Original Research Article

Role of Histopathology in the Diagnosis of Lytic Lesions of Bone: A Five Year Retrospective and Prospective Study

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Abstract

Background: The clinical and radiological features of many bone lesions overlap. Some benign processes such as osteomyelitis can mimic malignant tumors, a callus with an associated fracture can mimic osteosarcoma, whereas some malignant and metastatic lesions may mimic benign lesions. Even an orthopedic surgeon and radiologist together cannot come to a conclusion precisely. Therefore, the histopathological examination is the final guide to the orthopedic surgeon for the treatment of patients. The aim of this study to evaluate the histopathological examination of osteolytic lesions with assessment of their morphological pattern and their correlation with the clinicoradiological diagnosis. **Materials & Methods:** A retrospective and prospective analytical study done on all patients with the radiological diagnosis of lytic lesion of bone (as evaluated by a plain x-ray) attending the OPD of the orthopedics department, and admitted to Mahatma Gandhi Hospital and Mathura Das Mathur Hospital, Jodhpur during the period of July 2009- June 2014. Their biopsies were sent to the Department of Pathology, Dr. S.N.Medical College, Jodhpur. Data was entered and analyzed by using Microsoft Excel version 2007 and Statistical Package for social science ver.16(SPSS.16) and necessary and appropriate statistical tests were applied and p value less than 0.05 was considered statistically significant. **Results:** Our study shows that males were affected more commonly than females in most of the age groups except at the extremities of age where males and females were equally 1.Thebenign tumors when taken together were the most frequent lesions encountered (33.02%) followed by tumor like lesions (23.58%) and inflammatory lesions (22.65%). 16.98% cases were of malignant tumors and a small percentage (3.77%) were of metastasis from other sites.Pain was the most common presenting symptom singly as well as associated with other complaints like swelling, fever etc.The histopathological diagnosis was similar to the radiological diagnosis in 86 (81.1%) cases whereas it was not similar to the radiological diagnosis in 20 (18.9%) cases. **Conclusion:** We concluded that light microscopy or histopathology is the gold standard in the diagnosis of bone lesions and invariably accurate when correlated with clinicoradiological features.

KeyWords: Histopathology, Lytic Lesions, Bone, Radiographic, Clinical, Benign, Malignant.

Introduction

Bone is a structurally important dynamic tissue which provides mechanical support for movement, supports viscera and determine the size and shape of the body.

Bone lesions are diverse in size, gross and histological features and range from innocuous to rapidly fatal lesions which are diverse in nature. It is critical to diagnose these tumors and tumor like lesions correctly, stage them accurately and treat them appropriately, so that the patients not only survive but also maintain optimal function[1].Conventional radiographs usually are the basic means of evaluating skeletal lesions as they are inexpensive and easily available. Radiological diagnosis of any bone lesion takes into account the site of lesion, borders, type of matrix, type of bone destruction, number of lesions and the nature and extent of soft tissue involvement[2].

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Osteolytic lesions are frequently found radiological presentation of patients in orthopedic practice. A broad spectrum of pathological lesions ranging from inflammatory to neoplastic conditions can present in this form. They vary greatly in their aggressiveness and clinical behavior, thus requiring early diagnosis and a broad spectrum of treatment options. The behavior of these lesions varies from innocent nature requiring no active treatment to an aggressive and destructive nature with potentials of transforming into malignancy and even producing metastases[3,4]. These are diverse in size, gross and histological features and range from innocuous to rapidly fatal lesions. As a group, these affect all ages and virtually every bone[1].

However, keeping in mind the extremely wide spectrum of the osteolytic lesions and the inability of the plain x-ray films to accurately diagnose the disease, it can be said that radiography is just one of the steps in the diagnosis of the bone lesion.

The clinical and radiological features of many bone lesions overlap. Some benign processes such as osteomyelitis can mimic malignant tumors, a callus with an associated fracture can mimic osteosarcoma, whereas some malignant and metastatic lesions may mimic benign lesions. Even an orthopedic surgeon and radiologist together cannot come to a conclusion precisely. Therefore, the histopathological

examination is the final guide to the orthopedic surgeon for the treatment of patients.Histopathology is the current gold standard for the diagnosis of bone lesions[5].However, pathologists should be familiar with the clinical and radiological features of the various lesions, along with the sex, age group, and anatomical sites these lesions favour, all such crucial data must be considered when generating differential diagnosis. The pathologist's position is, in many ways, similar to that of a lens focusing on a single spot with multiple beams of light. A review of clinical information, surgeon's personal impression before and during surgery, and imaging findings should be correlated with the microscopic findings to achieve the most meaningful final diagnosis[6].

