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Original Research Article

To Assess the Significance of Histopathology in the Diagnostic Process of Lytic Bone Lesions at a Tertiary Centre

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Abstract

Background: The presence of lytic bone lesions is a common radiographic finding seen in patients seeking orthopaedic care. The histopathology's plays a crucial role in providing guidance to orthopaedic surgeons in the management of patients with lytic lesions.

Aims and Objectives: The purpose of this study is to assess the significance of histopathology in the diagnostic process of lytic bone lesions.

Materials and Methods: The selection criteria for patients included those with radiologically evident bone disease. A total of 50 cases were identified, and radiographic diagnosis confirmed the presence of lytic bone lesions in all patients. Histopathological biopsies were conducted in all patients to diagnose lytic bone lesions. The biopsy procedure mostly included the use of the scraping technique as well as the incision and excision methods. In the laboratory, soft tissue samples were immersed in a solution of 10% formalin for fixation. As for bone samples, slices with a thickness ranging from 3 to 5 mm were prepared and then fixed in a 10% buffered formalin solution. Decalcification of the bone specimens was then performed by immersing them in a 5% nitric acid solution for duration of 2 days.

Results: The findings of our investigation revealed that out of a total of 50 instances, there were 18 cases of inflammatory lesions, 22 cases of benign lesions, 3 cases of initial malignant lesions, and 7 cases of subsequent malignant lytic lesions. So, the most prevalent lytic lesion was a benign neoplastic lesion of bone. There were a total of 22 instances in the study. Out of a total of 18 inflammatory lytic lesions, 8 cases were of pyogenic osteomyelitis, and 10 cases were of tuberculous osteomyelitis. So, tuberculous osteomyelitis was slightly more common than pyogenic osteomyelitis in inflammatory lytic lesions. Out of a total of 22 lytic lesions classified as benign neoplastic, 14 instances were diagnosed as giant cell tumors, while 3 cases were identified as fibrous dysplasia. Giant cell tumors have a greater frequency of occurrence compared to other benign lytic lesions.

Conclusion: It has been determined that the identification of lytic bone lesions is an often used radiological finding utilized by orthopaedic surgeons in the evaluation of several individuals. Histopathology serves as the definitive diagnostic method for a wide range of disorders that result in lytic lesions, establishing itself as the benchmark for accuracy and precision.

Keywords: Histopathology, Lytic Bone Lesions, Inflammatory Lytic Lesions.

Introduction

The presence of lytic bone lesions is a common radiographic finding seen in patients seeking orthopaedic care. This shape may include a range of clinical abnormalities, spanning from inflammatory to neoplastic diseases. The histopathology's plays a crucial role in providing guidance to orthopaedic surgeons in the management of patients with lytic lesions. Lytic bone lesions are often seen in a variety of bone illnesses, including both inflammatory and neoplastic conditions, as shown by radiological findings. Osteolytic lesions manifest when the rate of bone destruction surpasses the rate of new bone formation. In order for lytic bone metastases to be detectable using x-ray imaging, they must have a minimum size of 1 cm and have caused a reduction in bone density ranging from 30% to 50% [1, 2]. It

is crucial to bear in mind, meanwhile, that some non-malignant processes, such as osteomyelitis, have the potential to imitate malignant tumors, while certain malignant lesions, such as metastases or myeloma, have the potential to imitate benign conditions. The differentiation between benign and malignant lytic lesions is challenging to ascertain radiologically with plain film imaging. A more precise approach is assessing whether the process exhibits aggressive or non-aggressive characteristics. Pyogenic osteomyelitis is an acute inflammatory disorder mostly attributed to the pathogenic bacterium Staphylococcus aureus [3]. The osteolytic lesions associated with TB may bear a strong resemblance to those caused by multiple myeloma or subsequent malignant deposits [4]. Neoplastic lesions, including both benign and malignant (primary and secondary) tumors, are capable of inducing lytic lesions within the skeletal system. Typical manifestations include a gradual onset of discomfort, swelling, soreness, and, in some instances, the occurrence of an abrupt pathological fracture. In the context of benign lesions, the differential diagnosis of lytic lesions encompasses several conditions such as simple bone cyst, aneurysmal bone cyst, osteochondroma (exostosis), enchondroma, giant cell tumor, fibrous dysplasia, osteoblastoma, chondroblastoma, non-ossifying fibroma, and brown tumor of the bone. Primary bone tumors, such as Ewing's sarcoma, osteosarcoma, multiple myeloma, and adamantinoma, are often seen among malignant neoplasms. The incidence of primary bone cancer is much lower compared to bone metastases [5, 6]. The skeletal system is identified as the third most prevalent location for the occurrence of metastatic illness, as supported by previous studies [7, 8]. Regarding secondary tumors, it has been shown that primary sites such as the lung, kidney, thyroid, breast, gastrointestinal tract, and melanomas predominantly generate lytic lesions, while other initial sites elicit a combination of lytic and sclerotic reactions. Carcinomas have a higher propensity for bone metastasis compared to sarcomas. The axial skeleton has a greater abundance compared to the appendicular skeleton, mostly because of the enduring presence of red bone marrow inside the former. Typically, the first bones afflicted in this context are the ribs, pelvis, and spine, whereas distal bones are seldom impacted. The identification of all lytic lesions is achieved by the use of radiographic modalities such as plain X-rays, CT scans, MRIs, and bone scintigraphy.

