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Malignant bone tumors in Kuwait

A 10-year clinicopathological study

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Abstract Between 1995 and 2004, 142 malignant bone tumours comprising 76 primary and 66 secondary tumours were identified in the Pathology Department of Al-Sabah Hospital, Kuwait. Pathological fracture was the presenting sign in 35% of the cases. The mean incidence of primary tumours/year was 3.3 cases/million inhabitants. The primary tumours showed a male predilection and 42% occurred below the age of 20 years. The most frequent in the descending order of frequency were Ewing's sarcoma, multiple myeloma, osteosarcoma, chondrosarcoma and non-Hodgkin's lymphoma. The femur was the most common site for secondary tumours; more than half of the tumours with metastases at this site originated in the breast. The high frequency of Ewing's sarcoma is noteworthy and requires further investigation.

Résumé Entre 1995 et 2004, 142 tumeurs osseuses malignes composées de 76 tumeurs primaires et 66 tumeurs secondaires ont été identifiées dans le Département de Pathologie de l'hôpital Al Sabah au Koweït. Une fracture pathologique était le signe révélateur dans 35% des cas. La fréquence moyenne des tumeurs primaires par année était de 3,3 cas par million d'habitants. Les tumeurs primaires ont montré une prédilection masculine et 42% sont survenues avant l'âge de 20 ans. Les plus fréquentes, en ordre décroissant, était le sarcome d'Ewing, le myélome multiple, l'ostéosarcome, le chondrosarcome et le lymphome

non hodgkinien. Le fémur était l'emplacement le plus fréquent des tumeurs secondaires, et, plus de la moitié des tumeurs métastasées sur ce site était d'origine mammaire. La haute fréquence du sarcome d'Ewing est remarquable et exige une enquête supplémentaire.

Introduction

Malignant bone tumours are relatively uncommon lesions that constitute less than 1% of all cancers worldwide [14]. Apart from secondary tumours, a variety of primary malignant tumours of different histogenesis arise in the bone because of its structural complexity. Some of these primary tumours display marked inter- and intra-national variations in incidence, site and age distribution [4, 5, 11]. Despite this observation, epidemiological studies have not been able to clarify the role of environmental and genetic factors in their aetiology [3, 10]. Similarly, there is a wide difference in the reported ratio of primary to metastatic tumours [2, 13]. This may be a reflection of the nature of hospital practice and availability of adequate diagnostic facilities. In some centres, suspected bone secondaries in patients with known primary cancers do not even have a biopsy. The contrary holds true for others, where orthopaedic surgeons have a more aggressive approach. Resection of metastatic bone tumours may prolong the patient's survival [1]. While in most cases, the assumption that the bone lesions in patients with known primary cancers are metastases may be right, it is pertinent to note that a small percentage of these patients may have a different concomitant malignant tumour [8]. Furthermore, inadequate manpower, a lack of cooperation between the surgeon, radiologist and pathologist, and the absence of good diagnostic facilities may result in under-diagnosis or misdiagnosis of malignant bone tumours in some parts of the world [2].

The objective of this retrospective study, covering a 10-year period (1995 to 2004), is to establish the pattern of primary malignant and secondary bone tumours in Kuwait. During this period Al-Razi Orthopaedic Hospital was the referral centre for bone tumours. Biopsies of the skull and

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Fig. 1 Age and sex distribution of all malignant bone tumours

some vertebral tumours were taken by the Department of Neurosurgery, Ibn Sina Hospital. All materials from the two hospitals were examined by the Pathology Department of Al-Sabah Hospital.

Materials and methods

All malignant bone tumours diagnosed between 1995 and 2004 in the Pathology Department of Al-Sabah Hospital, Kuwait were taken from the departmental records. Age, sex, site and clinical presentation, and pathological findings were analysed from the records available. In addition to routine haematoxylin and eosin stains, special stains and immunohistochemistry were used in relevant cases.

Results

During the study period, 142 patients (83 male, 59 female) had histologically confirmed malignant bone tumours. These comprised 76 patients (58 male, 18 female) with primary and 66 patients (27 male, 39 female) with secondary tumours.

The age distribution curve of all malignant tumours as a group was bimodal with peaks in the age ranges 10 to 19 years and 50 to 59 years (Fig. 1). The first peak, unlike the second, showed a strong male predominance.

In 50 patients (35%) a pathological or impending fracture was the presenting clinical picture. Thirteen patients had primary malignant tumours, while 37 had secondaries.

