

# Radiology - Pathological Correlation of Osteosarcoma in a Tertiary Care Hospital - A Retrospective Study

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## Abstract

**Introduction:** The study was conducted to understand the clinical algorithm of osteosarcoma. Correlation was done by clinical presentation with radiological features and histopathology. The stress on to understand the necessity for a team approach between the clinician, radiologist, and pathologist and vice versa is emphasized. With the establishment of magnetic resonance imaging (MRI) scan, pathological procedures, chemotherapy, and limb salvage surgery, a revolution has taken place in the treatment.

**Aim:** The aim of this study to study the radiological and pathological correlation of osteosarcoma.

**Materials and Methods:** This is a retrospective study of 62 bone tumors, among which 27 cases were diagnosed by histopathology as osteosarcoma at Thoothukudi Medical College, India over 5 years. All the relevant clinical data of the patients were searched from the ward records. The various radiological features were collected. The data were stored in the department computer server, which were very much useful in the retrospective histopathology and radiology correlation study.

**Results:** The total number of bone tumors reported during the 5 years was 62 cases, among which 27 cases were diagnosed by histopathology as various types of osteosarcoma. MRI was found essential in planning treatment modality of osteosarcoma, to study skip lesions, blood vessels, tissue content, involvement of adjacent tissue, planning preoperative chemotherapy, choosing the right candidate for limb salvage surgery, and postoperative evaluation of the lesion. Surgical treatment of extremity osteosarcoma should be a wide excision. This means that the tumor, its adjacent reactive zone, and a normal cuff of tissue in all planes should be respected. A wide excision includes amputation or a disarticulation, which is essentially an amputation through a joint.

**Conclusion:** The vast majority of osteosarcomas that occur in children, adolescents, and young adults are high-grade lesions that arise in the intramedullary cavity of the bone and include the conventional as well as the telangiectatic subtypes. All tumors require surgery. Bone tumors need correlation between radiologist, pathologist, and clinician.

**Keywords:** Angiogram, Chemotherapy, Computerized tomography, H and E stain, Limb salvage surgery, Magnetic resonance imaging, Radiograph

## INTRODUCTION

Osteosarcoma is defined by the production of tumor osteoid by the neoplastic cells. The importance of the Rb

and p53 genes in osteosarcoma development derives from the frequent derangements of these pathways in tumor specimens.<sup>1</sup> Patients with Rothmund-Thomson syndrome have a 30% incidence of develop osteosarcoma.<sup>2</sup> Genetic lesions in the Rb gene itself, mapped to 13q14, have been shown to be present in approximately 70% of primary osteosarcoma tumors.<sup>3-5</sup> Virtually, all osteosarcoma tumors have some lesion in the p53 pathway. The most common genetic losses in Rb gene located on chromosome 13 and p53 located on chromosome 17.<sup>6,7</sup> Loss of expression of Fas appears to be necessary for the survival of metastatic osteosarcoma cells in the lungs.<sup>8</sup>

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The five basic parameters of importance are the age of the patient, bone involved, specific area within the bone, radiographic appearance, and microscopic appearance. Osteosarcoma of bone is divided into conventional, telangiectatic, small cell, low-grade, secondary, parosteal, periosteal, and high-grade surface variants.<sup>9</sup> These entities can be divided by their apparent origin from the intramedullary cavity or the surface of the bone. The histologic diagnosis of conventional osteosarcoma is usually straightforward although considerable variability can exist between different tumors and even within single tumors.<sup>10,11</sup>

### Aim

The aim of this study is to study the radiological and pathological correlation of osteosarcoma.

## MATERIALS AND METHODS

This retrospective study was conducted at the Department of Pathology, Thoothukudi Medical College Hospital. A total of 62 cases were reported, among which 27 cases were diagnosed by histopathology as various types of osteosarcoma. All the relevant clinical data of the patients were searched from the ward records. Magnetic resonance imaging (MRI) helps in monitoring tumor response to neoadjuvant chemotherapy in osteosarcoma and helps to determine the appropriate adjuvant (postoperative) chemotherapy in the postoperative period. An indication of tissue content of a lesion such as fat, hemorrhage, fibrosis, and fluid levels can be made out using MRI. Serum levels of lactic acid dehydrogenase (LDH), alkaline phosphatase, calcium, and phosphate levels are needed periodically. Tests to assess general health include: A complete blood count, differential count, tests for serum electrolytes including calcium, magnesium, and phosphate, liver function studies, blood group typing, a coagulation profile, as well as tests for hepatitis and human immunodeficiency virus infection were recorded. The initial step in the assessment of patients with bone tumors is a good medical history, including age, gender, type and duration of symptoms, and localization of the mass.