Aims and Objective

To assess the significance of histopathology in the diagnostic process of lytic bone lesions

Materials and Methods

The present randomized cross-sectional prospective study was hospital-based and included 120 patients with radiologically evident bone disease of both genders in the pathology department. The study was conducted in the pathology department at Anugrah Narayan Magadh Medical College and Hospital, Gaya, Patna, Bihar, India, after approval from the institutional ethical committee. All the study participants were briefed about the study, and written informed consent was obtained. This study was done between January 2022 and June 2022. Demographic details such as age and gender, clinical history, and radiological findings were noted in all the cases. FNAC was done whenever possible. All bone biopsies and resected specimens were received in 10% formalin, and gross findings were noted during the study period.

Keeping power (1-beta error) at 80% and confidence interval (1-alpha error) at 95%, the minimum sample size required was 60 patients; therefore, we included 120 (More than the minimum required number of cases) patients in present study.

Inclusion Criteria

All the cytological samples got histological follow-up during the study period.

Exclusion Criteria

To exclude cytological samples showing only blood.

The selection criteria for patients included those with radiologically evident bone disease. A comprehensive medical history was obtained, including key demographic information such as age, gender, location of residence, and work. Additionally, specific inquiries were made about the presence of fever, weight loss, cough, haemoptysis, or other indications of systemic involvement. All patients had a comprehensive physical examination, including both systemic and general assessments. The pathological investigation included a standard complete blood count (CBC), erythrocyte sedimentation rate (ESR), and urine examination for all patients. Additionally, sputum and body fluid examinations, as well as serum calcium and alkaline phosphatase tests, were conducted selectively in certain instances. Histopathological biopsies were conducted in all patients to diagnose lytic bone lesions. The biopsy procedure mostly included the use of the scraping technique as well as the incision and excision methods. In the laboratory, soft tissue samples were immersed in a solution of 10% formalin for fixation. As for bone samples, slices with a thickness ranging from 3 to 5 mm were prepared and then fixed in a 10% buffered formalin solution. Decalcification of the bone specimens was then performed by immersing them in a 5% nitric acid solution for duration of 2 days. Subsequently, all tissue specimens underwent a series of alcohol

solutions with progressively higher concentrations, followed by the preparation of paraffin blocks. The tissue sections were subjected to staining using hematoxylin and eosin. Subsequently, all slides were subjected to microscopic examination, leading to the final diagnosis being classified into categories of inflammatory, benign, and malignant lesions, as appropriate. A few IHCs were conducted in order to validate the histological observations.

Statistical Analysis

The data was analysed using Microsoft Excel (2016). Results were expressed as mean, frequency, and range. Tables and figures were used as required. The statistical analysis was done by the software Statistical Package for the Social Sciences (SPSS), version 21.0. When the difference's p value was less than 0.05, it was considered significant.

Results

Out of 120 patients studied, it was observed that 77 individuals, constituting 64.17% of the total, were male, while the remaining 43 individuals, accounting for 35.83% of the total, were female (Figure 1). The mean age of patients was 44.73±12.65 years.

