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HISTOPATHOLOGICAL EVALUATION OF 114 OSTEOSARCOMA CASES*

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Summary: 114 cases (75 males and 39 females, M:F ratio 1.9/1) within the age range of 5-75 (median 27) with osteosarcomahad been admitted to Ankara University School of Medicine from 1970 to 1990. These cases were evaluated and discused with statistical and histopathological aspects. Osteoblastic subtype was encountered more frequently than fibroblastic or telangiectatic subtypes.

Key words: Osteosarcoma, histopathology, epidemiology.

Next to multiple myeloma, osteosarcoma is the most common primary malignant tumor of bone in which the malignant proliferating spindle cells directly produce osteoid or immature bone (5,6,12,14,16,19). Males were affected more frequently than females, the ratio being about 1.3 to 2.1 (5, 9, 12, 16, 19). Approximately 50% of tumors occur around the knee joint and the metaphyses of long bones were the usual sites of involvement (5,12,14,16,17,20,21).

Clinical presentation of osteosarcoma varies widely (5,11,14). Metastases may be found in almost every organ but they occur most frequently in the lung and bone (5,8,11,14,16,19). The radiographic appearance of osteosarcoma is characterized by periosteal new bone formation (Codman's triangle), calcification, bone production and osteolysis (11,16,19).

114 Osteosarkom vakasının Histopatolojik Değerlendirmesi

Özet: 1970 - 1990 yılları arasında Ankara Tıp Fakültesi'ne kabul edilmiş 5 - 75 yaşlar arasında (median: 27) 114 osteosarkomlu hastanın (75 erkek, 39 kadın E/K -1.9/1) kayıtları değerlendirildi, demografik ve histopatolojik özellikleri tartışıldı. Osteoblastik alt tip ile telanjiektazik ve fibroblastik tipe nazaran daha fazla karşılaşılmış olduğu görüldü.

Anahtar Kelimeler: Osteosarkom, histopatoloji, epidemiyoloji

Histopathological evaluation of osteosarco - ma has been made on the basis of predominant tissue produced in the tumor as osteoblastic, fibroblastic and chondroblastic subtypes (5,6,8,11,16,17).

Some lesions may contain considerably mineralized osteoid which may show maturation to readily recognized bony trabeculae. These were called as osteoblastic osteosarcomas. About one-fourth of osteosarcomas show predominant chondroid differentiation and called as chondroblastic osteosarcomas. Another subtype is fibroblastic osteosarcoma which resembles predominantly fibrosarcoma except for areas of osteoid production (5,6).

MATERIALS AND METHODS

Starting from 1970 a 20 years collection of all clinical and pathological records of pati-

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ents with the diagnosis of osteosarcoma were reviewed at the pathology department of Ankara University School of Medicine. These cases were evaluated Statistically. Histological Material studied included both biopsy and amputation specimens. Any case with unavailable or technically insufficient specimen was excluded from the study. After this comprehensive search 114 cases of osteosarcoma were evaluated.

Histopathologic subclassification was performed according to the predominant cell type as suggested by Dahlin (6) classifying the osteogenic tumors as osteoblastic, fibroblastic, chondroblastic and telangiectatic osteosarcomas. The numbers and percentages are also calculated and presented in tables.

RESULTS

There were 75 (65%) female patients in this study ranging in age from 5 to 75 years. The median age was 27. The most frequently affected age group was adolescent in the second decade of life, especially those in the age range of 12-16 years. The youngest patient was a 5 year old boy and the oldest one was a 75 year old female. Approximately 64% of the patienst were in their second and third decades (Table I).

Males were affected more frequently than females, the ratio was 1.9/1. The most common region involved was the knee (58%), being localized distal femur in 40.4%, proximal tibia in 17.5%, and proximal femur in 10.6% of the cases (Table II).

After classifying according to subtypes, it was clearly demonstrated that the osteoblastic subtype was the most commonly encountered one (in 70.2% of cases). The ratio of fibroblastic subtype was 3.5 % (Table III).

