	39-78, 69 62.2 (18.1)	0	5 (100.0)	-	-	-	-	-	-	-	5
Osteofibrous dysplasia	(1.5:1)	9-47, 19 23.2 (15.4)	1 (20.0)	-	-	-	-	-	-	4 (80.0)	-	5
Sarcoma NOS	(All male)	22-54, 39.5 38.75 (13.4)	-	-	-	-	-	-	-	4 (100.0)	-	4
Langerhans cell histiocytosis	(0.3:1)	17-37, 27 27 (14.1)	-	2 (50.0)	-	-	-	-	-	2 (50.0)	-	4
Osteoid osteoma	(All male)	6, 7, 17[#]	-	-	-	-	-	-	-	3 (100.0)	-	3
Ewing sarcoma / PNET	(0.5:1)	15, 19, 19[#]	-	-	1 (33.3)	-	-	-	1 (33.3)	1 (33.3)	-	3
Aneurysmal bone cyst	(2:1)	12, 15, 24[#]	-	1 (33.3)	-	-	-	-	-	2 (66.7)	-	3

Table 2. The distributions of gender, age, and location of bone tumors (cont.)

Tumors	(M:F ratio)	Age in year Range, median Mean (SD)	Location, n(%)									Total (N)
			Cranio-facial bone	Spine and sacrum	Scapula	Clavicle	Rib	Sternum	Pelvic bone	Bone of limb	Bone marrow biopsy	
Non-ossifying fibroma	(1:1)	12, 35#	-	-	-	-	-	-	-	2 (100.0)	-	2
Hemangioma	(All male)	41, 64#	-	1 (50.0)	-	-	-	-	-	1 (50.0)	-	2
Chondromyxoid fibroma	(All male)	24#	-	-	-	-	-	-	-	1 (100.0)	-	1
Osteoblastoma	(all female)	6#	-	-	-	1 (100.0)	-	-	-	-	-	1
Desmoplastic fibroma	(All male)	11#	-	-	-	-	-	-	-	1 (100.0)	-	1
Benign fibrous histiocytoma	(All male)	48#	-	-	-	-	-	-	-	1 (100.0)	-	1
Mixed tumor of long bone	(All female)	43#	-	-	-	-	-	-	-	1 (100.0)	-	1
Juvenile xanthogranuloma	(All female)	23#	1 (100.0)	-	-	-	-	-	-	-	-	1
Total	(1.2:1)	0.58-88, 44 44.2 (18.8)	45 (4.5)	34 (3.4)	6 (0.6)	4 (0.4)	3 (0.3)	1 (0.1)	22 (2.2)	222 (22.2)	664 (66.3)	1001

age of each patient; NOS = Not otherwise specified

and plasma cell myeloma (n = 71, 7.1%) (Tables 1, 2). The primary non-hematologic bone tumors (n = 202) included 106 (52.5%) benign and 96 (47.5%) malignant lesions. The common benign lesions were giant cell tumor (n = 37), osteochondroma (n = 25), and chondroma (n = 15). The common malignant lesions were osteosarcoma (n = 58), chondrosarcoma (n = 10), and adamantinoma of the jaw (n = 10).

Discussion

By comparing the frequency of bone tumors in the present study with those from the large series of the Mayo Clinic[5], the U.S.Surveillance Epidemiologic and End Results (SEER) Program[6], and the report of Dorfman HD, et al[7]; the authors found the same groups of common tumors as hematologic bone tumors, osteosarcoma, osteochondroma, chondrosarcoma, and giant cell tumors. Excluding adamantinoma of the jaw, 86/192 (44.8%) of the primary non-hematologic bone tumours were malignant compared to 63.0% in the latest AFIP fascicle[8] (Table 3). In the present study, the frequency of chondrosarcoma among the primary non-hematologic malignant lesions (11.6%) is not as high as those reported from the Mayo Clinic (25.1%), the SEER (30%), the Dorfman HD, et al (25.8%)[7] and the latest AFIP fascicle[8] (26.9%). However, it correlates very well with the frequencies of chondrosarcoma cases from two other centers in Thailand, Chulalongkorn (10.3%) and Siriraj (9.5%) Hospitals[9,10]

As the most common primary non-hematologic malignant tumor of bone, the frequency of osteosarcoma in the present series is relatively high (67.4%) compared to those reported from the same two university hospitals in Bangkok (41.2%, 51.0%)[9,10], from the Mayo Clinic (39.8%)[5], from SEER (36%)[6], from Dorfman HD, et al (35.1%)[7] and from the AFIP fascicle (41.2%)[8]. These findings might be influenced by the fact that Chiang Mai University hospital is the largest university hospital in Northern Thailand and it is the only one hospital in this area that provides the full spectrum of bone tumor management.

