Original Article

Neglected orthopedic oncology - Causes, epidemiology and challenges for management in developing countries

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Abstract

BACKGROUND: Management of malignant bone and soft tissue tumors remains an overwhelming confront to orthopedic surgeons. The challenge is discriminating in developing countries due to inadequate diagnostic and therapeutic amenities and unawareness. A lot has been discussed about the neglected orthopedic trauma, but the published literature on the causes and management of neglected bone and soft tissue tumors is sparse. Hence, current study was undertaken to highlight the causes of neglect and therapeutic challenges for managing these neglected tumors in developing countries. **AIMS AND OBJECTIVES:** To determine the causes of neglect of malignant bone and soft tissue tumors, their epidemiology (including their relative frequencies, age, gender discrimination, anatomical sites of occurrence and histological characteristics) and difficult aspect of management due to neglect or delayed presentation. **MATERIALS AND METHODS:** This was an appraisal of the neglected malignant bone and soft tissue tumors presented to J. N. Medical College and Hospital from June 2008 to May 2013. Criteria for labeling the tumor as neglected malignant bone and soft tissue tumor was delayed presentation (>3 months), locally advanced disease, ulceration, sepsis, fungating mass or metastasis at the time of presentation. All the cases were reviewed and analyzed for age, gender, histological types, educational status and socioeconomic status of the family, any prior treatment by traditional bone setters or registered medical practitioner, cause of delay for seeking medical advice. We have also analyzed the treatment given at our institute and the outcome of the tumor. **OBSERVATIONS AND RESULTS:** Eighteen patients fulfilled the criteria for neglected malignant bone and soft tissue tumors, hence were included in study. Eight cases were of osteosarcoma, five cases were of Ewing's sarcoma, three cases were of chondrosarcoma and 1 case each was of pleomorphic liposarcoma and primary lymphoma of bone. According to Enneking staging system 11 cases were of stage III (distant metastasis) and 7 were stage II-B. Seven were females, and 11 were males. Age range was 5–68 years. 15 patients (83.3%) belonged to low socioeconomic status with 17 patients (94.4%) belonged to uneducated background. Cause of delay in seeking medical advice was neglect by the patient and family due to financial constraints, cultural and religious believes, lack of access to health care facilities, consultation with traditional bone setters and even misdiagnosis by qualified orthopedic surgeons. The tumors included were all unresectable and of huge sizes, hence were managed with amputation/dis-articulation, chemotherapy or radiation. **CONCLUSION:** The current study tries to highlight the causes and quantity of neglect of malignant bone and soft tissue tumors prevalent in our country, which poses a therapeutic challenge for management and consequent mutilating surgeries with poor outcome resulting in loss of extremity and existence.

Key Words: Bone/soft tissue tumors, malignant, metastatic, neglected, orthopedic oncology

Introduction

Although the incidence of bone and soft tissue tumors is relatively low constituting only 0.5% of the total world cancer incidence,[1] but the management of malignant bone and soft tissue tumors remains an overwhelming confront to orthopedic surgeons worldwide. The challenge is more discriminating in developing countries due to inadequate diagnostic and therapeutic amenities and unawareness. There are two types of bone tumors; primary and secondary. However, the precise cause for primary bone tumors is indefinite, but the predisposing factors to primary bone tumors include trauma,[2] irradiation,[3] foreign bodies[4] and mutation.[5] Bone tumors affect males more than females and occur more in the second and third decades of life.[6] The blight of bone and soft tissue tumors in developing countries remains distressing. Our inability to embark upon with this problem primarily arises from the interplay of the certain epidemiological factors viz; unawareness, low socio-economic status of our population and inadequate diagnostic and therapeutic amenities. Unawareness is mainly caused by misdirected cultural and religious beliefs prevalent in our society. Neglected tumors tend to be exceptionally symptomatic and prejudice the patient's quality of life. Extremity tumors, especially of the lower limbs prejudice ability to walk and to accomplish daily activities, further aggravating the problem and impairing the patient's quality of life. The neglected tumors may present with severe pain, sepsis, tumor fungation, hemorrhage, thrombosis, pathologic fractures, radiation-induced necrosis and severe functional impairment.[7] By and large malignant bone and soft tissue tumors carry a poor prognosis with high morbidity and mortality, their neglect or improper management makes the outcome even worse leading to loss of extremity and existence. A lot has been discussed about the neglected orthopedic trauma, but the published literature on the causes and management of neglected bone and soft tissue tumors is sparse. Hence the current study was undertaken to highlight the causes of neglect and therapeutic challenges for managing these neglected tumors in developing countries.