## RESULTS

This retrospective study covered a total number of 62 cases reported, among which 27 cases were diagnosed by histopathology as various types of osteosarcoma. The primary osteosarcoma involves age group of 15-25 years, and long bones are involved in 80% of cases. The presenting symptoms are pain and swelling over the lesion. The case distribution in the study of 27 cases of osteosarcoma at this center is summarized based on the types, age, and bones involved (Table 1).

The correlation study was conducted with histopathological features with radiographic findings. The various radiological patterns are osteoid/ossification production, mixed sclerotic and lytic, purely lytic, and purely blastic. Histopathological sections studied show malignant stromal cells with malignant osteoid is production (Table 2).

### Osteosarcoma

Osteosarcoma is the most frequent primary malignant bone tumors, exclusive of hematopoietic malignancy. Intramedullary osteosarcoma is the lesions arising within the medullary space of the bone is the most common type. Juxtacortical osteosarcoma is the lesions arising on the surface of the bone in apposition to the cortex. Intracortical osteosarcoma is the lesions arising from the cortex of the bone.

Based on the histologic appearance and origin from various anatomical parts of bone osteosarcoma is divided into variants. These entities can be further divided by their apparent origin from the intramedullary cavity or the surface of the bone. High-grade lesions arise in the intramedullary cavity of the bone (Table 3).

From its usual origin in the metaphysis of a long bone, the tumor may spread to the adjacent cortex and extend into the soft tissues. It may even reach beneath the skin. It may extend into the epiphysis and the joint space. The “skip” metastases are responsible for an increased incidence of local recurrences. Metastasis through the bloodstream to distant sites, particularly the lung, is seen. Factors to be considered in regard to development and prognosis of osteosarcoma are the following: Paget’s disease, external radiation therapy as a modality of treatment for other cancers, radiation exposure in nuclear accidents, and chemotherapy for children for retinoblastoma. Total hip replacement, due to the presence of foreign body, germ-line and somatic mutations of p53, which is a cancer suppressor gene, the above factors carries very bad prognosis.

Osteoblastic, chondroblastic, fibroblastic, parosteal, periosteal osteosarcoma variants, and jaw and distal extremities have a relatively good prognosis. The other variants and predisposing factor-induced osteosarcoma have a bad prognosis (Table 4).

Tumors associated with serum elevations of LDH and alkaline phosphatase have an increased metastatic rate. The system uses histological grade and anatomical location of tumor. Grading varies from well differentiated to low grade, (1-2: Low grade, 3-4: High grade). Staging varies from anatomic location: One compartment (confined to bone) or two compartments (tumor has broken through the bone into soft tissue) (Table 5).

**Table 1: Various types of osteosarcoma with bones involved**

Tumor	Number of cases	Bones involved	Age group involved
Osteoblastic osteosarcoma	15	Nine cases were involving lower end of the femur. Two cases were involving upper end of the humerus. Two cases were from upper end of tibia and two cases from lower end of the fibula	12-28 years
Chondroblastic osteosarcoma	4	All the cases were male patients; two lesions involved the lower end of the femur, one upper end of the tibia, and one lower end of the humerus	13-18 years
Periosteal osteosarcoma	3	All three cases were males. Two cases involved femur and one upper end of the humerus	15-19 years
Parosteal osteosarcoma	2	Two cases were reported, both were females, involving lower end of the femur	22-28 years
Telangiectatic osteosarcoma	3	Three cases of telangiectatic Osteosarcoma were reported. Three cases were reported, two cases were male children and one case a female. Two lesions involved femur and one involved humerus	11-16 years