The key to the accurate diagnosis of any osteolytic lesion is the utilization of an integrated approach that assesses and correlates the clinical findings including age, involved bone and the specific part of the bone involved, radiological and morphological behavior of these lesions[7-9]. Rapid and correct diagnosis is important for early institution of the therapy. Therefore, a systemic approach to clinical history, radiographic evaluation and histopathology is necessary for accurate diagnosis[2].Morphological analysis disconnected from the clinical and radiographic context may lead to misinterpretation[6].

Hence, to diagnose bone lesions, there should be a team approach including orthopedic surgeon, radiologist, pathologist and a clinician, who is specialized in treatment of these patients.[9] The aim of this study to evaluate the histopathological examination of osteolytic lesions with assessment of their morphological pattern and their correlation with the clinicoradiological diagnosis.

Materials & Methods

A retrospective and prospective analytical study done on all patients with the radiological diagnosis of lytic lesion of bone (as evaluated by a plain x-ray) attending the OPD of the orthopedicsdepartment, and admitted to Mahatma Gandhi Hospital and Mathura Das Mathur Hospital, Jodhpur during the period of July 2009- June 2014. Their biopsies were sent to the Department of Pathology, Dr. S.N.Medical College, Jodhpur.

Inclusion Criteria

The study group included all patients with the radiological diagnosis oflytic lesion of bone (as evaluated by a plain x-ray).

Exclusion Criteria

Inadequateandautolysedsamples.

Methods

Following information was obtained from requisition forms and hospital records-

1. Name, age and sex
2. Clinical findings
3. Plain x-ray
4. Biopsy examination: sections were stained with Hematoxylin and Eosin.

Processing of Bone Biopsy Tissue: Formalin fixed biopsy specimen ofbone was kept in nitric acid for decalcification after sawing of bone.

1) **Sawing-** Bone saw was used for this purpose
   - Any soft-tissue adherent to the bone was removed.
   - The bone was cut in slabs of 3-5mm thickness.

2) **Decalcification-** The bony tissue was dimineralised by keeping it in 5% aqueous nitric acid solution for 24-48 hours. The stage of completion of demineralization was checked by 5% ammonium hydroxide solution by assessing residual calcium.
3) **Fixation –** The decalcified tissues were kept in 10% formalin (the volume offormalin was 10-20 times of tissue volume) for 24 hours for fixation.
4) **Dehydration-** This was done with acetone. One to two hourly in three increasing strength i.e. 60%-80% followed by 100%.
5) **Clearing-** This was done by keeping the processed material in xylene for one to two hours.
6) **Impregnation-** Processed material was kept in molten wax overnight.
7) **Embedding-** Biopsy material was embedded in paraffin wax and molded in a square block.
8) **Section Cutting-** The sections were cut with a microtome at a thickness of 5*u*. Sections were taken on albuminized slides, placed on hot plates at a temperature of 54°C to 56°C to melt the wax.The sections were put in xylene to remove wax for half an hour followed by descending serials of alcohol and then in distilled water.
9) **Staining-** Staining was done with hematoxylin and eosin.

Hematoxylin and Eosin (H& E) Staining Procedure

1. Sections were deparaffinized and then hydrated by passing through decreasing concentration of alcohol bath and water. Then washed in tap water and rinsed in distilled water.
2. Harris's Hematoxylin solution was poured on slides for 3-5 minutes and then slides were washed in running tap water.
3. Slides were differentiated in 1% acid alcohol.
4. After rinsing the slides in tap water, they were dipped in Lithium Carbonate.
5. Then slides were washed in tap water and agitated in Eosin solution for 1-2 minutes.
6. After draining solution, slides were dehydrated through increasing concentration of alcohol.
7. Then slides were cleared in xylene.
8. After draining the excess xylene, slides were mounted in DPX with a cover slip.