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Aims and objectives

To determine the causes of neglect of malignant bone and soft tissue tumors, their epidemiology (including their relative frequencies, age, gender discrimination, anatomical sites of occurrence, and histological characteristics) and difficult aspect of management due to neglect or delayed presentation.

Materials and Methods

This was an appraisal of the neglected malignant bone and soft tissue tumors presented to J. N. Medical College and Hospital from June 2008 to May 2013. Criteria for labeling the tumor as neglected malignant bone and soft tissue tumor was delayed presentation (>3 months), locally advanced disease, ulceration, sepsis, fungating mass or metastasis at the time of presentation [Figures 1a and 2a]. Locally advanced disease was defined as the tumor involving all the compartments of the extremity or a major adjacent structure such as the neurovascular bundle

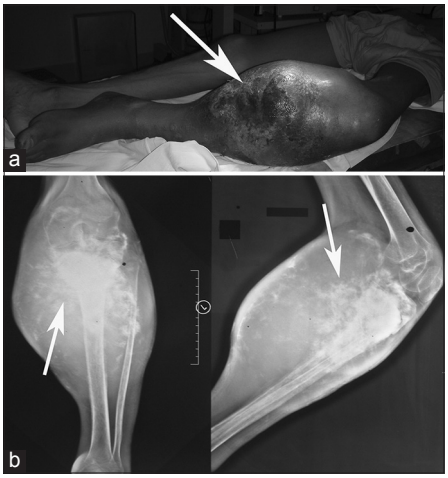

Figure 1: (a) Clinical photograph of patient showing (case 1) massive growth arising from the proximal aspect of leg with ulceration (arrow head). Also note the distal extremity edema (b) Plain radiograph of the patient showing osteosclerotic lesion involving the metaphyseo-diaphyseal region of proximal tibia with islands of new bone formation in soft tissues (arrow heads). Also note the massive soft tissue shadow and peri-articular osteoporosis. Patient was clinico-radiologically diagnosed as a case of osteosarcoma with lung metastasis (Enneking stage III). The diagnosis was confirmed by histological examination. This case demonstrates the amount of neglect prevalent in our country, rendering the tumor amenable to resection and reconstruction. Patient was managed with palliative above knee amputation and multi-agent chemotherapy to improve the quality of life

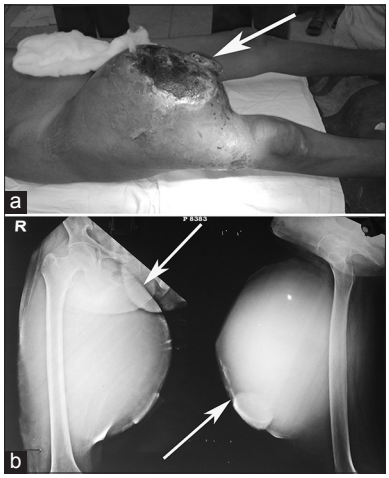

Figure 2: (a) Clinical photograph of patient showing (case 14) huge growth arising from the right thigh with fungation and ulceration (arrow head). This tumor was biggest in our series. The observation of such case in current study highlights the quantity of neglect of bone and soft tissue tumors prevalent in our country, which can lead to loss of extremity and existence (b) Plain radiograph of the thigh showing massive soft tissue shadow involving whole length of femur (arrow heads). The patient was managed with hip disarticulation