Microscopically, production of osteoid by malignant cells even in very small amounts in diagnostic for osteosarcoma. Seventy percent of these tumors showed abundant osteoid production by the tumor cells, termed as osteoblastic osteosarcoma (Figure 1), Some cases of osteoblastic osteosarcoma illustrated obviously malignant pleomorphic and bizzare tumor cells surrounding homogenous eozinophilic osteoid tissue. In these cases compact, richly vascularized mass of tumor cells jhich show prominent atypism with hyperchromatic often bizzare nucleus, prominent nucleolus and many atypical mitosis were observerd. (Figure 2). Tumor cells whch show prominent atypism with hyperchromatic often bizzare nucleus, prominent

TABLE-I: Age and Sex Distribution of the Osteosarcoma Cases

Ages	Male number	Female number	Total	%
0-9	5	-	5	4.4
10-19	35	17	52	45.6
20-29	15	6	21	16.4
30-39	3	2	5	4.4
40-49	6	2	8	7.0
50-59	4	2	6	5.3
60-69	4	9	15	11.4
70-79	3	1	4	3.5
TOTAL	75	39	114	100.0

TABLE II: Primary Localization of Osteosarcomas

Localization	Case number	%
Right distal femur	25	22.9
Left distal femur	20	17.5
Right proximal tibia	12	10.5
Left proximal femur	8	7.0
Right proximal femur	6	5.3
Left proximal femur	6	5.3
Proximal humerus	8	7.0
Mandibula	6	5.3
Maxilla	5	4.4
Skull	5	4.4
Ilium	5	4.4
Fibula	2	1.7
Left foot	2	1.7
Scapula	2	1.7
Clavicula	1	0.9
Rib	1	0.09
TOTAL	114	100.0

TABLE III: Subclassifications of Osteosarcoma

Type	Case number	%
Osteoblastic	80	70.2
Fibroblastic	18	15.8
Chondroblastic	12	10.5
Telangiectatic	4	3.5
TOTAL	114	100.0

nucleolus and many atypical mitosis were observed. (Figure 2). Tumor cells with several pleomorphic bizzare nuclei and multinucleated giant cells of osteoclast type jhich have numerous and typical nuclei were observed (Figure 3). This feature was observed in 15 (18.8%) osteoblastic osteosarcoma cases. Eighteen (15.8%) cases were evaluated as fibroblastic osteosarcoma. They predominantly resemble fibrosarcoma excepting for osteoid production (Figure 4). In chondroblastic cases, there were predominant chondroifferentiation in random samples of the tumors. Sometimes osteoid tissue were rather