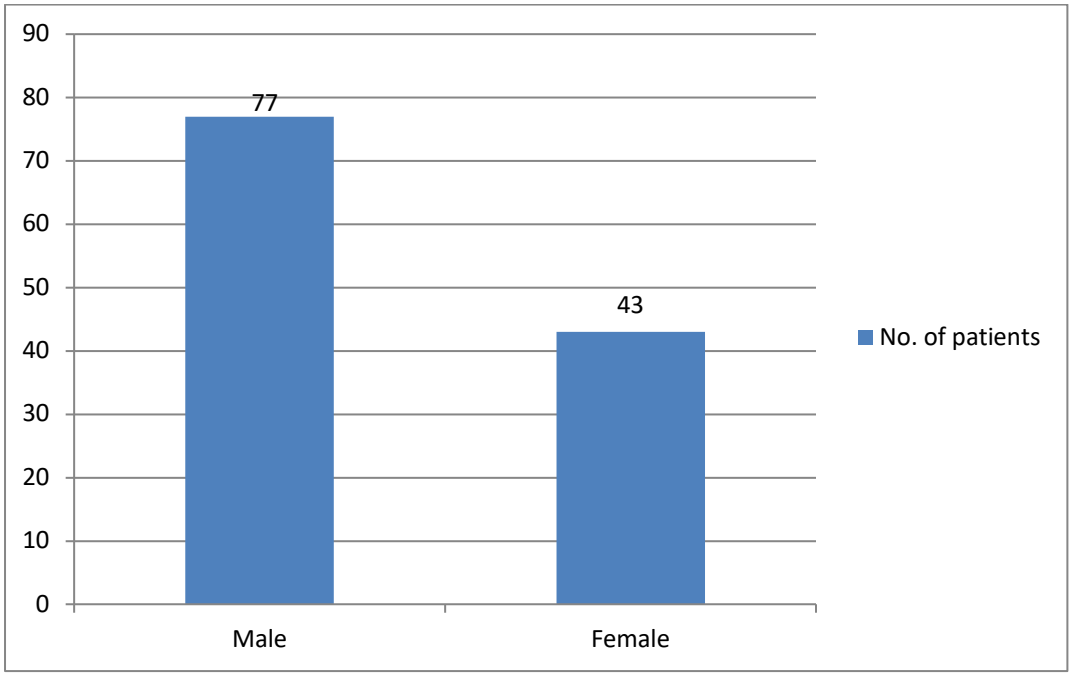

Figure 1: Gender wise distribution of patients

The findings of our investigation revealed that out of a total of 120 instances, there were 43 cases of inflammatory lesions, 53 cases of benign lesions, 7 cases of initial malignant lesions, and 17 cases of subsequent malignant lytic lesions. So, the most prevalent lytic lesion was a benign neoplastic lesion of bone. The provided information is in the form of a table, specifically labelled "Table 1".

Table 1: Showing proportion of different lytic lesion

Lytic Lesion	No. of patients	Percentage
Inflammatory	**43**	**35.83**
Bacterial osteomyelitis	19	15.83
Tuberculous	24	20
Neoplasm	**77**	**64.17**
Benign	53	44.17
Malignant primary	07	05.83
Malignant	17	14.17

Among the male patients, 24 cases were classified as inflammatory lesions, 36 were identified as benign lesions, and 17 cases were identified as malignant lesions. In the female patients, 17 were identified as benign lesions, 19 were classified as inflammatory lesions, and 7 were determined to be malignant lesions. Benign neoplastic lesions were found to be the most prevalent among individuals of both sexes (Table 2).

Table 2: Gender-wise distribution of the lytic lesions of bone

Histological type	lytic lesions	Male (n=77)	Female(n =43)
Inflammatory	**43**	**24**	**19**
Bacterial osteomyelitis	19	7	12
Tuberculous	24	17	07
Neoplasm	**77**	**53**	**24**
Benign	53	36	17
Malignant primary	7	05	02
Malignant	17	12	05

Among the various age groups examined, the age group with the highest prevalence of lytic lesions was those between the ages of 10 and 19 years, with a total of 43 instances identified. A total of 41 instances with lytic lesions were identified within the age range of 20–40 years. In the age category of individuals aged 40 years and older, a total of 34 instances of lytic lesions were identified. Only two incidences were identified in the age range below 10 years (Table 3).

Table 3: Age-wise distribution of the lytic lesions of bone

Age (in Years)	Lytic lesion	Percentage
<10	02	1.67
10-19	43	35.83
20-40	41	34.17
>40	34	28.33

Out of a total of 43 inflammatory lytic lesions, 19 cases were of pyogenic osteomyelitis, and 24 cases were of tuberculous osteomyelitis. So tuberculous osteomyelitis was slightly more common than pyogenic osteomyelitis in an inflammatory lytic lesion (Table 4).