or organs like the chest wall or vertebra.[7] All patients were admitted and investigated for staging the tumor. Antero-posterior and lateral radiographs of the involved extremity [Figures 1b and 2b], and the plain radiograph of the chest were done. Complete blood count with general blood picture, blood urea nitrogen, liver function test including alkaline phosphatase, serum electrolytes (sodium, potassium and calcium) were done. MRI of the involved extremity and computed tomography scan of the chest were also done when required. Fine-needle aspiration cytology (FNAC) or biopsy of the lesion was made for establishing histological diagnosis of tumor. The histological classification was based on the current World Health Organization system of bone and soft tissue tumors.[8] Enneking staging system was used for staging the tumor. All the cases were reviewed and analyzed for age, gender, anatomical site involved, histological types, educational status and socioeconomic status of the family, any prior treatment by traditional bone setters or registered medical practitioner, cause of delay for seeking medical advice. We have also analyzed the treatment given at our institute and the outcome of the tumor.

Observations and Results

Eighteen patients fulfilled the criteria for neglected malignant bone and soft tissue tumors, hence were included in the study. Cause of delay in seeking medical advice was neglect by the patient and family due to financial constraints or low socioeconomic status (83.3%), unawareness (94.4%), lack of access to health care facilities (72.2%), consultation with traditional bone setters (66.6%) and even misdiagnosis by qualified orthopedic surgeons – 11.1% [Table 1]. Delayed presentation in our series ranged from 3½ months to 18 months (mean = 8.2 months).

Table 1: Demonstrating the causes of delayed presentation of malignant bone and soft tissue tumors in our series of neglected cases

Case no.	Low socio-economic status	Unawareness (Illiteracy)	Lack of access to health care facilities	Visit to bone setters	Misdiagnosis at hospital
1	+	+	+	+	-
2	+	+	+	+	-
3	-	+	-	-	-
4	+	+	-	-	+
5	+	+	+	+	-
6	+	+	+	+	-
7	+	+	-	-	-
8	-	+	-	-	-
9	+	+	+	+	-
10	+	+	+	+	-
11	+	+	+	+	-
12	+	+	+	+	-
13	+	+	+	+	-
14	+	+	+	+	-
15	-	-	-	-	+
16	+	+	+	-	-
17	+	+	+	+	-
18	+	+	+	+	-
Total (%)	15 (83.3)	17 (94.4)	13 (72.2)	12 (66.6)	2 (11.1)

Among the 18 patients included in the study, 8 cases were of osteosarcoma (44.4%), 5 cases were of Ewing's sarcoma (27.7%), 3 cases were of chondrosarcoma (16.7%) and 1 case each was of pleomorphic liposarcoma (5.6%) and primary lymphoma of bone (5.6%). Seven were females, and 11 were males. Age range was 5–68 years. In the present study, a significant proportion of neglected neoplastic bone lesions were seen to occur in children constituting about 72.1% [Table 2]. According to Enneking staging system 11 cases (61.1%)

were of stage III (distant metastasis) and 7 (38.9%) were stage II-B. The tumors included were all unresectable and of huge sizes, hence were managed with amputation/dis-articulation, chemotherapy or radiation [Table 3]. Seven (38.9%) patients refused surgery. Survival following diagnosis of tumor was ranged from 8 months to 3 years.