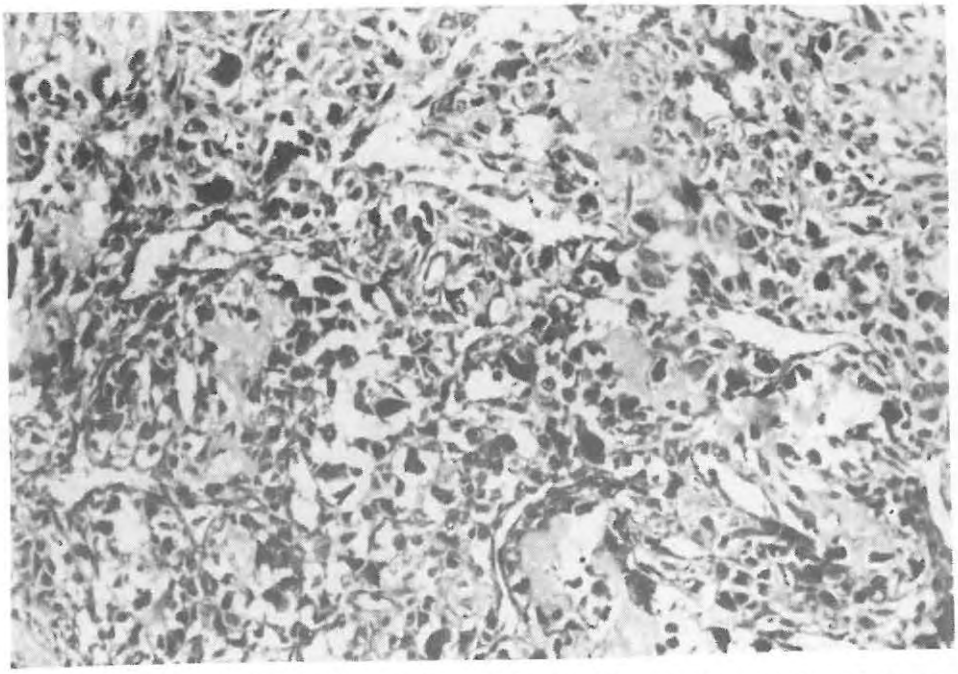

Figure 1: Osteoblastic osteosarcoma. Abundant osteoid areas with a background of atypical osteoblastic proliferation. (Hematoxylin-Eosin, X100).

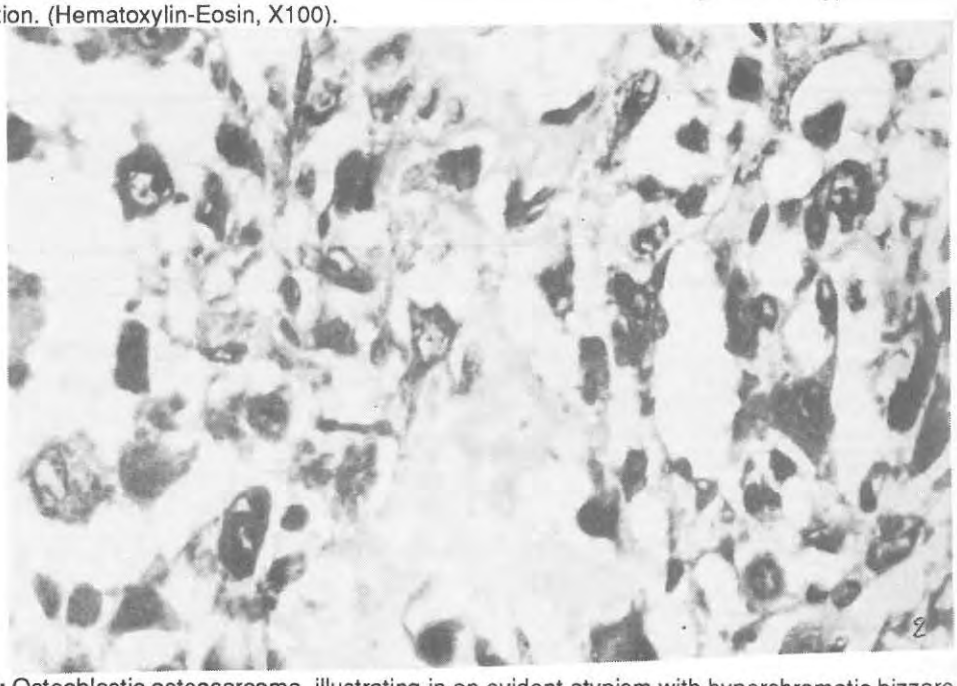

Figure 2: Osteoblastic osteosarcoma, illustrating in an evident atypism with hyperchromatic bizzare nuclei, prominent nucleoli and many atypical mitosis. (Hematoxylin-Eosin, X400).