Data Entry and Analysis

Data was entered and analyzed by using Microsoft Excel version 2007 and Statistical Package for social science ver.16(SPSS.16) and necessary and appropriate statistical tests were applied and p value less than 0.05 was considered statistically significant.

Results

Our study shows that males were affected more commonly than females in most of the age groups except at the extremities of age where males and females were equally affected (table 1).

The present study found that benign tumors when taken together were the most frequent lesions encountered (33.02%) followed by tumor like lesions (23.58%) and inflammatory lesions (22.65%). 16.98% cases were of malignant tumors and a small percentage (3.77%) were of metastasis from other sites.

Pain was the most common presenting symptom singly as well as associated with other complaints like swelling, fever etc (table 2).

The histopathological diagnosis was similar to the radiological diagnosis in 86 (81.1%) cases whereas it was not similar to the radiological diagnosis in 20 (18.9%) cases (table 3).

Table 1: Age Wise Gender Distribution of the Cases

Age Group (Yrs)	Male	Female	Total
≤ 10	6 (50)	6 (50)	12 (100)
11-20	21 (61.8)	13 (38.2)	34 (100)
21-30	18 (64.3)	10 (35.7)	28 (100)
31-40	7 (70)	3 (30)	10 (100)
41-50	4 (66.7)	2 (33.3)	6 (100)
51-60	5 (71.4)	2 (28.6)	7 (100)
61-70	5 (71.4)	2 (28.6)	7 (100)
≥71	1 (50)	1 (50)	2 (100)
TOTAL	**67**	**39**	**106**

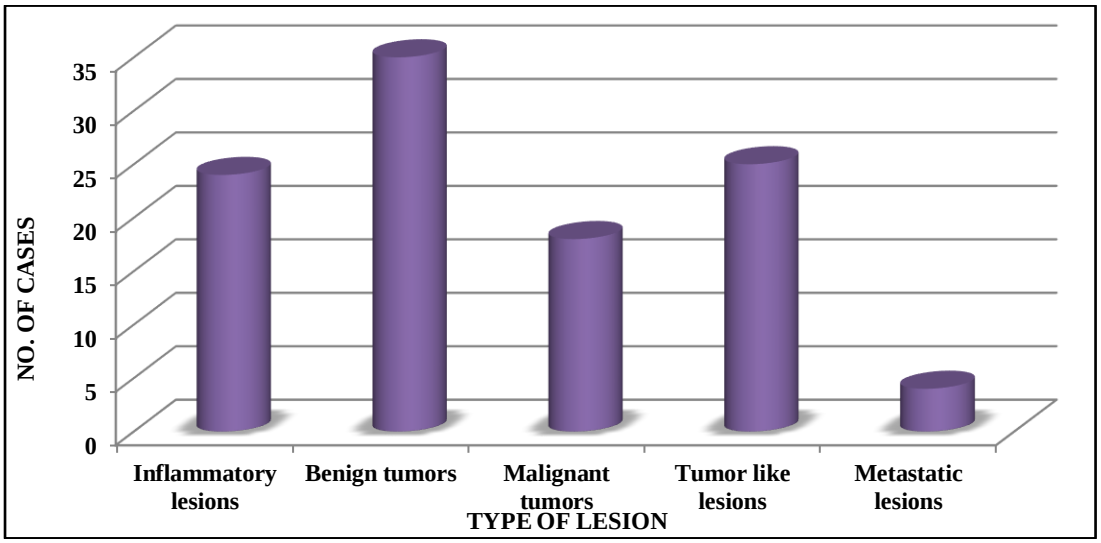

Figure 1: Distribution of Cases Based on the Behaviour of Lytic Bone Lesions

Table 2: Distribution of Cases on the Basis of Clinical Symptoms

Presenting Symptoms	No. of Cases
Pain	38
Swelling	19
Pathological fracture	7
Pain + swelling	37
Pain + fever	2
Pain+discharging sinus	1
Pain+swelling+fever	2