Discussion

This appraisal of the neglected malignant bone and soft tissue tumors describes the causes, epidemiology and difficult aspect of management due to neglect or delayed presentation at a tertiary referral center at J.N. Medical College and Hospital, A.M.U., Aligarh. Problem of neglect is almost indigenous to developing countries and is unheard of in developed nations and hence western literature is devoid of such studies. Thus, the study is relevant in that it addresses the problem of neglect of malignant bone and soft tissue neoplasms for which there are relatively few reports emanating from our nation,[9] emphasizing the need of the hour to create awareness among the masses regarding the neglect of bone and soft tissue tumors and their hazardous consequences. Eighteen cases of neglect of malignant bone and soft tissue tumors at our center over a period of 5 years gives an annual average of 3.6 cases/year. We believe that these cases are only the tip of the iceberg, with many of such patients dying without any conventional medical care or definitive diagnosis. Hence, this statistics may not be falsely taken to reflect the rarity of the tumors in our environment, but it particularly highlights the reluctance of our people to exploit conventional medical services while patronizing traditional bone setters and spiritual homes. In developed countries, statistics regarding the occurrences of bone and soft tissue tumors are

Table 2: Demonstrating relative incidence of occurrence of tumors in different age groups in our series of neglected cases

Age groups (years)	No. of cases	% of cases
0-10	3	16.6
11-20	10	55.5
21-30	1	5.6
31-40	0	0
41-50	1	5.6
51-60	2	11.1
61-70	1	5.6

Table 3: Illustrating age/sex, anatomical site, delay in presentation, Enneking staging, management and outcome of malignant bone and soft tissue tumors in our series of neglected cases

Case no.	Age (years) and sex	Anatomical location	Delay in presentation (months)	Enneking staging	Management	Outcome
1	15/M	Proximal tibia (Osteosarcoma)	10	III	Above knee amputation+ chemotherapy	Died after 10 months of diagnosis
2	11/M	Distal femur (Osteosarcoma)	5	II-B	Above knee amputation+ chemotherapy	Died after 1 and ½ years of diagnosis
3	14/F	Distal femur with skip metastases (Osteosarcoma)	7	III	Refused surgery Chemotherapy alone	Died after 11 months of diagnosis
4	7/M	Proximal tibia (Osteosarcoma)	5 and ½	II-B	Mid thigh amputation+ chemotherapy	Died after 2 and ½ years of diagnosis
5	11/M	Proximal fibula with common peroneal nerve palsy (Osteosarcoma)	8	II-B	Refused surgery Chemotherapy alone	Lost to follow up at 2 years
6	14/F	Proximal tibia (Osteosarcoma)	9	III	Above knee amputation+ Chemotherapy	Died after 9 months of diagnosis
7	15/M	Proximal humerus (Osteosarcoma)	7	III	Refused surgery Chemotherapy alone	Died after 13 months of diagnosis
8	10/F	Distal femur (Osteosarcoma)	7 and ½	III	Refused surgery Chemotherapy alone	Died after 8 months of diagnosis
9	5/M	Scapula (Ewing sarcoma)	5	III	Chemoradiation	Died after 15 months of diagnosis
10	18/M	Calcaneum with skip metastases (Ewing sarcoma)	7	III	Refused surgery Chemotherapy alone	Lost to follow up at 1 year
11	18/F	Clavicle (Ewing sarcoma)	5	II-B	Surgery+chemotherapy	Died after 11 months of diagnosis
12	12/F	Sacrum (Ewing sarcoma)	7	III	Chemoradiation	Died after 14 months of diagnosis
13	13/M	Femur (Ewing sarcoma)	8	III	Chemoradiation	Died after 10 months of diagnosis
14	60/F	Ilium (Chondrosarcoma)	10	II-B	Refused surgery Chemotherapy alone	Lost to follow up at 1 and ½ years
15	68/M	Ilium (Chondrosarcoma)	18	III	Chemoradiation	Died after 8 months of diagnosis
16	45/M	Proximal femur with pathological fracture (Chondrosarcoma)	15	II-B	Refused surgery+ chemoradiation alone	Died after 12 months of diagnosis
17	59/F	Thigh (Liposarcoma)	10	III	Hip disarticulation	Died after 1 and ½ years of diagnosis
18	23/M	Proximal humerus with pathological fracture (Lymphoma)	3 and ½	II-B	Chemoradiation	Died after 3 years of diagnosis

