Role Of Histopathology In Lytic Lesions Of Bone – A Study Of Seventy Cases Of Lytic Lesion Of Bone.
V Popat, V Sata, D Vora, V Bhanvadia, M Shah, L Kanara

Citation

Abstract
Aims: Histopathological study of lytic lesions of bone with evaluation of types and occurrence of different lesions with correlation in different age and sex. Material & method: A study of 70 cases of lytic lesion of bone was carried out during two years duration (January 2008 to December 2009). Result: In our study, out of 70 cases of lytic lesion of bone, 24 cases were of inflammatory lesions, 30 cases were of benign tumors, 6 cases of Primary malignant bone tumours and 10 cases of metastatic lytic lesions were found. Most of the patients belonged to the middle age group with the age incidence varying with the type of lesion. Out of these 70 cases, 46 were males and 24 were females. The lytic lesions occur more commonly in the males within the age group of 11-20 years. Conclusion: Benign tumors are more common amongst all lytic lesions with giant cell tumour ranking first in benign tumors. Tuberculous osteomyelitis is more common than pyogenic osteomyelitis. Secondaries in the bone are a more frequent finding than primary malignant tumors.

The present study was carried out in the Dept. Of Histopathology & Radiology, M. P. Shah medical college, Jamnagar, Gujarat state of India and cases were referred from Dept. of Orthopaedics. Of G. G. Hospital, M. P. Shah Medical College, Jamnagar.

INTRODUCTION
Lytic lesion of bone is a frequently found radiological presentation of patients seen in orthopedic practice. A spectrum of pathological lesions can be presented in this form from inflammatory to neoplastic conditions. The histopathologist is the final person to guide an orthopedic surgeon for the treatment of patients with lytic lesion. Lytic lesions of the bone are the most common radiological findings in various bone diseases including inflammatory and neoplastic lesions. In osteolytic lesions are present where the destructive processes outstrip the laying down of new bone. Lytic bone metastases must be greater than 1 cm and have destroyed 30-50% of the bone density in order to be seen by x-ray. [1] It is important to remember, however, that some benign processes such as osteomyelitis can mimic malignant tumours, and some malignant lesions such as metastases or myeloma, can mimic benign. It is difficult to determine radiologically with plain film imaging whether a lytic lesion is benign or malignant. It is more accurate to describe whether the process looks aggressive or nonaggressive. Pyogenic osteomyelitis is an acute inflammatory condition most commonly caused by staphylococcus aureus.[2] The osteolytic lesions of tuberculosis may closely mimic those due to multiple myeloma or secondary malignant deposits. [3] Neoplastic lesions, benign, malignant (primary and secondary) also produce lytic lesion in bones. Common presentations are progressive pain, swelling, tenderness & in some cases, acute pathological fracture. Within benign lesions, the differential diagnosis of lytic lesions includes simple bone cyst, aneurysmal bone cyst, osteochondroma (exostosis), enchondroma, giant cell tumor, fibrous dysplasia, osteoblastoma, chondroblastoma, non ossifying fibroma and brown tumour of the bone. Among the malignant tumors, the most common are primary bone tumors which include Ewing’s sarcoma, osteosarcoma, multiple myeloma and adamantinoma. Primary bone cancer is much rarer than bone metastasis.[4] Bone is the third most common site of metastatic disease.[5] As far as secondary tumors are concerned primary sites like lung, kidney, thyroid, breast, gastrointestinal and melanomas produce mainly lytic lesion while others elicit mixed lytic and sclerotic reaction. Carcinomas are much more likely to metastasize to bone than sarcomas. The axial skeleton is seeded more than the appendicular skeleton, partly due to the persistence of red bone marrow in the former. The ribs, pelvis and spine are normally the first bones involved and distal bones are rarely
affected. Diagnosis of all lytic lesions is made by 
radiological modalities like plain X-ray, CT scan, MRI and 
bone scintigraphy.

MATERIALS & METHODS

The study was carried out at departments of orthopedic, 
radiology and pathology. 
The criteria for the selection of patient are cases of 
radiologically apparent bone disease. 
Total seventy cases were selected and in all patients lytic 
lesion of bone was diagnosed 
radiologically. In orthopedic OPD, patients clinically 
presented with pain, swelling, non healing 
fracture. Detailed history was taken which mainly included 
age, sex, place of residence, 
occupation, fever, weight loss, cough, haemoptysis or 
history suggestive of systemic 
involvement. All patients were subjected to through physical 
examination both, systemic and 
general examination.