**Table 2: Correlation study between radiology and histopathology of various types of osteosarcoma**

Tumor	Radiology features	Histopathology features
Osteoblastic osteosarcoma	The radiographs show a metaphyseal lesion with osteoid/calcifications destroying the cortex, producing a soft-tissue mass with Codman's triangle	The histopathological sections showed malignant osteoid with sarcomatous stromal cells with high mitotic activity and permeating pre-existing bone. The chemotherapy features show areas of necrosis of tumor cells and coagulation necrosis of bone
Chondroblastic osteosarcoma	The radiographs show expansile lesion arising in the metaphyseal region with destruction of cortex, producing a soft-tissue mass, and multiple calcifications were present	Histopathology sections showed the malignant chondrocytes in lacunae with plenty of malignant stromal cells producing malignant osteoid matrix
Periosteal osteosarcoma	X-ray shows a diaphyseal lesion on surface of bone; medullary canal is uninvolved. Spiculated or sunburst periosteal reaction is seen. Partial matrix mineralization is seen consistent with chondroblastic nature	The histopathological sections studied show chondromyxoid areas with few atypical cells with malignant osteoid deposition
Parosteal Osteosarcoma	X-ray features are lobulated and ossified exophytic mass adjacent to the cortex, radiodense centrally, and cortical thickening	Microscopic pathology demonstrates a fibroblastic tumor that is producing bone and osteoid. The islands of bone are interspersed among fibrous-appearing tissue
Telangiectatic osteosarcoma	X-ray showing purely lytic lesion resembling aneurysmal bone cyst	Histopathology sections showed blood-filled spaces separated by septa. The septa contain malignant cells

**Table 3: Osteosarcoma classification based on the location in the bone and lineage of differentiation**

Intramedullary (75%)	Juxtacortical/surface (7-10%)
Conventional	Parosteal
Osteoblastic (82%)	Periosteal
Mixed and Sclerosing	High-grade surface
Chondroblastic (5%)	Intracortical
Fibroblastic	Secondaries
MFH-like	Paget's disease (67-90%);
Osteoblastoma-like	Post radiotherapy,
Giant cell-rich	Bone infarct, fibrous dysplasia, metallic implant, and osteomyelitis
Small cell	Osteosarcoma with specific syndrome
Epithelioid (5%)	Familial,
Telangiectatic (3%)	Retinoblastoma,
Well differentiated	Rothmund-Thomson syndrome
	Multifocal, osteogenesis imperfecta

### Osteoblastic Osteosarcoma

Nearly 50% of conventional osteosarcoma was osteoblastic osteosarcoma. The sites are long bones in 70-80% of cases.

Conventional osteosarcoma is composed of pleomorphic, obviously malignant, cells that demonstrate at least focal evidence of osteoid production. The constituent malignant cells of conventional osteosarcoma include round, ovoid, epithelioid, spindled, and bizarre mononuclear or multinucleated giant cells in varying numbers with interspersed, benign-appearing osteoclastic giant cells. Conventional osteosarcomas are high-grade tumors. Surgical treatment of extremity osteosarcoma should be a wide excision. This means that the tumor, its adjacent reactive zone, and a normal cuff of tissue in all planes should be respected. Wide excisions can be achieved through a variety of means, the most ablative being an amputation or a disarticulation, which is essentially an amputation through a joint.

**Surgery:** Wide surgical resection of the primary tumor involves both the complete extirpation of the tumor and its ensuing bone and soft-tissue reconstruction. Amputation (extremity lesions) was done with postoperative (adjuvant) chemotherapy, same regimen as preoperatively 4 cycles were administered. **Limb salvage surgery:** The surgeon removes

the entire tumor, saving the nearby tendons, nerves, and blood vessels, to keep as much of the limb's functions and appearance as possible. The section of the bone that is removed along with the osteosarcoma is replaced with a bone and with an internal prosthesis made of metal and other materials. Two cases with stage IA underwent the procedure. One case underwent radical resection of distal femur osteosarcoma and reconstruction with distal femur prosthesis. The final outcome is that the patient can perform normal life activities with adequate physiotherapy. The other cases underwent radical resection of proximal humerus and scapula. Reconstruction was done with prosthetic replacement of scapula, creation of shoulder joint, and proximal humerus reconstruction. The patient can perform normal life activities with adequate physiotherapy. A total of 13 cases underwent amputation with wide excision.

X-ray fibula shows an osteolytic mass lesion with Codman's triangle. X-ray humerus shows an osteolytic mass lesion with Codman's triangle. Histopathological sections in the first two rows show malignant osteoid with sarcomatous stromal cells with high mitotic activity and permeating pre-existing bone. The third row shows that the chemotherapy features show areas of necrosis of tumor cells and coagulation necrosis of bone. The histopathological features correlated with radiological features perfectly (Figures 1 and 2).