Osteoid osteoma accounted for 13.3% of all benign bone tumors found in the series of Mayo Clinic[5]. Interestingly, there are only three cases (2.8%, 3 out of 106) in the present study. The present finding is in keeping with the value of 5.8% reported from Chulalongkorn Hospital[9].

Specific types of tumors target certain age groups and anatomic sites[11]. As a group, bone neoplasms affect all ages and arise in virtually every bone but most develop during the first few decades of life and have a propensity to originate in the long bones of the extremities[1]. In the present study, approximately 60% of non-hematologic bone tumor cases were younger than 30 years (data not shown). And by excluding the bone marrow biopsy specimens, bones of limbs were the major site affected (222/337, 65.9%). The predilection of bone in specific tumor types (Table 2) correlates very well with the results of previous reports[1,2,5,8,9,12,13].

In conclusion, the present series summarizes the data available on 1001 bone tumors from a single health care center in terms of the tumor subtype, frequency, site of occurrence and patient demographics. This is the first report of this sort from the Northern

Table 3. Comparison of the frequencies of primary non-hematologic bone tumors: Chiang Mai University and Mayo clinic[8]

	CMU total N (%)	CMU malignant N (%)	Mayo total N (%)	Mayo malignant N (%)
Cartilaginous	57 (29.7)	10 (11.6)	(37.6)	(26.9)
Osteogenic	76 (39.6)	58 (67.4)	(32.0)	(41.2)
Fibrogenic	1 (0.5)	1 (1.2)	(3.7)	(5.8)
Ewings	3 (1.6)	3 (3.5)	(7.5)	(11.8)
Histiocytic	6 (3.1)	5 (5.8)	(1.3)	(1.8)
Vascular	2 (1.0)	0 (0)	(3.1)	(2.3)
Giant cell	37 (19.3)	0 (0)	(8.1)	(0.7)
Chordoma	5 (2.6)	5 (5.8)	(5.3)	(8.4)
Sarcoma NOS	4 (2.1)	4 (4.6)	Not listed	Not listed
Mixed tumor	1 (0.5)	0 (0)	Not listed	Not listed
Total	192 (100)	86 (100)	7742 (100)	4882 (100)

CMU = Chiang Mai University; NOS=Not otherwise specified

region of Thailand based on WHO 2002 diagnostic criteria. While a similar spectrum is seen in these cases when compared to studies on Western populations, some differences emerge (Table 3). A lower percentage of bone tumors seen in our centre are malignant (44.8%, 86 out of 192) compared to 63.0% in the latest AFIP fascicle[8]. Of interest, the present study showed a higher frequency of osteosarcoma (67.4%, 58 out of 86) and lower frequencies of chondrosarcoma (11.6%, 10 out of 86) and Ewing sarcoma (3.5%, 3 out of 86) amongst the primary malignant bone tumors, and a lower frequency of osteoid osteoma (2.8%, 3 out of 106) among primary benign bone tumors. These differences may be related to local patterns of practice and referral. For example, some benign bone lesions such as osteoid osteoma are not frequently biopsied at our center, whereas there are many cases of giant cell tumor. Secondly, our centre is a tertiary referral institution and the spectrum of bone tumors may differ for primary or secondary health care providers. Our center does not have a large pediatric patient population and some tumors such as Ewing sarcoma may be underrepresented in the present series for that reason. Alternatively, some tumors like osteogenic sarcoma can have a genetic predisposition that may differ in different racial groups and subpopulations. Further studies on cases from the presented patient population can help establish to what extent there are differences in tumor demographics among specific ethnic populations.