Table 3: Clinico- Radiological V/S Histopathological Diagnosis

	Histopathological Diagnosis																		
Clinico Radiological Diagnosis	**Osteomyelitis**	**Osteoid Osteoma**	**Osteoblastoma**	**Osteosarcoma**	**CMF**	**Chondroblastoma**	**Enchondroma**	**Chondrosarcoma**	**GCT**	**Ewings Sarcoma**	**SBC**	**ABC**	**Fibrous Dysplasia**	**NOF**	**GCRG**	**LCH**	**Plasma Cell Myeloma**	**Metastasis**	**Total**
Osteomyelitis	20	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	21
Osteoid Osteoma	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	5
Osteoblastoma	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Osteosarcoma	0	0	0	4	0	0	0	0	1	0	0	0	0	0	0	0	0	0	5

CMF	0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	4
Chondroblastoma	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Enchondroma	0	0	0	0	0	0	3	0	1	0	0	0	0	0	3	0	0	1	8
Chondrosarcoma	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	3
GCT	2	0	0	0	1	2	0	0	16	0	0	1	0	0	0	0	0	1	23
Ewings Sarcoma	2	0	0	1	0	0	0	0	0	7	0	0	0	0	0	0	0	0	10
SBC	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	0	0	6
ABC	0	0	0	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0	3
Fibrous Dysplasia	0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0	6
NOF	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	4
GCRG	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LCH	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1
Plasma Cell Myeloma	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	2	5
Metastasis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Total	24	5	1	5	4	3	3	3	18	7	7	4	6	5	3	1	3	4	106

Discussion

Histological examination of lytic bone lesions is one of the difficult subjects in pathology. These are comparatively uncommon lesions. Low incidence of these lesions and the resulting limited experience is probably a major factor in the differences between the initial diagnosis made on clinicoradiological assessment and pathological diagnosis. A total of 106 cases which were radiologically described as osteolytic lesions were studied and analyzed. The study included inflammatory lesions, primary tumors and tumor like lesions and metastatic lesions.

In our study, the age of the patient ranges from 6 to 85 years. Most common age group was between 11-20 years (32.09%) followed by the third decade of life.(26.42%).Mean age in the study was 28.23years. These results were similar to the studies done by Patil P (2012)[10] and Nayar M (1979)[11] who concluded that bone tumors were most common in 2nd decade of life (29.4% and 37.7% respectively). The mean age for males was 29.23 years (n=67) and females was 26.51 years (n=39).

A total of 106 cases were analyzed out of which 69 (65.09%) were males and 37(34.91%) were females with a male: female ratio of1.78:1.The findings of G.A.A. Oyemade et al (1982)[12] was in concordance with the present study. They analyzed 170 cases with bone neoplasms diagnosed over the 17-year period 1960-1976. There were 119(70%) male and 51(30%) female patients. V Popat et al (2010)[5] in a study of 70 cases found that 46(65.7%) were males and 24(34.3%) were females.P Patil (2012)[10] in a study of 64 cases found that 69% were males and 31% were females.

In the present study, benign tumors were found to be the most common lesions when taken together comprising of 35 cases out of 106 cases (33.02%) followed by tumor like lesions (23.58%), inflammatory lesions(22.65%), malignant tumors(16.98%) and metastatic lesions(3.77%) in that order. The results are comparable to the study done by Simon MA et al (1993), Lewis MM et al.(1993)[13,14] in which they concluded that among all the bone tumors, benign bone tumors were very common, but prevalence was not calculated.Unni K et al. (1996)[15] studied the general aspect of data on 11,087 cases and revealed benign tumors were more common in comparison to malignant tumors and the ratio between them was 1000:1.V Popat et al. (2010)[5]studied the role of histopathology in lytic lesions of bone in 70 patients in a 2 year durationfound that 24 cases were of inflammatory lesions, 30 cases were of benign lesions, 6 cases were of primary malignant tumors and 10 cases of metastatic lytic lesions and Patil P (2012)[10] in a study of 64 cases found that benign tumors constituted 38.2%, malignant tumors 51.5% and tumor like lesions constituted 10.3% of total bone lesions.