Table 4: Showing the distribution of inflammatory lesions

Inflammatory lesion	No. of patients (n=43)	Percentage
Pyogenic Bacterial osteomyelitis	19	15.83
Tuberculous osteomyelitis	24	20

Out of a total of 53 lytic lesions classified as benign neoplastic, 34 instances were diagnosed as giant cell tumors, while 7 cases were identified as fibrous dysplasia. Giant cell tumors have a greater frequency of occurrence compared to other benign lytic lesions (Table 5).

Table 5: Showing the distribution of benign lesions

Benign lesion	No. of patients (n=53)	Percentage
Giant cell tumor	34	28.33
Fibrous Dysplasia	07	05.83
Simple Bone cyst	03	02.50
Aneurysmal bone cyst	03	02.50
Chondroblastoma	02	01.67
Enchondroma	02	01.67
Langerhans cell histiocytosis	02	01.67

Out of the total of 24 malignant lesions, 7 instances were identified as initial malignant lesions, while the other 17 cases were classified as secondary malignant lesions. In the context of malignant lytic lesions, it was shown that secondary lesions had a higher prevalence compared to original lesions (Table 6).

Table 6: Showing distribution of malignant lytic lesion

Malignant lytic lesion	No. of patients (n=24)	Percentage
Primary		
Ewing sarcoma	5	4.17
Osteosarcoma	2	1.67
Secondary		
Secondary in bone from follicular variant of papillary carcinoma of thyroid	6	5
Renal cell carcinoma	5	4.17
Squamous cell carcinoma of lungs	4	3.33
Adenocarcinoma Lungs	2	1.67

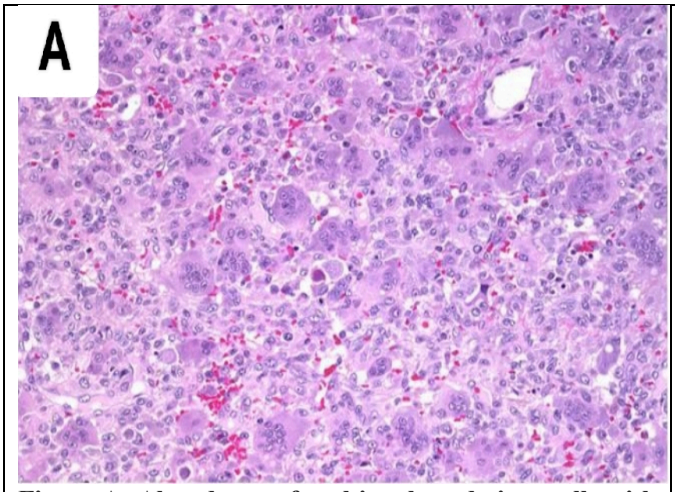

Figure A: Abundance of multinucleated giant cells with a background of mononuclear stromal cells.

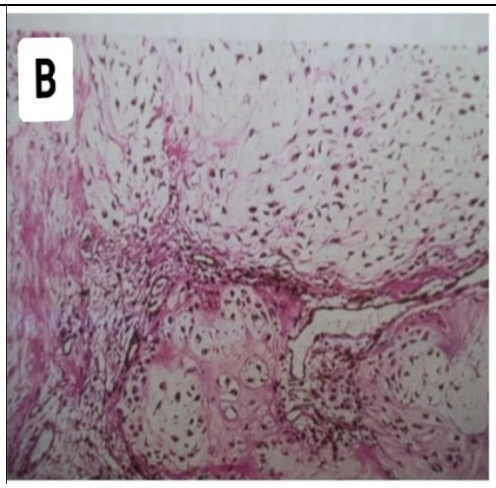

Figure B: The tumour has a typical lobulated appearance.