Fig. 2 Trend analysis: incidence of primary malignant bone tumours

Primary tumours

The incidence of primary malignant bone tumours in the population during the study period varied from about 0.5 to 5.5/million (mean $\pm$ SD=3.3 $\pm$ 1.88). Male-specific incidence ranged from 0 to 7.2/million (mean $\pm$ SD=4.28 $\pm$ 2.46. Female-specific incidence ranged from 0 to 4.6/million (mean $\pm$ SD=2.2 $\pm$ 1.68). Trend analysis showed no consistent pattern on a yearly basis. However, when pooling each pair of successive years, there was a general rise, which was more pronounced in male patients than in female patients (Fig. 2).

Most patients with primary cancers irrespective of sex were aged between 10 and 19 years (Fig. 3). The frequency of the various histological types of primary bone cancers is shown in Table 1. The most common primary bone cancers in a descending order of frequency were Ewing's sarcoma/primitive neuroectodermal tumour (PNET), multiple myeloma/plasmacytoma, osteosarcoma and chondrosarcoma.

Ewing's sarcoma/PNET

Ewing's sarcoma/PNET was a predominantly male disease (17 male: 6 female). The patients were aged 8 to 31 years, with most (15 out of 23) being in the age range 10 to 19 years. The pelvic bone was the most common site of this tumour.

Multiple myeloma/plasmacytoma

There were 19 patients (15 male and 4 female), aged 38 to 75 years, with multiple myeloma/plasmacytoma. Most (16) were aged 50 years and above. Out of the four women, three had a preoperative diagnosis of metastatic bone disease, while tuberculosis was suspected in the fourth. Ten patients presented with pathological or impending fracture of long bones. Five of these were known cases of multiple myeloma and did not pose a preoperative diagnostic prob-

Table 1 Frequency of the various histological types of primary bone cancers

Histological type	Number of cases (%)
Ewing's sarcoma/PNET	23 (30.3)
Multiple myeloma/plasmacytoma	19 (25.0)
Osteosarcoma	16 (21.0)
Chondrosarcoma	6 (7.9)
Non-Hodgkin's lymphoma	5 (6.5)
Chordoma	3 (3.9)
Sarcoma (not otherwise specified)	1 (1.3)
Hemangiopericytoma	2 (2.6)
Malignant giant cell tumour	1 (1.3)
Total	76 (100)

PNET primitive neuroectodermal tumour

lem. The remaining five were clinically diagnosed as bone metastases (four cases) or benign lytic bone lesion (one case). Two of the former were undergoing treatment for breast or colonic cancer while the other two were assumed to have an unknown primary tumour.

Osteosarcoma

Twelve male patients and four female patients had osteosarcomata. Their ages varied from six to 22 years with a median of 16 years. Most (eight out of 16) were in the age range ten to 19 years. The tumour arose in the bones of the lower extremities in 13 patients and in the humerus in the remaining three. Thirteen patients had conventional intramedullary osteosarcoma, while the remainder had telangiectatic (2) or small cell variant (1).

Chondrosarcoma

Patients with chondrosarcomata were aged between 36 and 68 years with a median of 44 years. They comprised three

Fig. 3 Age and sex distribution of primary malignant bone tumours

Fig. 4 Age and sex distribution of secondary bone tumours

men and three women. The bones involved were as follows: vertebra, base of skull, humerus, femur and rib. The tumour was undifferentiated in the last two sites and well differentiated (grade 1) at the base of the skull, whereas it was histological grade 2 or 3 at the remaining sites.

Non-Hodgkin's lymphoma

There were five men with non-Hodgkin's lymphoma (NHL) with an age range of 30 to 63 years and a median age of 36 years. All had diffuse B-cell lymphoma, which was of the large cell type in three cases, small cleaved cell in one case and lymphoplasmacytoid in the fifth case. The following bones were involved: vertebra, pelvis and tibia.

Secondary tumours

Most (50 out of 66) metastatic bone tumours occurred after the age of 40 years. The peak age frequency for women was in the age range 50 to 60 years, while that of men occurred a decade later (Fig. 4). The femur (45.5%) was the most common bone involved, followed by the vertebra (28.8%). The frequency of bone involvement is shown in Table 2. The breast (20) was the most common site of primary cancer. Other common sites are shown in Table 3. Signif-

icant sex differences were observed in tumours metastasising to the femur, vertebra and pelvis (Fig. 5). While the majority of patients with femoral (23 out of 30) and pelvic (six out of eight) metastases were females, the converse (five out of 19) was true for vertebral secondaries. Pathological or impending fracture was a presenting clinical sign in 37 patients. Fifteen had breast cancer.