### Chondroblastic Osteosarcoma

In chondroblastic osteosarcoma, the defining matrix is cartilaginous. The histologic distinction between

chondroblastic osteosarcoma and chondrosarcoma may be difficult or impossible particularly in tumors with limited osteoid production with limited amounts of biopsy material; the tumor tissue is inadequately removed surgically. Distinction of these two entities is critical as their treatment and expected outcome are different. In such cases, MRI plays a key role in making a crucial diagnosis preoperatively.

Four cases of chondroblastic osteosarcoma were reported. The presenting age group was between 13 and 18 years of age and all the cases were male patients. Two lesions involved the lower end of the femur, one upper end of the tibia and one lower end of the humerus. The cases underwent wide surgical resection.

The radiographs show expansile lesion arising in the metaphyseal region with destruction of the cortex and producing a soft-tissue mass; multiple calcifications were



Figure 1: X-ray humerus showing an osteolytic mass lesion with Codman's triangle

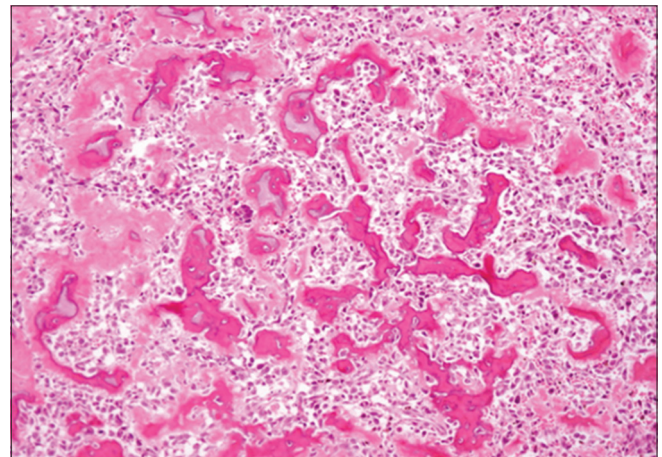


Figure 2: Histopathological sections show malignant osteoid with sarcomatous stromal cells with high mitotic activity

**Table 4: The prognostic indicators of various types of osteosarcoma and the predisposing conditions that lead to the development of osteosarcoma**

Conditions	Prognosis
Paget's disease	Highly malignant
Prior irradiation	Highly malignant
Jaw and distal extremities	Good
Multifocal	Fatal
Osteoblastic, chondroblastic, fibroblastic, parosteal, and periosteal osteosarcoma	Good
Telangiectatic osteosarcoma	Highly malignant
Young age, male sex, large size, and poor response to chemotherapy	Bad prognosis

**Table 5: Grading and staging of osteosarcoma**

Tumor grade	Tumor differentiation	Tumor grade	TNM	Stage
G1	Well differentiated	G1, G2	T1 N0 M0	IA
G2	Moderately differentiated	G1, G2	T2 N0 M0	1B
G3	Poorly differentiated	G3, G4	T1 N0 M0	IIA
G4	Undifferentiated	G3, G4	T2 N0 M0	IIB
Gx	Not assessable	Any G	Any T, N1, M0	IVA



present. Histopathology sections showed the malignant chondrocytes in lacunae with plenty of malignant stromal cells producing malignant osteoid matrix. The correlation is up to the mark (Figures 3 and 4).

### Telangiectatic Osteosarcoma

The criteria to diagnose telangiectatic osteosarcoma are X-ray showing purely lytic lesion resembling aneurysmal bone cyst. The gross appearance is that of spaces filled with blood clots. The lesion consists of spaces separated by septa. The septa contain malignant cells.

Three cases of telangiectatic osteosarcoma were reported. The presenting age group was between 11 and 16 years of age, 2 cases were male children and 1 case a female. Two lesions involved femur and one humerus. The treatment was wide surgical resection.

The X-ray shows telangiectatic osteosarcoma of distal femur showing radiolucent area with destruction of cortex and Codman's triangle. Femoral artery angiogram of telangiectatic osteosarcoma of upper femur shows large, tortuous pathological tumor vessels. The histopathological sections show aneurysmal cyst-like lesion with multiple cystic spaces filled with blood separated by septa that contain atypical stromal cells with malignant osteoid deposition. The correlation is crystal clear (Figures 5 and 6).