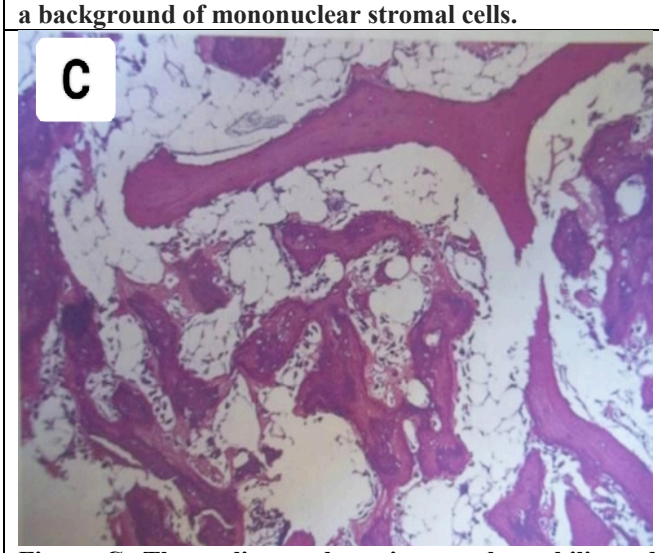

Figure C: The malignant bone is more basophilic and has more irregular borders.

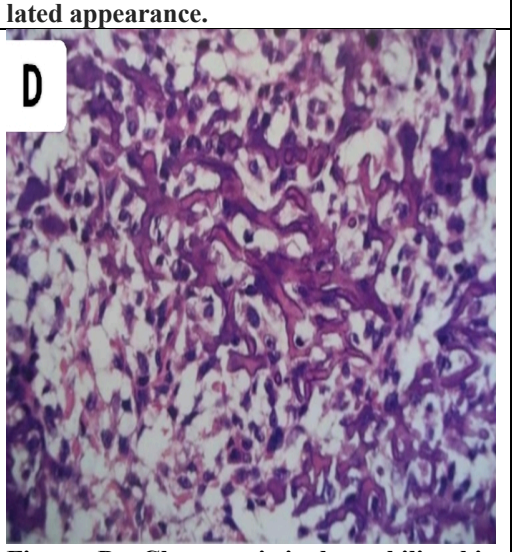

Figure D: Characteristic basophilic thin bony trabeculae of neoplastic bone.

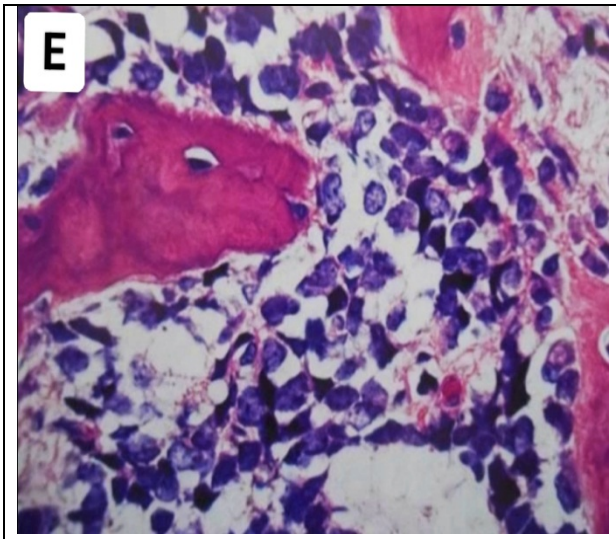

Figure E: Uniform cells with darkly staining nuclei and very scanty cytoplasm infiltrate marrow spaces around the bony trabeculae.

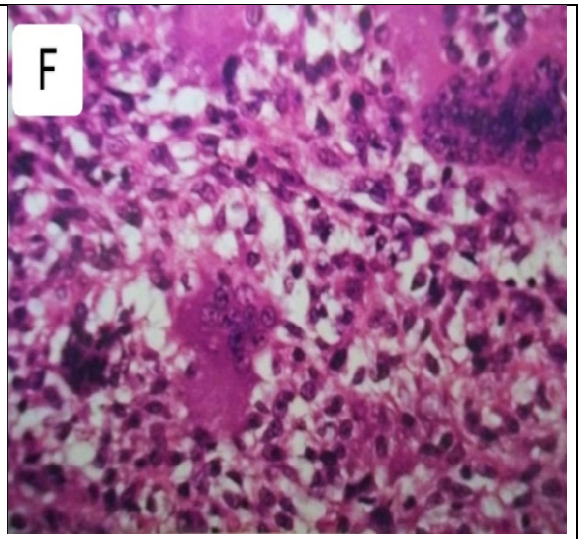

Figure F: Small round tumors cells are accompanied by scattered osteoclasts.