Femoral metastases

All seven of the male patients with femoral secondaries were more than 50 years old, while 48% of the 23 women were under 50. Information on clinical presentation was not available for one patient. The rest presented as follows: pathological fracture 24; impending fracture three; pain one; and swelling one. The breast was the most common site of primary tumours that had metastasised to the femur (17 out of 30).

Vertebral metastases

All 14 male patients were more than 40 years old. Five had unknown primary tumours. In the rest, prostatic and hepa-

Table 2 Frequency of bones involved in secondary bone tumours

Bone	Number of cases (%)
Femur	30 (45.5)
Vertebra	19 (28.8)
Pelvic bone	8 (12.1)
Humerus	7 (10.6)
Skull	1 (1.5)
Fibula	1 (1.5)
Total	66 (100)

Table 3 Frequency of site of primary cancer that has metastasised to bone

Site	Number of cases (%)
Breast	20 (30.3)
Prostate	7 (10.6)
Liver	5 (7.5)
Kidney	4 (6.1)
Thyroid	4 (6.1)
Lung	3 (4.5)
Colon	3 (4.5)
Other	10 (15.2)
Unknown	10 (15.2)
Total	66 (100)

Fig. 5 Site and sex distribution of secondary bone tumours

tocellular carcinomas were the most common. There were five female patients with vertebral metastases.

Pelvic bone metastases

There were six female and two male patients with pelvic bone metastases. The primary tumour was not identified in one of the patients. There were two cases each of metastatic breast cancer and neuroblastoma, one case each of metastasis from the kidney, prostate gland and Hodgkin's lymphoma.

Metastases to humerus

The four female and three male patients were between 38 and 71 years old with a median age of 53.5 years. All presented with fractures. There were two cases each of metastatic lung and colonic cancers, and one each from breast, thyroid and skin cancers (melanoma).

Discussion

The results of this study demonstrate some peculiarities in the pattern of malignant bone tumours in Kuwait. Contrary to most reports from Asia and Africa [2, 13], Ewing's sarcoma/PNET is the most common primary malignant tumour encountered in this study. This is, however, similar to a report from the Greater Bombay Cancer Registry [14]. The reason for this is not apparent and calls for a detailed epidemiological investigation. Multiple myeloma/plasmacytoma is the second most frequent primary malignant bone tumour. Significantly, most (40%) were diagnosed from the femur rather than from the pelvic bone. This is a reflection of the nature of hospital practice as the majority of the patients were seen in an orthopaedic hospital because

of pathological fracture or bone pain. Pathological fractures were encountered more frequently in patients with secondary (56%) than in those with primary (17%) tumours. The majority of the latter (77%) had multiple myelomas. The predominance of the former group of patients is consistent with other reports [7] and underlies the preoperative presumptive diagnosis of a metastatic tumour in some patients. Such a presumptive diagnosis was made in three patients who were later proven to have multiple myelomas. This finding strengthens O'Connor's emphasis on the need to avoid a rush to judgment and treatment of metastatic bone tumours [9].

As expected, the age and sex distribution of bone tumours in this study showed a bimodal curve. Primary tumours had an early peak in the age range 10–19 years and a strong male predominance. This is explained by the high frequency of Ewing's sarcoma and osteosarcoma. Both together comprised about half (51%) the primary tumours. On the other hand metastatic tumours occurred much later in life and displayed a slight female predominance. The differential sex prevalence may be attributed to the relatively high frequency of metastatic breast cancer. Consistent with other reports [12] the femur was the most common site of metastatic tumours. Different sex predilections were observed in tumours metastatic to the femur and vertebrae. While the former showed a strong female preference the converse was true for the latter. This can be explained by the type of primary tumours that metastasise to both sites. About 57% of tumours metastatic to the femur were from cancer of the female breast. It has been estimated that about 85% of patients with breast cancer develop bone metastases some time during the course of the disease [6]. Prostatic and hepatocellular cancers were the most common metastatic tumours in the vertebrae in this series. Both are predominantly male disorders.

The results of the study suggest a rising incidence of primary malignant bone tumours, especially in men. This is worrisome and highlights the need for further epidemiological study.

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