### Periosteal Osteosarcoma

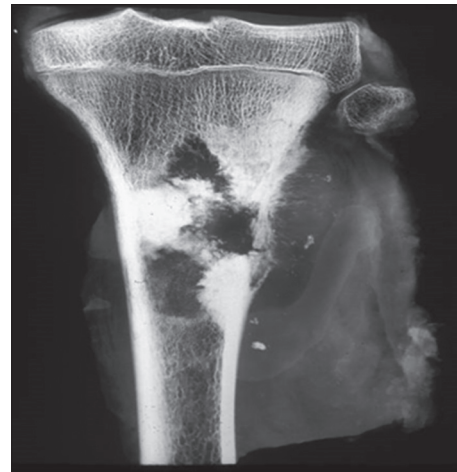
Low-grade to intermediate-grade bone forming sarcoma with predominant chondroblastic differentiation tumor. The tumor arises from the inner layer of the periosteum. The age group involved is between 10 and 20 years of age, with male predominance. Location is diaphysis of long bones.

Radiology: X-ray shows a diaphyseal lesion on surface of the bone; medullary canal is uninvolved. Spiculated or sunburst periosteal reaction is seen. Partial matrix mineralization is seen consistent with chondroblastic nature.

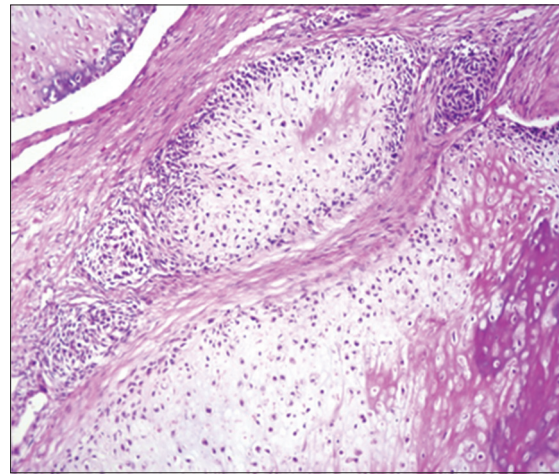
Three cases of periosteal osteosarcoma have been reported. All 3 cases were males. The age group was between 15 and 19 years of age presenting with pain and swelling. Two cases involved femur and one case involved upper end of the humerus.

Treatment: Three patients underwent *en bloc* resection and reconstruction surgically.

The X-ray shows well-defined sclerotic lesion with translucent medullary space and underlying clear bone. The histopathological sections studied show chondromyxoid



**Figure 3: Radiographs show expansile lesion arising in the metaphyseal region in the upper end of the tibia with destruction of cortex and producing a soft-tissue mass**



**Figure 4: Histopathology sections show the malignant chondrocytes in lacunae with plenty of malignant stromal cells producing malignant osteoid matrix**

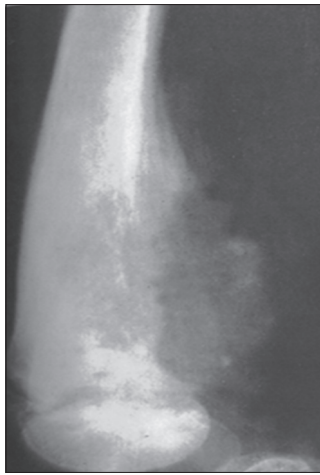
areas with a few atypical cells with malignant osteoid deposition. The histopathology and radiology correlation holds well here (Figures 7 and 8).

### Parosteal Osteosarcoma

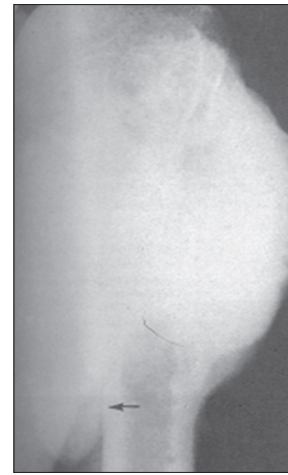
The tumor arises from outer layer of periosteum, with involved age group is between 20 and 30 years of age.

The location is posterior distal femur metaphysis 65% and long bones, and clinical feature is a painless mass in the posterior distal thigh. Radiology: X-ray features are lobulated and ossified exophytic mass adjacent to the cortex, radiodense centrally and cortical thickening. MRI/CT evaluation needs to demonstrate medullary invasion.