Among the various lesions, osteomyelitis was the most common, seen in 22.64% cases. GCT was the most commonnon inflammatory lesion encountered comprising ofabout 17% of the total cases, followed by Ewing's sarcoma(6.6%) and simple bone cyst(6.6%). Other lesions encountered were fibrous dysplasia (5.6%), osteoid osteoma, osteosarcoma, CMF(4.72%), NOF, ABC and metastatic lesions(3.77%), chondroblastoma, chondrosarcoma, enchondroma, plasma cell myeloma and GCRG (2.83%). One case each of osteoblastoma and LCH were seen. These findings were consistent with the data obtained in other studies- Yeole BB et al. (1998)[16] revealed that in all bone tumors, Ewing's sarcoma, chondrosarcoma and osteosarcoma are the principal malignant tumors involving bone. Howard D Dorfman (1995)[17] found that osteosarcoma was the most frequently diagnosed primary sarcoma of bone(35.1%), followed by chondrosarcoma (25.8%), Ewing's sarcoma (16.0%). Makashir R et al. (1991)[18] concluded that primary small bone tumors are rare. In this retrospective study of small bone tumors over the period of 5 years, the commonest tumor encountered was enchondroma. Next in frequency were exostosis, giant cell tumor and benign chondroblastoma. Similarly, K.C.Katchy(2005)[19] studied between 1995 and 2004, 142 malignant bone tumors comprising 76 primary and 66 secondary tumors. The most frequent in the descending order of frequency were Ewing's sarcoma, multiple myeloma, osteosarcoma, chondrosarcoma and Non Hodgkin's lymphoma.

After analyzing the data, it was found that pain and swelling were the most common presenting symptoms of bone lesions. These findings were in concordance to study done by G.A.A. Oyemade et al. (1982)[12] who analyzed 170 cases with bone neoplasms and observed that the most common symptom was painful swelling. The same findings were observed by Buckley JD et al. (1998)[20] who reviewed 305 cases of bone tumor and described pain and swelling as most common presenting symptom. Also, Simon MA et al. (1993), Lewis MM et al. (1993)[13,14] concluded that presenting symptoms of bone tumors were noted to be very important parameters indicating the diagnosis. Among all the bone tumors, benign bone tumors were very common and characterized by painless swelling of long duration while malignant bone tumors on the other hand most commonly presented with pain and swelling of short duration. Similar to this, B JorhWidhe et al. (2000)[21] conducted a study on a

group of patients and revealed that pain was the initial symptom and swelling was the initial sign of these tumors.

As exact diagnosis ofbone lesions is at times difficult, a joint approach integrating clinical, radiological and histopathological findings is recommended to increase accuracy.

In the present study, there was a good correlation between the clinicoradiological and histopathological diagnosis. Among the 106 cases studied, histopathological diagnosis was same as the radiological diagnosis in 86 (81%)cases. However, 20 (19%) cases were discordant radiopathologically. The Pearson's correlation coefficient between radiological and histopathological diagnosis was calculated as 0.763(P value < 0.0001). The Cohen's Kappa coefficient calculated was 0.761 which indicates that the strength of agreement between the clinicoradiological and histopathological diagnosis is good. This is in concordance to the studies done by Bayush E Nagesh et al. (2009)[2] Kappa value 0.82,Wamisho BL et al. (2009)[22] Kappa value 0.82, Patil P (2012)[10] Kappa value 0.817.

Taking the individual osteolytic lesion into account, maximum discordance is seen in GCT in which discrepancy was seen in 7 out of 23 radiologically diagnosed GCT cases. There was concordance in 16 cases. Among the discordant cases, 2 cases were of osteomyelitis, 2 cases of chondroblastoma and 1 case each of CMF, ABC and metastatic lesion. 8 cases of enchondroma were suspected radiologically. However, on biopsy only 3 cases proved to be enchondroma while 3 others were diagnosed as giant cell reparative granuloma and 1 case each of GCT and metastasis. Among the 10 radiologically defined cases of Ewings sarcoma, 2 were of osteomyelitis and 1 was of osteosarcoma. Among the 5 cases of osteosarcoma, 1 proved to be GCT histologically. 1 case of ABC was misdiagnosed as osteomyelitis and another 1 case of ABC as SBC on X-ray. Among the 5 cases of radiologically suspected plasma cell myeloma, 2 proved to be metastatic lesions when biopsy was done.

Conclusion

We concluded that light microscopy or histopathology is the gold standard in the diagnosis of bone lesions and invariably accurate when correlated with clinicoradiological features.

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