readily available from the properly maintained records and appropriate documentation of tumors by tumor registration. In developing countries, including India, such statistics is not available as there are no properly maintained records and appropriate documentation of tumors by tumor registration. In our study, the causes of neglect leading to delayed presentation were low socioeconomic status (poverty), unawareness (Illiteracy), lack of access to health care facilities, initial visit to traditional bone setters and even misdiagnosis at reputed hospitals by qualified orthopedic surgeons [Table 1]. The epidemiological factors viz; Low socio-economic status (poverty), unawareness (Illiteracy) and lack of access to health care facilities acts in a vicious circle as illustrated in Figure 3, propelling the family and patient to consult traditional bone setters, and thus leading to the hazardous consequences of neglect and delayed presentation. Two of our patients were misdiagnosed elsewhere as osteomyelitis (case 4) and radiculopathy (case 15). It is not uncommon that the tumors (whether benign or malignant) may be misdiagnosed as other entities owing to overlap in clinical presentation, as was reported in the literature.[10,11] One of our patients with osteosarcoma of the proximal tibia was misdiagnosed as osteomyelitis, operated for the same elsewhere, resulting in a delay in definitive treatment. Another patient with chondrosarcoma of ilium was misdiagnosed with radiculopathy since clinical presentation was consistent with the above diagnosis as the patient presented with weakness of ankle due to involvement of the sciatic nerve by tumor mass. These cases typically underscore the difficulties encountered in the diagnosis of malignant neoplasm, as early diagnosis difficult because of their rarity leading to lack of suspicion, overlapping clinical presentation, inexperience and lack of schooling on the part of the surgeon in managing such cases. Hence, we recommend all suspicious lesions on radiographs either subtle or obvious should be supplemented effectively with FNAC or needle biopsy for establishing the diagnosis as inappropriate diagnosis and treatment may delay and minimize the chances of a salvage procedure. Moreover, value of careful history is taking and clinical examination cannot be overemphasized.

In the present study, a significant proportion of neglected neoplastic bone lesions was seen to occur in children constituting about 72.1%. This figure is alarming as children contribute to the nation's progress, often becomes a burden on the family, and the nation following mutilating surgeries as a result of neglect and delayed presentation. In developing countries, like India it is not uncommon to find poor and unaware parents from villages, requesting the surgeon to save the extremity of their child when all the damage has already been done.

Osteosarcoma was the most commonly neglected primary bone tumor observed in our series, followed by Ewing's sarcoma, chondrosarcoma, pleomorphic liposarcoma and primary lymphoma of bone. Six cases of osteosarcoma were concentrated around knee, with one case each of the proximal humerus and proximal fibula. High proportions of osteosarcoma cases were probably due to its most common incidence in children and adolescents. It occurs

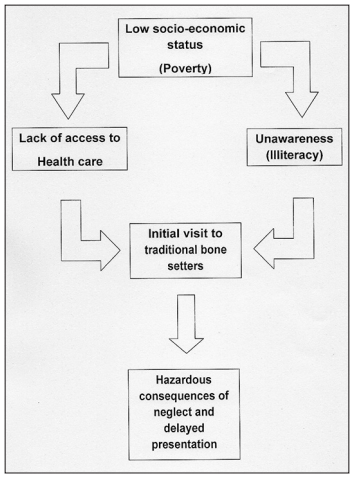

Figure 3: Illustrating the Epidemiological factors acting in a vicious circle propelling the family and patient to consult traditional bone setters, and thus leading to the hazardous consequences of neglect and delayed presentation