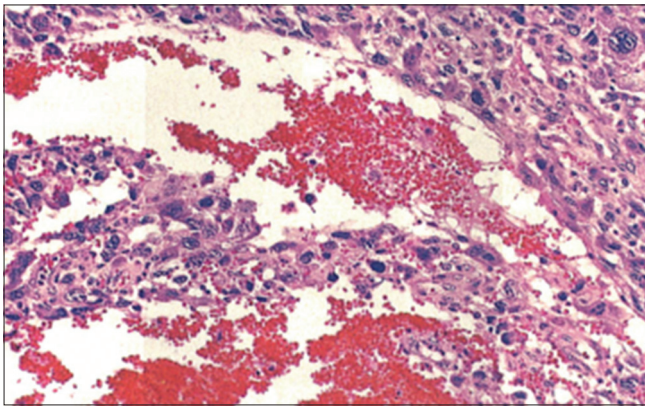
Microscopic pathology demonstrates a fibroblastic tumor that is producing bone and osteoid. The islands of bone



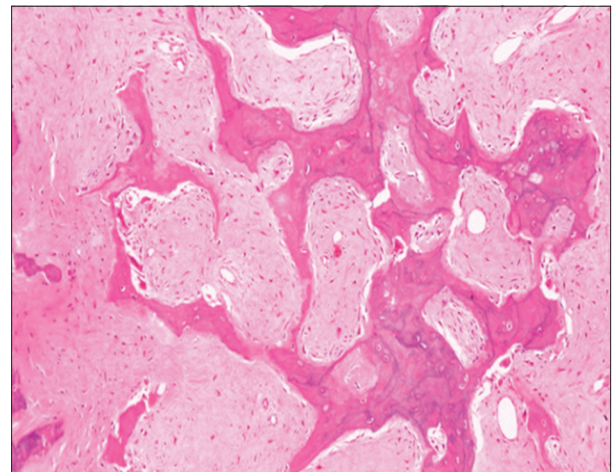
**Figure 5:** X-ray shows telangiectatic osteosarcoma of distal femur showing radiolucent area with destruction of cortex and Codman's triangle



**Figure 7:** X-ray shows well-defined sclerotic lesion with translucent medullary space and underlying clear bone



**Figure 6:** Histopathological sections show aneurysmal cyst-like lesion with multiple cystic spaces filled with blood separated by septa that contain atypical malignant stromal cells with malignant osteoid deposition



**Figure 8:** Histopathological sections studied show chondromyxoid areas with a few atypical cells with malignant osteoid deposition

are interspersed among fibrous-appearing tissue. The tumor is typically a low-grade tumor. The higher-grade variants spread and may be treated with chemotherapy in addition to surgery.

Two cases were reported, both were females. The presenting age group was between 22 and 28 years of age with symptoms of swelling for few months. The two patients underwent surgery. X-ray features are lobulated and ossified exophytic mass adjacent to the cortex with a lucent cleavage plane between lesion and the cortex. Histopathology shows bone trabeculae with abundant collagen matrix with stromal tumor cells interspersed within the matrix. The correlation study between histopathology and radiology holds good (Figures 9 and 10).

#### Metastatic Tumors

The lungs were the only metastatic site in 70% of cases. A metastasis indeed may be the presenting feature. In all

bones, metastases are preferentially situated in the red bone marrow. When located in the long bones, the area usually involved is the metaphysis. Periosteal bone proliferation may rarely accompany a metastatic lesion. This is more likely to occur in certain sclerosing lesions such as those of the prostate and can lead to diagnostic confusion with osteosarcoma. It is important metastatic lesions to bone be biopsied to avoid treatment designed for primary malignant bone tumors.

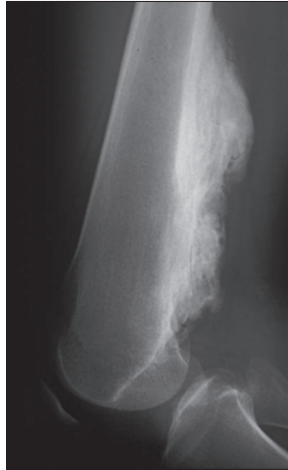
The high-grade tumors showed a poor 3-year disease-free survival. Only stage cases responded to the treatment (Table 6).