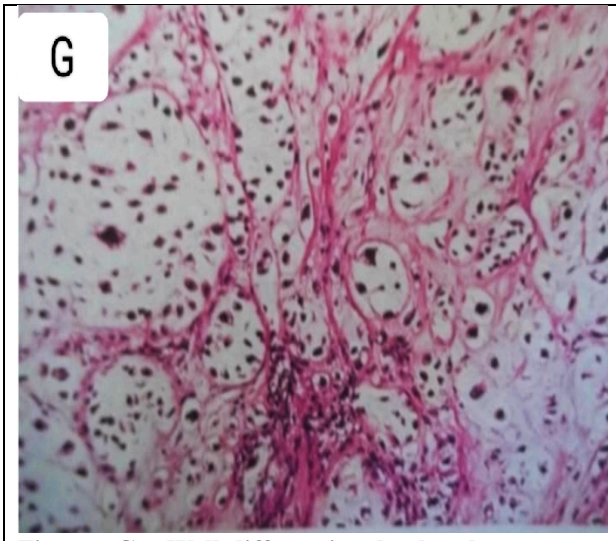

Figure G: Well-differentiated chondrosarcoma. The tumour retains a lobulated appearance, but nuclear atypicality is obvious.

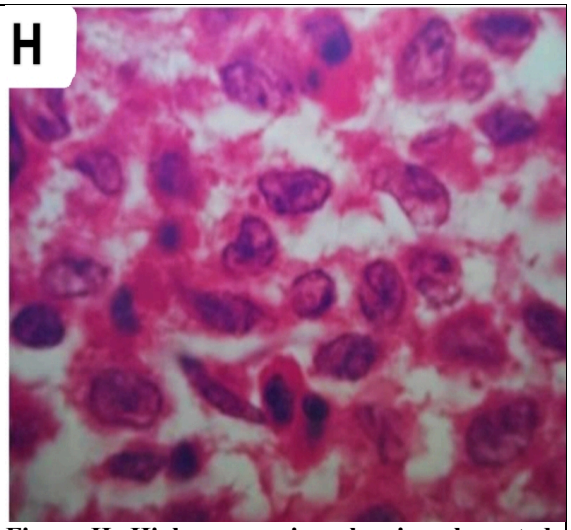

Figure H: High power view showing elongated nuclei with occasional longitudinal grooves in the Langerhans cells

Discussion

The primary objective of this research was to accurately identify various lytic lesions of the bone. One crucial factor to be taken into consideration is the patient's age. Certain age groups are more likely to experience lytic lesions. For instance, infants and young children are primarily affected by metastatic neuroblastoma, while middle-aged and elderly individuals are more prone to metastasis and multiple myeloma. Lymphomas that specifically target bones typically manifest in adulthood, with the majority of cases occurring after the age of 25. Ewing's sarcoma and simple bone cysts are often seen in the long bones of pediatric patients and early adolescents, whereas giant cell tumors tend to affect individuals in the young to middle-aged adult demographic, namely those between 20 and 50 years of age [9, 10]. However, our analysis revealed that the highest numbers of instances were mostly seen throughout the second decade of life.

Among the male patients, 24 cases were classified as inflammatory lesions, 36 were identified as benign lesions, and 17 cases were identified as malignant lesions. In the female patients, 17 were identified as benign lesions, 19 were classified as inflammatory lesions, and 7 were determined to be malignant lesions. Benign neoplastic lesions were found to be the most prevalent among individuals of both sexes.

Among the various age groups examined, the age group with the highest prevalence of lytic lesions was those between the ages of 10 and 19 years, with a total of 43 instances identified. A total of 41 instances with lytic lesions were identified within the age range of 20–40 years. In the age category of individuals aged 40 years and older, a total of 34 instances of lytic lesions were identified. Only two incidences were identified in the age range below 10 years.

Osteomyelitis was seen throughout all age cohorts over 10 years in our research investigation. The diagnosis of chronic recurrent multifocal osteomyelitis mostly relies on excluding other potential causes. Infective osteomyelitis and malignancy are the primary differential diagnoses [11]. It is important to distinguish the osteolytic lesions associated with TB occurring at various locations from those caused by multiple myeloma, secondary metastasis, and bacterial osteomyelitis. The delay in diagnosis sometimes stems from individuals seeking medical attention at a later stage or from a lack of knowledge of the condition's subtle start [12]. Histopathological investigation has been shown to yield a substantial proportion of positive findings, as evidenced by previous studies [13, 14]. In our histological investigation, it was shown that TB had a higher prevalence compared to bacterial osteomyelitis in cases of inflammatory lytic lesions, particularly among individuals in the older age demographic. Ewing sarcoma and lymphoma are significant differential diagnoses that need consideration in clinical practice. In the present investigation, a total of 120 instances of lytic bone lesions were examined.