In all patients X-ray of lesioned bone had been taken while 
CT scan and MRI were done 
according to the need and advice of orthopedic surgeon. 
Pathological investigation included 
routine CBC, ESR and Urine examination in all patients 
while sputum, body fluid examination, 
Serum Calcium and alkaline phosphatase were done in 
selected cases.

Biopsy for histopathology was performed in all patients for 
the diagnosis of lytic lesions 
of bone. Biopsy was taken mainly by scrapping method, 
incision and excision method. 
In laboratory soft tissue were fixed in 10% formalin while 
for bone 3 to 5 mm thick 
sections were made and adequately fixed in 10% buffered 
formalin and then decalcification was 
achieved by placing the specimens in 5% nitric acid for 2 
days. After that all tissue were 
processed by increasing concentrations of alcohol and 
paraffin wax blocks were prepared. 
Sectioned were stained with haematoxylin and eosin. After 
that all slides were examined under 
microscope, the final diagnosis was made into inflammatory, 
benign and malignant lesion 
accordingly. In selected cases IHC was performed to 
confirm histopathological findings.

RESULTS

In results of our study 24 cases of inflammatory, 30 cases of 
benign, 6 cases of primary 
malignant and 10 cases of secondary malignant lytic lesions 
were found out of total 70 cases. So, 
the most common lytic lesion was benign neoplastic lesion 
of bone. (30 cases) [Table -1].

Figure 1

Table 1: Showing proportion of different lytic lesion.

<table>
<thead>
<tr>
<th>Lesions</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>24 (34.28%)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td></td>
</tr>
<tr>
<td>Benign</td>
<td>30 (42.85%)</td>
</tr>
<tr>
<td>Malignant Primary</td>
<td>6 (8.57%)</td>
</tr>
<tr>
<td>Malignant Secondary</td>
<td>10 (14.28%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>70</td>
</tr>
</tbody>
</table>

Out of 70 patients, 46 (65.71%) were male and 24 (34.28%) 
were female. In male patients 20 cases were of benign 
neoplastic lesion, 14 cases were inflammatory lesion and 12 
cases were malignant lesion. Where as in female, 10 cases 
were benign lesion, 10 cases were inflammatory lesion and 4 
cases were malignant lesion. So, benign neoplastic lesions 
were the most common among both the sex. [Table- 2].

From different age group, the most common age group was 
11-20 years, in which total 24 cases of lytic lesion were 
found, in which benign neoplastic lesions (18 cases) were 
most common. In age group 21-40 years, total 22 cases of 
lytic lesion were found, in which benign lesion (10 cases) 
was most common. In age group of above 40 years, total 22 
cases of lytic lesion were found, in which 10 malignant 
lesions were found. In below 10 year group only 2 case 
found which was of malignant types. [Table-3].

Figure 2

Table 2: Gender distribution of the lytic lesions of bone.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>6 (8.57%)</td>
<td>18 (25.71%)</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>10 (14.28%)</td>
<td>12 (17.14%)</td>
</tr>
<tr>
<td>Benign</td>
<td>20 (28.57%)</td>
<td>24 (34.28%)</td>
</tr>
<tr>
<td>Malignant Primary</td>
<td>6 (8.57%)</td>
<td>2 (2.85%)</td>
</tr>
<tr>
<td>Malignant Secondary</td>
<td>10 (14.28%)</td>
<td>2 (2.85%)</td>
</tr>
<tr>
<td>TOTAL</td>
<td>66 (95.71%)</td>
<td>24 (34.28%)</td>
</tr>
</tbody>
</table>
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Table 3: Age wise distribution of the lytic lesions of bone.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Age Groups (in years)</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-10</td>
<td>11-20</td>
<td>21-40</td>
<td>Above 40</td>
</tr>
<tr>
<td>Inflammatory</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyogenic Osteomyelitis</td>
<td>0</td>
<td>45.71%</td>
<td>45.71%</td>
<td>2.83%</td>
</tr>
<tr>
<td>Tuberculous osteomyelitis</td>
<td>0</td>
<td>0</td>
<td>48.74%</td>
<td>5.12%</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>0</td>
<td>15.15%</td>
<td>25.15%</td>
<td>2.83%</td>
</tr>
<tr>
<td>Primary malignant lesion</td>
<td>0</td>
<td>25.75%</td>
<td>25.75%</td>
<td>25.75%</td>
</tr>
<tr>
<td>Secondary malignant lesion</td>
<td>0</td>
<td>25.75%</td>
<td>25.75%</td>
<td>25.75%</td>
</tr>
<tr>
<td>TOTAL</td>
<td>25.75%</td>
<td>25.75%</td>
<td>25.75%</td>
<td>25.75%</td>
</tr>
</tbody>
</table>

