Limb Saving Management in Osteosarcoma in Developing African Countries

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ABSTRACT

Osteosarcoma is still quite common in african countries. The disease which involves mostly poorer members of the community presents late. Treatment has been by amputation, chemotherapy and radiotherapy where amputation is impractical. Patients are now reluctant to have amputation hence exploration of limb saving procedures, find and overcome impedents to this kind of surgery. What do we need to do in future to make this kind of surgery available and affordable?

INTRODUCTION

Osteosarcoma is defined as spindle cell neoplasm that produces osteoid. There are several variations to this basic definition due to the cell variations in the various tumours encountered. At the Kenyatta National Hospital (KNH) the commonest type of osteosarcoma seen is the high-grade intramedullary osteosarcoma. Unfortunately our pathologists make no effort to differentiate between the various types. Other types include parosteal, telangiectatic, that originating from paget's disease and that from radiation. The majority of these tumours affect the young age groups . The high grade variety seen at KNH also comes in various forms of cell dorminance. i.e. chondroblastic, osteoblastic or fibroblastic (1). The prognosis appears to be more or less the same. Simply put grading of osteosarcoma can be put as stage IA being low grade tumour limited to the bone medullary cavity and cortex and 1B involving the surrounding soft tissues as well. IIA is high grade intermedullary osteosarcoma limited to the medullary cavity and cortex and IIB having invaded the surrounding soft tissue. Grade III will be with distant metastasis (2,3).

Age: The tumour affects mostly children and adolescents. The affected age group being 5 -30 years. However, from 1972 it has been noted that age has risen now affecting mostly the 3rd and 4th decades.

Distributions: The tumour affects areas around the knee i.e. distal femur, proximal tibia. Other areas are proximal femur, proximal humerus, distal radius and the pelvis. However, no bone is immune. The distribution is similar to that of osteomyelitis.

Presentation: There are three main forms of presentation namely pain, swelling and occasionally fracture. The most consistent and early presentation is pain, and detected at this stage the treatment is likely to have a good outcome. Unfortunately in most of Africa, the tumour presents at the stage of a mass. By this time the patient has been on treatment for many other conditions but the tumour. In developed countries it is noted that at the time of presentation 10-20% already have pulmonary metastasis. In Africa this figure is about 40-50% but detection methods are poor .

Examination: Examination usually reveals a tender bone in the area complained of. A mass may be felt which is an indication of late presentation. The temperature at the affected area is usually elevated leading to erroneous diagnosis of osteomyelitis. There may be a fracture clinically. Those real late presentations, the child is markedly wasted in contrast to the very large tumour (Figure 1).

Investigations: X-rays vary according to the stage of presentation. They may show hazy osteolytic areas, osteoblastic areas with outwardly extending bone; poorly defined endosteal margin or Codman's triangle formed by tumour, cortex and new bone reaction at elevation of periosteum.

Blood investigations unfortunately are still very limited but show mildly elevated erythrocyte sedimentation rate (ESR) and elevated serum alkaline

phosphatase. Other relevant tests mostly not available to poor african states include expression of P-glycoprotein, lactic dehydrogenase, alteration of DNA ploidy, anti shock protein 90 antibodies. Human epidermal growth factor receptor 2 (HEGFR2), CT, MRI and Isotopic scans have improved evaluation of extent of bone involvement and assessment of metastases. Only a few african states can afford these. The definitive diagnosis is made on biopsy and histological examination of the tumour.