#### DISCUSSION

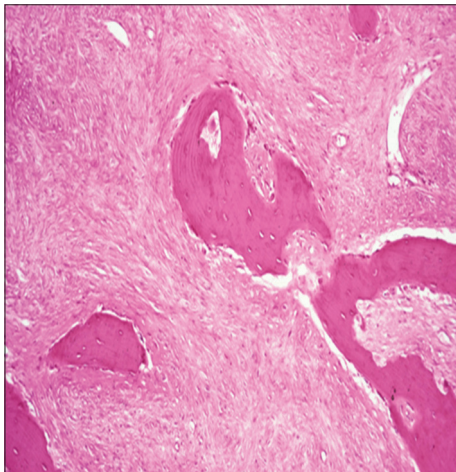
The risk factors for development of osteosarcoma are Paget's disease,<sup>12</sup> external radiation therapy.<sup>13</sup> The average latency



period varies from 10 to 15 years<sup>14,15</sup> Osteosarcoma may extend into the epiphysis<sup>16</sup> and to the metaphyseal region of the bone.<sup>17</sup> The grading and staging for osteosarcoma is the one formulated by Enneking *et al.* and it is the accepted system for musculoskeletal system tumors.<sup>18</sup> The histologic distinction between chondroblastic osteosarcoma and



**Figure 9: X-ray features are lobulated and ossified exophytic mass adjacent to the cortex with a lucent cleavage plane between lesion and the cortex**



**Figure 10: Histopathology shows bone trabeculae with abundant collagen matrix with stromal tumor cells interspersed within the matrix**

chondrosarcoma may be difficult or impossible particularly in tumors with limited osteoid production limited amounts of biopsy material received, as the tumor tissue is inadequately removed surgically.<sup>19</sup> In our study, the radiology and pathology correlation was perfect in all the 27 cases. With modern treatment, approximately 60-70% of newly diagnosed, resectable osteosarcoma patients can expect to be disease-free period of 3 years from diagnosis.<sup>13-15,20</sup> Goldsby *et al.* reported the feasibility of incorporating zoledronic acid to chemotherapy for patients with pulmonary metastatic osteosarcoma.<sup>15</sup> The use of multiagent chemotherapy and surgical resection has drastically improved the outcome of osteosarcoma patients and with modern therapy, and patients with localized, resectable osteosarcoma have a 3-year disease-free survival of 60%.<sup>16,17,19</sup> The lungs were the only metastatic site in 70%, showing secondary deposits if the lung fields in the CT scan.<sup>17,19,21</sup> Bony metastasis alone amounted to 25% of all deaths from other systemic malignant diseases.<sup>21</sup> In the palliative care setting, many would advocate the use of bisphosphonates or radiation therapy particularly in the context of painful bone metastases.<sup>22</sup> The outcome for patients with initially metastatic disease<sup>22-24</sup> remains much worse with reported 2-year survivals of 10-30%. Finally, radium-223 is approved for the treatment of selected adult cancers with bone metastases.

## CONCLUSION

The histopathology is the final tool for the diagnosis of various types of osteosarcoma; the study also explains the pain in diagnosing certain osteosarcoma that produces cartilage, in addition to production of malignant osteoid. Histopathology provides the final verdict for further treatment of the patient as the treatment modality for osteosarcoma differs from the treatment modality of other malignant tumors. The study provides the importance of other medical faculties include the surgeon, radiologist, and oncologist to work as a team for a successful outcome. We correlated the histopathological findings with radiological findings. This resulted in perfect correlation between the histopathology study and radiology study.

**Table 6: Cases reported for follow-up**

Tumor	Number of cases	Number of years since operated	General condition
Osteoblastic osteosarcoma	5	2 cases were operated with limb salvage surgery 3 years back with stage IA. 3 cases underwent wide excision 2 years back	2 cases with limb salvage surgery are keeping good health. The other two have entered treatment complications. 1 case is struggling with multiple organ failure
Chondroblastic osteosarcoma	3	2 cases were operated with wide excision 2 years back. 1 case was operated 1 year back	The general conditions of all the three patients are bad
Parosteal osteosarcoma	2	2 cases were operated 1 year back	The 2 cases show poor health conditions
Periosteal osteosarcoma	2	2 cases were operated 1 year back	The 2 cases show poor health conditions

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