Among these cases, the most often seen kind of lesion was benign neoplastic lesions, accounting for 53 cases. Among a total of 53 lytic lesions of a benign neoplastic nature, it was observed that 34 of these instances corresponded to giant cell tumors of the bone. In the current investigation, it was observed that the lower end of the femur and the higher end of the tibia were the prevailing locations for the occurrence of giant cell tumors. The prevalence of giant cell tumors in primary bone

tumors ranges from 4 to 10 percent. This bone tumor is very prevalent. The majority of patients have discomfort that progresses gradually, either accompanied by or without the presence of a mass. Symptoms manifest when the lesion initiates cortical destruction and irritation of the periosteum or when the tumor-induced weakening of the bone elicits pain as a result of an impending pathologic fracture. Certain large cell tumors may have a pathologic fracture. The radiological data indicate that the lesion is often located eccentrically in relation to the long axis of the bone [15]. The study also identified three instances of fibrous dysplasia as further examples of benign lytic lesions. In both cases, the location of the lesion was seen to be the upper end of the tibia. Langerhans cell histiocytosis often manifests as a pathological fracture or an unexpected discovery, and it tends to undergo spontaneous healing [11].

The current research focuses on a case of Langerhans cell histiocytosis in a 15-year-old male patient. The patient had been experiencing pain and a pathological fracture for duration of 10 months. Prior to our examination, another pathologist had first classified the condition as acute chronic osteomyelitis. However, the patient did not react to the prescribed therapy and was then transferred to our institution. A meticulous histological analysis is necessary in order to distinguish between osteomyelitis and Langerhans cell histiocytosis. The upper extremities are susceptible to this condition; however, it may also affect any long tubular bone. The metaphysis and diaphysis of the femur are the most often seen locations, with the tibia and humerus following suit.

In our research, we saw a total of 120 instances of lytic bone lesions. Among these cases, the main malignant lesion most often seen was Ewing's sarcoma. Specifically, we identified two cases located at the lower end of the femur and tibia, affecting individuals below the age of 20. Osteosarcoma has the potential to develop in any bone inside the human body; however, a majority of cases start in the long bones of the appendicular skeleton. Specifically, the distal femur is the most common site of occurrence, followed by the proximal tibia and proximal humerus, which are characterized by having very active growth plates. The cancer is often located in the metaphysis of long bones, less usually in the diaphysis, and rarely in the epiphysis [16]. In our research, we identified a total of one instance of osteosarcoma in senior male individuals. This particular kind of cancer was localized in the metaphysis region of the lower end of the femur.

The primary causes of morbidity associated with bone metastases are pain, pathological fractures, and hypercalcemia. The prevalence of pain as a primary symptom has been seen in 72% of patients diagnosed with bone metastases [17]. Pain arises due to the tumor-induced stretching of the periosteum as well as the activation of nerves inside the endosteum. The prevalence of pathological fractures is highest in cases of breast cancer, mostly attributed to the lytic characteristics of the lesions. The occurrence of hypercalcemia is limited to a minority of individuals, namely 10% [18].

Our study identified five instances of metastatic lytic lesions. These cases involved the metastasis of the follicular variant of papillary carcinoma of the thyroid to the upper end of the femur, as well as the metastasis of carcinoma of the kidney to the L3 vertebra. Additionally, squamous cell carcinoma of the lung and adenocarcinoma of the lung were found to metastasize to the upper end of the humerus. A total of twelve instances were seen, each exhibiting symptoms of discomfort, weight loss, and a non-healing pathological fracture. All seven instances had elevated levels of alkaline phosphatase, whereas it was observed that adenocarcinoma of the lung with bone metastases presented with hypercalcemia. The first manifestation of the follicular variety of papillary carcinoma of the thyroid was the presence of a lytic lesion located at the upper end of the femur. Notably, both the patient and the doctor were ignorant of the existence of thyroid malignancy at the time.

Limitations of the study: The short study period and small sample size.

Conclusion

It has been determined that the identification of lytic bone lesions is an often-used radiological finding utilized by orthopaedic surgeons in the evaluation of several individuals. Histopathology serves as the definitive diagnostic method for a wide range of disorders that result in lytic lesions, establishing itself as the benchmark for accuracy and precision.

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