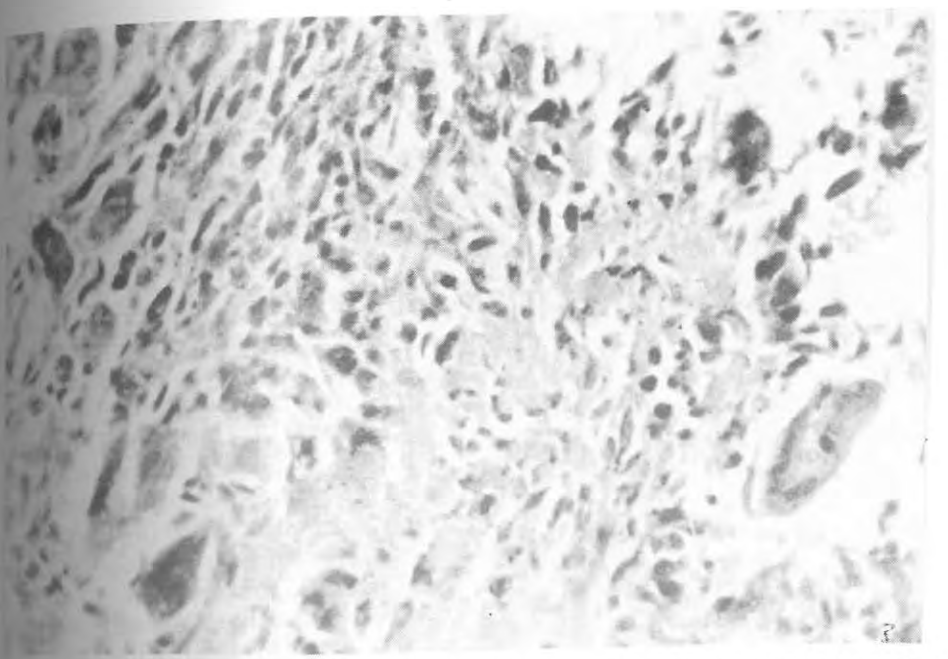

Figure 3: Photomicrograph of osteosarcoma illustrating the presence of osteoid productiion and typical multinucleated giant cells of osteoclast type. (Hematoxylin-Eosin, X200).

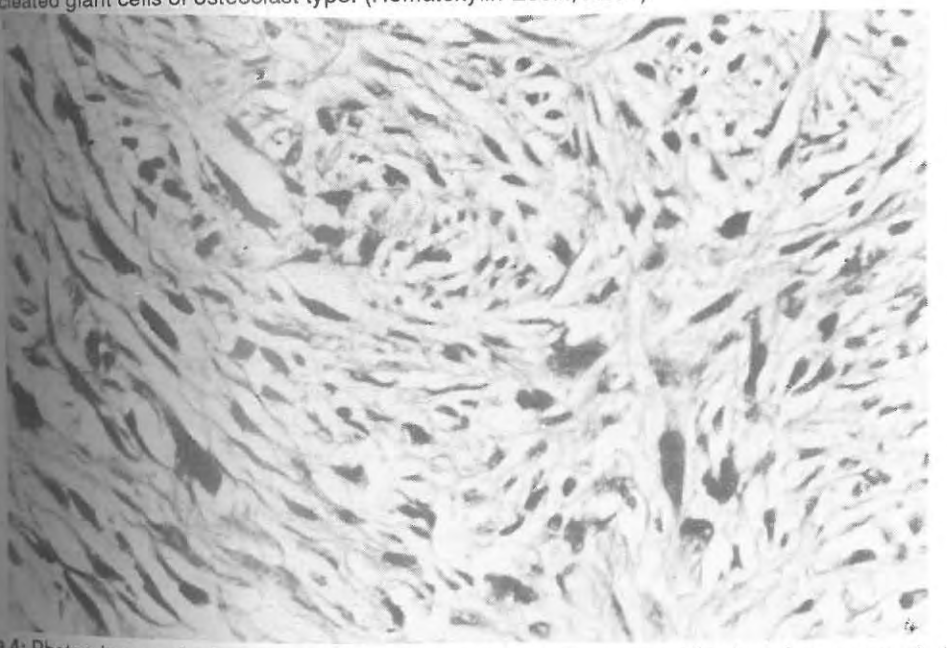

Figure 4: Photomicrograph of osteosarcoma, fibroblastic tyep, Rare osteoid trabeculae surrounded by spindle-celled tissue. (Hematoxylin-Eosin, X200).