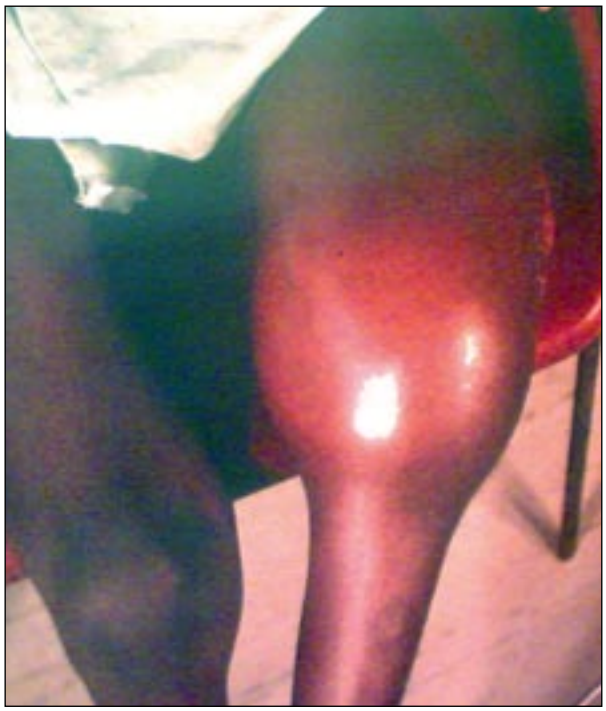

Figure 1: *Late presentation of osteosarcoma distal lt femur.*

Differential Diagnosis: In the African context the differentials lie between trauma, which patients almost always give as the cause of the pain. In actual sense, careful history taking will show that there was no trauma, but this history also contributes to delay in diagnosis. Other differentials include chronic osteomyelitis, stress fractures, bone cysts, chondrosarcoma, Ewing's tumour and fibrous dysplasia.

Management: Prognosis has markedly improved in other areas because of early diagnosis, better staging, increased average age at diagnosis and advances in chemotherapy. The mainstay of treatment at KNH is radical surgery and adjuvant chemotherapy. Radiotherapy has been tried in cases where parents have been reluctant to have radical therapy, which always means amputation, or where amputations are not practical. It does not seem to have much influence on tumour progression. In areas where it is affordable treatment consists of chemotherapy combining high dose methotrexate and other drugs preoperatively, surgery then postoperative chemotherapy.

Limb Saving Surgery: Is limb saving management of osteosarcoma possible in an african situation? When one is considering limb salvaging procedures a number of conditions need to exist. In most centres the average age is about 14 years. The tumour is diagnosed early; the tumour grading is good, preoperative chemotherapy is available and tumour necrosis rate assessed before surgery. Post operatively chemotherapy should be continued. The patient should be able to afford chemotherapy and the fare to come back for treatment and follow up. Some of the factors affecting prognosis includes radical therapy, grade of differentiation, histological subtype, soft tissue infiltration, reaction to preoperative chemotherapy and type of chemotherapy (4). It should be pointed out that even in most advanced centres complication rates for surgery is fairly high. They are early and late and include mechanical problems, infection and local recurrence. Local recurrence has ranged between 2.5 and 13% (5). Secondary amputation goes upto 10%, and reoperations upto 65%. Prediction of outcome of surgery is very difficult and tumour necrosis related to chemotherapy alone is no accurate indicator of surgical outcome. The local procedures carried out have included local excision of tumour and rotationplasty.

Additional surgical techniques may include arthroplasty, allografting, endoprosthetic replacement, autografting or resection without reconstruction (5). In some really good centres, with this measures actuarial survival curve plateau at 71% has been achieved at six years.

To illustrate the prevailing situation in some of our hospitals two cases will be reported here.

Case 1

CM was a 37 year old female who was seen in the author's clinic on 21st March 2000 with a one year history of pain in the left knee. The pain which was erroneously diagnosed to be due to osteoarthritis continued unabated inspite of treatment. The early X-rays taken showed a cyst in the patella and nothing else. She was started on nonsteroidal anti-inflammatory drugs (NSAIDs) pending surgery. Patient when reviewed on

6th April 2000 still had pain although she claimed she felt better. Two months later she still felt pain. In the following six months she had NSAIDs, local steroid injections, anxiolytic drugs and physiotherapy. On 12th September 2000 knee pain had stopped and she now had pain in the left thigh. Examination revealed a large mass in the mid thigh. She was admitted following X-rays showing a tumour in the mid thigh. Biopsy was done, and tumour excised six days later. Amputation was not done as patient flatly refused this. So CT scan was done to show extent of tumour spread in the bone, tumour excised, bone sterilized and re-implated and plated patient was put on chemotherapy. Had follow up to 10th April 2004 when she was seen with recurrence, was admitted again, this time with lung metastasis and died on 16th April 2004.

Figure 2: *A 37 year old female who was seen in my clinic on 21st March 2000 with a one year history of pain in the left knee.*

CASE 2

HH was a 14 year old female of Somali origin. She was seen on 12th November 2001 with history of pain of the left humerus for one year. Earlier X-rays showed tumour left humerus proximal end. Biopsy had confirmed osteogenic sarcoma. She was treated by chemotherapy alone by a physician. When she was first seen by a surgeon, the tumour was very big and had ulcerated. Plain X-rays and Tc 99 scan showed no obvious pulmonary metastasis. Parents completely refused to give consent for amputation. When the child was admitted to the ward for surgery, the mother escaped from the ward with her and it was only two weeks later she was readmitted after capture by the child's father. Tumour was excised and a fibula graft done. She was sent back to her physician for follow up chemotherapy. She was readmitted on 17th February 2002 with large chest metastases and she succumbed.