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References

1. Rosenberg AE. Bones. In: Kumar V, Abbas AK, Fausto N, editors. Robbins and Cotran. Pathologic basis of disease. 7th ed. Philadelphia: Elsevier saunders; 2005: 1273-324.
2. Dorfman HD, Czerniak B, Kotz R. WHO classification of tumours of bone: Introduction. In: Fletcher CDM, Unni KK, Mertens F, editors. WHO classification of tumour. Pathology and genetics of tumours of soft tissue and bone. Lyon: IARC Press; 2002: 227-32.
3. Settakorn J, Rangdaeng S, Arpornchayanon O, Lekawanvijit S, Bhoopat L, Attia J. Why were limbs amputated? An evaluation of 216 surgical specimens from Chiang Mai University Hospital, Thailand. Arch Orthop Trauma Surg 2005; 125: 701-5.
4. Lorvidhaya V, Srisukho S. Chiang Mai cancer registry. Annual report 1995. Chiang Mai: Faculty of Medicine. Chiang Mai University; 1998.
5. Unni KK. Dahlin's bone tumors. general aspects and data on 11,087 cases. 5th ed. Philadelphia: Lippincott-Raven; 1996.
6. Ries LA, Wingo PA, Miller DS, Howe HL, Weir HK, Rosenberg HM, et al. The annual report to the nation on the status of cancer, 1973-1997, with a special section on colorectal cancer. Cancer 2000; 88: 2398-424.
7. Dorfman HD, Czerniak B. Bone cancers. Cancer 1995; 75(1 Suppl): 203-10.
8. Unni KK, Inwards CY, Bridge JA, Kindblom LG, Wold LE. Tumors of the bones and joints. AFIP Atlas of Tumor Pathology. Fourth series, Fascicle 2. Washington, DC: AFIP; 2005.
9. Sampatanukul P, Pattanaruanglai A, Siriungkul S, Chaiwun B, Viratchai C. Bone tumors and tumor-like lesions - A retrospective study of 431 cases. Chula Med J 1987; 31: 303-9.
10. Dharamadhach A. Primary malignant bone tumors collected in the department of Pathology: Siriraj Hospital, Bangkok, from B.E.2500 to 2516. Mahidol University Annual Research Abstracts 1975. Bangkok: Secretariat of the Cabinet Printing Office; 1976.
11. Senac MOJ, Isaacs H, Gwinn JL. Primary lesions of bone in the 1st decade of life: retrospective survey of biopsy results. Radiology 1986; 160: 491-5.
12. Fechner RE, Mills SE. Tumors of the bones and joints. Washington, D.C.: AFIP; 1993.
13. Mirra JM, Picci P, Rosen G. General considerations. In: Mirra KM, editor. Bone tumors. Clinical, radiologic, and pathologic correlations. Philadelphia: Lea&Febiger; 1989: 13-34.

การศึกษาชนิดของเนื้องอกกระดูกของผู้ป่วยจำนวน 1,001 ราย จากคณะแพทยศาสตร์เชียงใหม่ตาม WHO Classification ปี 2002

จงกลณี เศรษฐกร, สุรีย์ เลขวรรณวิจิตร, โอฬาร อาภรณ์ชยานนท์, สำเริง รางแดง, ปราโมทย์ วณิตย์ธนาคม, ศราวุธ คงการค้า, เรืองรอง ชีพสัตยากร, ชรินทร์ ยาอินทร์, พอล เอส ธอร์นเนอร์

จุดประสงค์ของการศึกษานี้ คือ (1) เพื่อศึกษาความถี่ของเนื้องอกกระดูกชนิดต่างๆที่พบ ณ คณะแพทยศาสตร์ มหาวิทยาลัยเชียงใหม่ และ (2) เพื่อศึกษาอายุ และ เพศ ของผู้ป่วยเนื้องอกกระดูกและตำแหน่งที่เกิดโรค พบว่าจากบันทึกของภาควิชาพยาธิวิทยา มีชิ้นเนื้อส่งตรวจที่เป็นเนื้องอกกระดูกทั้งหมด 1,176 ชิ้น จากผู้ป่วย 1,001 ราย ซึ่งในจำนวนนี้ เป็นก้อนที่คล้ายเนื้องอก 41 ราย และ เป็นก้อนเนื้องอก 960 ราย ก้อนเนื้องอกแบ่งออกเป็นเนื้องอกปฐมภูมิ 856 (89%) ราย และ มะเร็งที่กระจายมาจากอวัยวะอื่น 104 (11%) ราย ในกลุ่มเนื้องอกปฐมภูมินั้น เป็นเนื้องอกที่มีต้นกำเนิดมาจากเซลล์เม็ดเลือด 654 (76%) ราย และ เป็นเนื้องอกที่ไม่ได้มีต้นกำเนิดมาจากเซลล์เม็ดเลือด 202 (24%) ราย เนื้องอกชนิด benign ที่พบบ่อย คือ giant cell tumor (n = 37), osteochondroma (n = 25), และ chondroma (n = 15) เนื้องอกชนิด malignant ที่พบบ่อยได้แก่ lymphoma-leukemia (n = 583), metastatic malignancy (n = 104), plasma cell myeloma (n = 71), และ osteosarcoma (n = 58) เป็นที่น่าสนใจว่าในการศึกษานี้พบความถี่ของเนื้องอกชนิด osteosarcoma สูงกว่าที่พบในคนผิวขาว แต่กลับพบ chondrosarcoma และ Ewing sarcoma ได้น้อยกว่า