Out of total 24 inflammatory lytic lesions, 10 cases were of pyogenic osteomyelitis and 14 cases were of tuberculous osteomyelitis. So, tuberculous osteomyelitis was slightly common than pyogenic osteomyelitis in inflammatory lytic lesion.[Table 4]. From total 30 benign neoplastic lytic lesions, 16 cases were of giant cell tumor, 4 cases were of fibrous dysplasia. Giant cell tumours show a higher incidence than other benign lytic lesion.[Table 5].

Table 4: Showing distribution of inflammatory lesion.

<table>
<thead>
<tr>
<th>Lesion</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pyogenic Osteomyelitis (Bacterial)</td>
<td>16</td>
</tr>
<tr>
<td>Tuberculous ( Koch’s) osteomyelitis</td>
<td>14</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 5: Showing distribution of benign lesion.

<table>
<thead>
<tr>
<th>Benign Lesion</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Giant Cell Tumor</td>
<td>16</td>
</tr>
<tr>
<td>Fibrous Dysplasia</td>
<td>4</td>
</tr>
<tr>
<td>Simple Bone Cyst</td>
<td>2</td>
</tr>
<tr>
<td>Anetomyssal Bone Cyst</td>
<td>2</td>
</tr>
<tr>
<td>Chondroblastoma</td>
<td>2</td>
</tr>
<tr>
<td>Enchondroma</td>
<td>2</td>
</tr>
<tr>
<td>Langhans Cell Histiocytoma</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>30</td>
</tr>
</tbody>
</table>

While in 16 malignant lesions, 6 cases were primary and 10 cases were secondary malignant lesions. So, Secondary lesions were more common than primary in malignant lytic lesions.[Table 6].

Figure 3

Figure 4

Figure 5

Figure 6

Table 6: Showing distribution of malignant lytic lesion.

<table>
<thead>
<tr>
<th>Malignant lesion</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
</tr>
<tr>
<td>Ewing’s sarcoma</td>
<td>4</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>2</td>
</tr>
<tr>
<td>Secondary</td>
<td></td>
</tr>
<tr>
<td>Secondary in Bone From Eosinophilic Variant Of Papillary Carcinoma Of Thyroid</td>
<td>2</td>
</tr>
<tr>
<td>Secondary in Bone From Renal Cell carcinoma</td>
<td>4</td>
</tr>
<tr>
<td>Secondary In Bone From Squamous Cell</td>
<td>2</td>
</tr>
<tr>
<td>Carcinoma of lung</td>
<td>2</td>
</tr>
<tr>
<td>Secondary From adenosarcoma Lung</td>
<td>2</td>
</tr>
<tr>
<td>TOTAL</td>
<td>16</td>
</tr>
</tbody>
</table>

KEY HISTOPATHOLOGICAL FEATURES OF LYTIC LESION IN OUR STUDY

INFLAMMATORY LESIONS- In cases of pyogenic osteomyelitis, large areas of necrosis, focal area of hemorrhage and acute inflammatory cells are found. In cases of tuberculous osteomyelitis, presence of epitheliod cells and caseation necrosis were inevitable. Few langhans giant cells and evident granuloma could be seen.