small foci that the matrix substance showed the finer ramification and deeper red staining with Hematoxlyin and Eosin. These areas showed deeper red staining with van Gieson stain (Figure 5). Specimens from telangiectatic osteosarcoma cases contained prominent blood-filled spaces (Figure 6), fairly numerous benign giant cells and sparse osteoid tissue. Parosteal osteosarcoma comprised about 3.5 percent of the total tumors in this series. Microscopically, they were well differentiated osteosarcoma highly resembling grade 1 fibrosarcoma (Figure 7).

DISCUSSION

The origins of osteosarcoma are as mysterious as those of all other forms of tumor; however, a number of interesting cases observations have been observed that eould have been considered under the categories of genetic, constitutional and environmental factors (13,14).

Osteosarcoma comprises neoplastic bone and osteoid with cytologically malignant osteocytes and osteoblasts; these are accompanied by a malignant stroma that may be undifferentiated with fibrosarcomatous features. Osteosarcomas may have large areas of cytologically malignant cartilage may develop epitheloid features, may be unusually vascular with anevrysmal areas, may have foci characteristic of malignant fibrous histiocytoma, and may have small round cells. A variable combination of tehese many histologic findings may be present (8,9,11,12).

At the Pathology Department of Ankara University School of Medicine 237 osteoblastic bone tumors have been were diagnosed between 1970 and 1990. In this study 48% of cases were osteosarcomas. Approximately 64% of the cases were in the second and third decades of life. This percentage is 55% teh USA and 65% in Denmark (8,10,19).

Males are affected more frequently than fermales, the ratio being 1.9/1. This ratio has been reported between 1.3 and 2.1/1 in the various articles (5,9,10,12,16,19,20). Higher incidence in males may be related the longer period of skeletal growth and higher bone mass and volume (8,19).

In our cases the most common lolacilazition for osteosarcoma was surrounding hnee goint. This finding was consistent with the data published previously (5, 8, 10, 11, 12, 16, 19, 20,21). Until the cessation of growth period, the long bones are most frequently involved, but after this period all bones are almost equally affected (8,16). The majority of the lesions are metaphysial, but occasionally extend into the epiphysis (8,14,16). Articular cartilage is very resistant to the tumor invasion (13,14,19). Most of the cases also show irregular borders, periosteal spicules (Sunburst appearance) and Codman's triangle (11,16,19,20).

Classifying the subtypes, clearly demonstrated that the osteoblastic subtype is the most commonly encountered one (70.2% of cases) which is similar to other series where the ratios are 44.5% and 55% (6,12,16). Fibroblastic subtype is estimated as 15.8% and chondroblastic subtype is 10.5%. The percentile for felangiectatic subtype in our study is 3.5%, but according to other series the percentile of telangiectatic subtype is approximately 1-2% (3,8). The percentage of parosteal osteosarcoma is 3.5% which is similar to other series (1,4).

The differential diagnosis of osteosarcoma may require to exclude a remarkably high number of benign and malignant tesions, such as osteoblastoma, fibrous dysplasia, fracture callus, myositis ossificans, fibrosarcoma, chondrosarcoma, giant cell tumor, lymphoma and metastaic carcinoma (11,12,14,16,17,19).