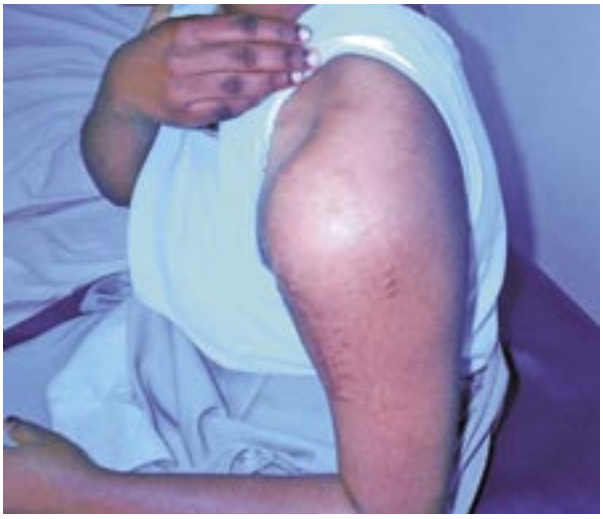

Figure 2: *A 14 year old female of Somali origin who was seen on 12th November 2001 with history of pain left humerus for one year.*

DISCUSSION

Osteosarcoma is still very commonly seen at KNH (7). In 2005 a total of 101 bone, and cartilage tumours were seen at KNH. Of these 24 were osteogenic sarcoma, which by the close of the year five had died. In 2006 a total of 80 bone tumours were seen of which 18 were osteogenic sarcoma and by end of the year four patients had died. The survival rate here is almost reminiscent of survival in most african state hospitals. Amputation as a form of treatment is becoming less acceptable and most of our practitioners have to seriously started looking at alternative limb saving therapies that are already prevalent elsewhere. The main impediments include:

Late Diagnosis: Patients present late. It used to be blamed on patients presenting late to the doctor but infact this is not the case. Pain takes patients to medical practitioners very early on in the disease. Patients are treated for many other conditions other than the osteosarcoma. The above two cases demonstrate this delay, patients first being seen a year after the symptoms began. All along they had seen medical personnel. It is a common observation that after biopsy, the tumour starts to grow much faster than before. It is important that the interval between biopsy and definitive treatment be not too long. This means longer discussion with the patient and guardians before the first cut into the tumour.Other forms of taking a biopsy will have to be considered.

Cost of Chemotherapy: Kenya now has a reasonable number of oncologists. The fact that a patient does not get adequate and relevant chemotherapy is more to do with cost than failure to develop the relevant regime of treatment. Most of the treatments available have methotrexate as the main drug with various combinations (7). Oncologists will need to identify credible generics in this regard as branded drugs are too costly. One study showed that two drug therapy of doxorubicin and cisplastin was not inferior to a three drug regime with methotraxate or multidrug therapy (5).

Treatment Protocol: There is an urgent need for a workshop between orthopaedic surgeons, oncologists, radiologists and pathologists to draw up a protocol of management so that a limb saving management be started at a number of centres to determine the feasibility of this kind of management that is highly desirable in this part of the world. Limb saving surgery is difficult and needs good back up with theatre space, good laboratory services, especially with bone bank , good radiological back up and good follow-up.

REFERENCES

1. Schajowicz F., Sissons H.A. and Sobin L.H. The World Health Organization's classification of bone tumours. *Cancer*. 1995; **75:** 1208-1214.
2. Kramarova E. and Stiller C.A. The international classification of childhood cancer. *Intl. J. Cancer*. 1996; **68:** 759-765.
3. Wolf R.E. and Enneking W.F. The staging and surgery of musculoskeletal neoplasms. *Orthop. Clin. North Amer.* 1996; **27:** 473-481.
4. Provisor A.J., Ettinge L.J., Nachman J.B., *et al*. Treatment of nonmetastatic osteosarcoma of the extremity with preoperative and postoperative chemotherapy: A report from the children's Cancer Group. *J. Clin. Oncol.* 1997; **15:** 76-84.
5. Grimmer R.J., Taminaiu A.M. and Cannon S.R. Surgical outcomes in Osteosarcoma *J. Bone & Joint Surg. (Brit)*. 2002; **3:** 395-400.
6. Weedens, Grimmer R.J., Cannon S.R., Taminiau A.H. and Usaniska B.M. European Osteosarcoma Intergroup. The effect of local recurrence on survival in resected Osteosarcoma. *Eur. J. Cancer*. 2001; **37:** 39-46.
7. Mulimba J.A.O. Osteogenic sarcoma at Kenyatta National Hospital. *Medicom*. 1998; **1:** 15-17.