most frequently in the second decade of life involving the metaphysis of the long bones, with most of the cases concentrating around knee as was observed in our series.[12-15] Five cases of Ewing's sarcoma were observed in the current study, involving scapula, clavicle, sacrum and calcaneum and femur. Ewing's sarcoma is a highly malignant nonosteogenic primary tumor of the bone. Originally, James Ewing described it in 1921 as a tumor arising from undifferentiated osseous mesenchymal cells; however, new studies advocate that Ewing's tumor may be neuroectodermally derived from the primitive neural tissue.[16] It occurs most frequently in long bones and flat bones of pelvic girdles and shoulder girdle, in first two decades of life, with male predominance.[17] Our study has matched with the available literature with male predilection in cases presented to our institute. Three cases of chondrosarcoma were noted concentrating around hip (two cases involving ilium and one leading to pathological fracture of the proximal femur). Chondrosarcoma is the most common primary malignant bone tumor in the age group of 40–60 years. It frequently involves pelvic girdle, shoulder girdle, ribs and vertebra with a male preponderance.[12-15] Among the 3 cases in our study, all the three cases had their usual anatomical site of involvement, with male to female ratio of 2:1. One case of pleomorphic liposarcoma was observed in the current series. This tumor was biggest in our series. The tumor was fungating at the time of presentation. The observation of such case in current study highlights the quantity of neglect of bone and soft tissue tumors prevalent in our country, which can lead to loss of extremity and existence. Pleomorphic liposarcoma is a rare, speedily growing subtype of liposarcoma that occurs most commonly in the deep tissues of the extremities, and is discriminated from other high-grade sarcomas by the presence of pleomorphic lipoblasts.[18] It behaves as a high-grade sarcoma that often metastasizes to the lungs. One case of primary lymphoma of bone was observed in the current series. Primary lymphoma of bone occurs commonly between 20 and 50 years of age, and it shows a male preponderance. Femur is the most commonly involved bone, followed by the pelvis, humerus, skull and tibia.[19] Our patient showed a clinically complete remission of the disease initially but later on developed multiple metastases leading to loss of existence.

After discussing the causes and epidemiology of neglected bone and soft tissue neoplasms, it is worthwhile to discuss the difficult aspect of management. By and large malignant bone and soft tissue tumors carry poor prognosis with high morbidity and mortality, their neglect or improper management makes the outcome even worse leading to loss of extremity and existence. Management of such cases has several difficulties viz, the advance and metastatic nature of the disease necessitates a life-threatening or highly mutilating surgical procedures. Furthermore, performing mutilating surgeries on such patients without any obvious improvement in life expectancy not only raises ethical issues, but also has potential to generate psycho-social and emotional trauma in patients. According to Malawer *et al*.,[20] the indications for palliative major amputations include-involvement of a proximal limb or a major joint, accompanied by intractable pain, sepsis, tumor fungation, hemorrhage, vascular thrombosis, pathologic fractures, radiation-induced necrosis; or a limb with severe functional impairment. We have performed 7 palliative surgeries on the above indications as described by Malawer *et al*. In our experience, patient's undergone palliative surgery showed great improvement in quality of life. As was expected acceptance of mutilating surgical procedures were low in our society, with 7 (38.9%) patients refusing surgery, even after long session of counseling by senior surgeon.

Conclusion

The current study tries to highlight the causes and quantity of neglect of malignant bone and soft tissue tumors prevalent in our country, which poses a therapeutic challenge for management and consequent mutilating surgeries with poor outcome resulting in loss of extremity and existence.

Problem of neglect is almost indigenous in developing countries. Growing number of neglected tumors requires a coordinated and determined effort from the orthopedic fraternity and the government to create awareness among the masses regarding the neglect of bone and soft tissue tumors and their hazardous consequences.

In developing countries reported cases of tumors are only the tip of the iceberg, with many of such patients dying without any conventional medical care or definitive diagnosis. Hence, it is the need of an hour that we should start maintaining records and appropriate documentation of tumors by tumor registration.

While managing such cases, the need for early physical, emotional and psycho-social rehabilitation is to be emphasized.

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