BENIGN NEOPLASTIC LESION- Out of sixteen cases of giant cell tumour, ten cases were from grade-I (conventional giant cell tumour), these tumours were showing many giant cells with plenty of nuclei located in central with abundant cytoplasm. Four cases of giant cell tumour were from grade-II. Two cases of giant cell tumour were having aggressive morphology (grade-III) in which number of giant cells were too less, number of nuclei in giant cells were less with atypical nuclear morphology and nuclei were arranged at the periphery of cell. Stromal cells were having aggressive nuclear morphology. Four cases of fibrous dysplasia were showing irregular, curvilinear bony trabeculae (Chinese letter pattern) lined by very few osteoblast in the background of bland fibrous stroma. Two cases of chondroblastoma were showing sheets of chondroblast having coffee-bean shaped nuclei along with chondroid matrix & giant cells. Two cases of enchondroma were composed of hyaline cartilage containing bland appearing chondrocytes. While simple bone cysts were showing cystic cavity lined by bland cell. In the two cases of aneurysmal bone cysts, hemorrhagic cystic cavity surrounded by bland fibrous stroma.
containing giant cell and reactive woven bone were seen. The two cases of langerhans cell histiocytosis showed plenty of eosinophils in the background of coffee bean shaped multilobated histiocyte.

MALIGNANT LESION- Four cases of Ewing’s sarcoma were showing small blue round cells having very scanty cytoplasm arrange in a sheets seperated by fibrovascular stroma. Two cases of osteosarcoma showed lace like neoplastic osteoid formed by anaplastic osteoblast and abnormal mitotic figure. Four cases of lung carcinoma metastasized to bone consisting of squamous cell carcinoma shows pleomorphic squamous epithelial cells in the back ground of bony trabeculae. Another two cases of adenocarcinoma of lung were showing malignant columnar cell arranged in adenoid pattern, which were confirmed at higher centre by IHC, tumours were positive for CEA and TTF-1. Two cases of secondaries were showing cells with ground glass nuclei, nuclear groove and arranged in a classical follicular pattern & thick colloid leads to diagnosis of follicular variant of papillary carcinoma in the clinically unsuspected cases (fig-1). Two cases were showing lobular arrangement of clear cells separated by vascular network leads to diagnosis of clear cell carcinoma of kidney, also confirmed at higher centre by IHC, tumours were positive for CK-7 and vimentin.

DISCUSSION

This study was carried out precisely to diagnose different lytic lesions of bone. One of the important point to be considered is the age of the patient. Some of the lytic lesions are most probably confined to certain age groups such as: metastatic neuroblastoma in the infant and young child, metastasis and multiple myeloma in the middle-aged and elderly, lymphomas affecting only bone usually occur during adult life; most cases after 25 years of age. Ewing’s sarcoma and simple bone cyst in the long bones of children and young teenagers, and giant cell tumor in the young to middle-aged adult (20 to 50 years of age).[5,6] But in our study, maximum number (10 out of 16) of cases were found in second decade only. Even the most common age group of all lytic lesions was 11-20 years, in which total 24 cases of lytic lesions were found composed of 18 cases of benign neoplastic lesions. In age group 21-40 years total 22 cases of lytic lesion were found, in which benign (10 cases) were the commonest. In age group above 40 years, a total of 22 cases were found, in which malignant lytic lesion was the most common diagnosis. In below 10 year group only 2 cases were found of Ewing’s sarcoma(fig-2). In our study, osteomyelitis was found in all age groups above ten years. The diagnosis of chronic recurrent multifocal osteomyelitis is essentially one
of exclusion. Infective osteomyelitis and malignancy are the main differential diagnoses.\[7\] The osteolytic lesions of tuberculosis at multiple sites need to be differentiated from multiple myeloma, secondary metastasis and bacterial osteomyelitis. Delay in diagnosis is usually due to the patients presenting late or it may be due to lack of awareness and its insidious onset.\[8\]

**Figure 8**

fig-2 Shows X-ray Lytic lesion of Ewing’s sarcoma at lower end of femur

Histopathological examination yields a high percentage of positive results.\[9,10\] In our histopathological study, tuberculosis was more common than bacterial osteomyelitis in inflammatory lytic lesion and mostly found in elderly age groups. Ewing sarcoma and lymphoma are important differential diagnoses.

In our study, out of 70 cases of lytic bone lesions, most common were benign neoplastic lesions making 30 cases. Out of 30 benign neoplastic lytic lesions, 16 cases were giant cell tumour of bone(fig-3). In present study, the most common site of giant cell tumor was lower end of femur and upper end of tibia. Giant cell tumor accounts for 5 to 9 percent of all primary bone tumors. It is the most common bone tumor. Most patients present with slowly progressive pain, with or without a mass. Symptoms arise when the lesion begins to destroy the cortex and irritate the periosteum or when the weakening of the bone caused by the tumor causes pain due to imminent pathologic fracture. Some giant cell tumors present with a pathologic fracture. Radiological findings demonstrate the lesion is most often eccentrically placed to the long axis of the bone.\[11\]
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Figure 9
fig-3 Shows X-ray Lytic lesion of giant cell tumor at lower end of radius.

Other benign lytic lesions included 4 cases of fibrous dysplasia and in both cases site of lesion was upper end of tibia. Langerhans cell histiocytosis usually presents as a pathological fracture or an incidental finding and heals spontaneously.[7]

In our study, Langerhans cell histiocytosis was presented with pain and pathological fracture since 8 months in a 16 year male patient which was previously diagnosed as acute on chronic osteomyelitis by another pathologist and didn’t respond to treatment and after that referred to us. So careful histopathological examination is required to differentiate osteomyelitis and langerhans cell histiocytosis.

Ewing’s sarcoma is found in the lower extremity more than the upper extremity, but any long tubular bone may be affected. The most common sites are the metaphysis and diaphysis of the femur followed by the tibia and humerus. In our study, out of 70 cases of lytic bone lesion, most common primary malignant lesion was Ewing’s sarcoma, the four cases were found in lower end of femur & tibia, below 20 years of age. Osteosarcoma can arise in any bone of the body but majority originate in long bones of appendicular skeleton, especially the distal femur, followed by the proximal tibia & proximal humerus- sites containing the most proliferative growth plates. In the long bones the tumour is most frequently centered in the metaphysis (90%), infrequently in the diaphysis (9%), and rarely in epiphysis.[12] In our study, two cases of osteosarcoma were found in elderly male patients in lower end of femur which were confined to metaphysis.

Pain, pathological fractures and hypercalcemia are the major sources of morbidity with bone metastasis. Pain is the most common symptom found in 70% patients with bone metastases.[13] Pain is caused by stretching of the periosteum by the tumor as well as nerve stimulation in the endosteum. Pathological fractures are most common in breast cancer due to the lytic nature of the lesions. Hypercalcemia only occurs in 10% of patients.[14] In our study eight cases of metastatic lytic lesion were found, which included Follicular Variant Of Papillary Carcinoma of thyroid metastasize to upper end of femur, Carcinoma of kidney with metastasis to L3 vertebra, Squamous Cell Carcinoma of lung and adenocarcinoma of Lung metastasize to upper end of humerus. Six cases were presented with pain, weight loss and non healing pathological fracture. All the eight cases had shown increase level of alkaline phosphatase while adenocarcinoma of lung with metastasis to bone found to have hypercalcemia. In case of follicular variant of papillary carcinoma of thyroid lytic lesion over upper end of femur were the first noticeable sign and even the patient & clinician were unaware of thyroid malignancy.

Finally we conclude, lytic lesion of bone is a very used to
radiological finding for orthopedic surgeon in many patients. Even an orthopedic surgeon and radiologist together won’t be able to reach to the precise conclusion and further treatment. Histopathology is the gold standard for the precise diagnosis from a very large number of conditions leading to lytic lesion. Among the various diagnoses, benign tumors form the largest group (42.85%) of patients presenting with a lytic lesion on radiological findings. There is a male preponderance with 65.71% of the patients being males. Also, majority of the patients fall into the second decade with 34.28% of the patients in the age group of 11-20 years. The common diagnoses among the benign lesions were giant cell tumors, while there were a slightly higher number of cases of tuberculous osteomyelitis as against bacterial osteomyelitis in the inflammatory conditions. Among the malignant lesions, secondaries were a commoner diagnosis as opposed to the primaries, and they tend to occur more commonly in the elderly population. The commonest primary malignant lesion that showed up was Ewing’s sarcoma. Overall, giant cell tumor is the commonest diagnosis presenting with a lytic lesion on radiological finding. Occult malignancy can be presented as lytic lesion of bone in the form of secondary. All lytic lesions may have osteoclastic giant cells and they should not be misinterpreted as Giant cell tumor.

References
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