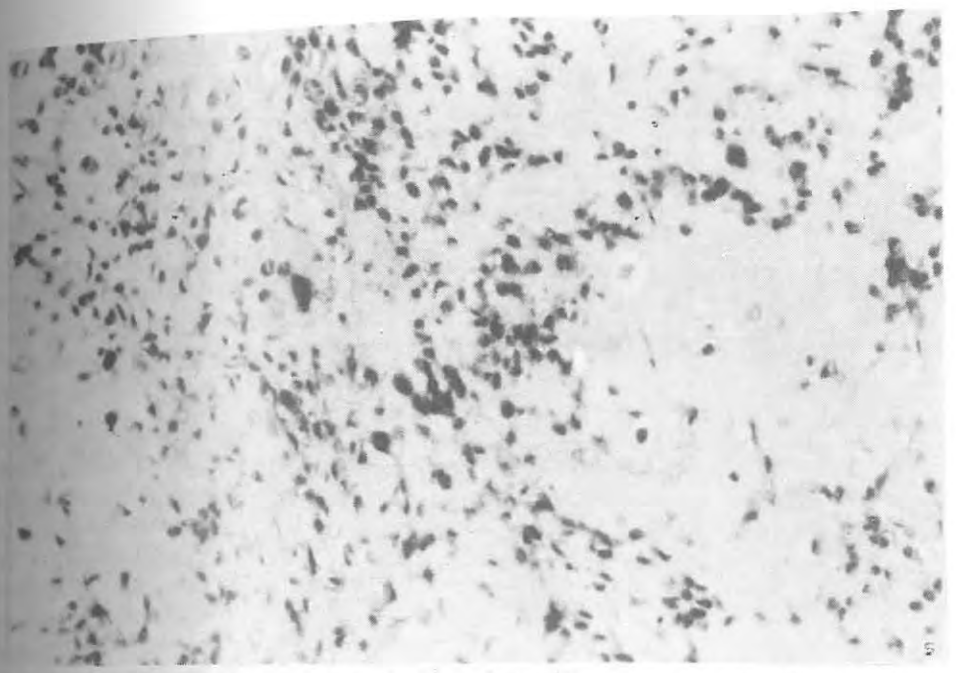

Figure 5: Chondroblastic osteosarcoma. Though there is prominent cartilaginous differentiation, osteoid is prominent in the cellular foci. (Van Gieson, X100).

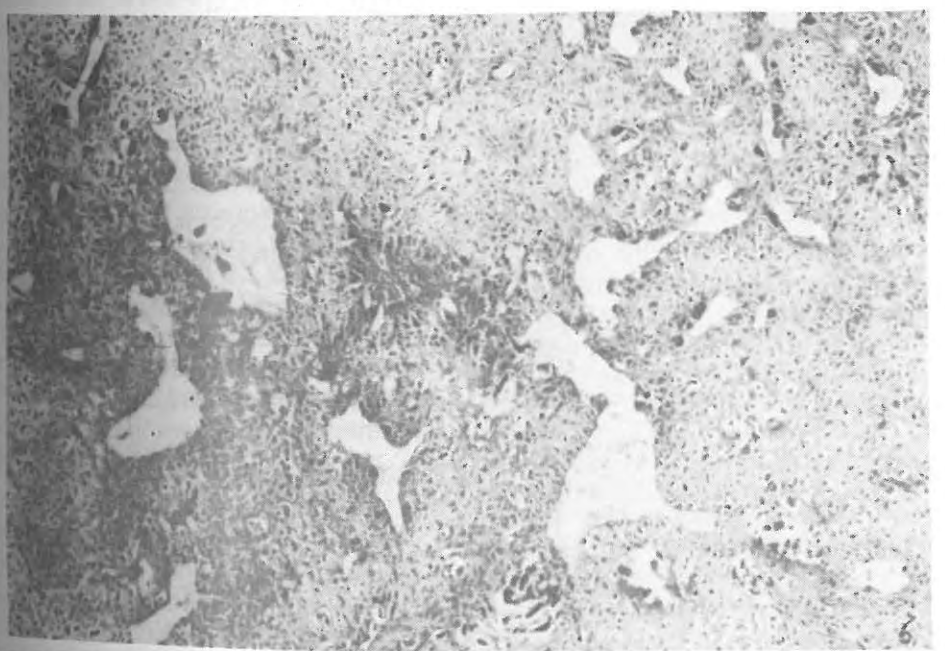

Figure 6: Telangiectatic osteosarcoma. A highly vascularised appearence (Hematoxylin-Eosin, X40).

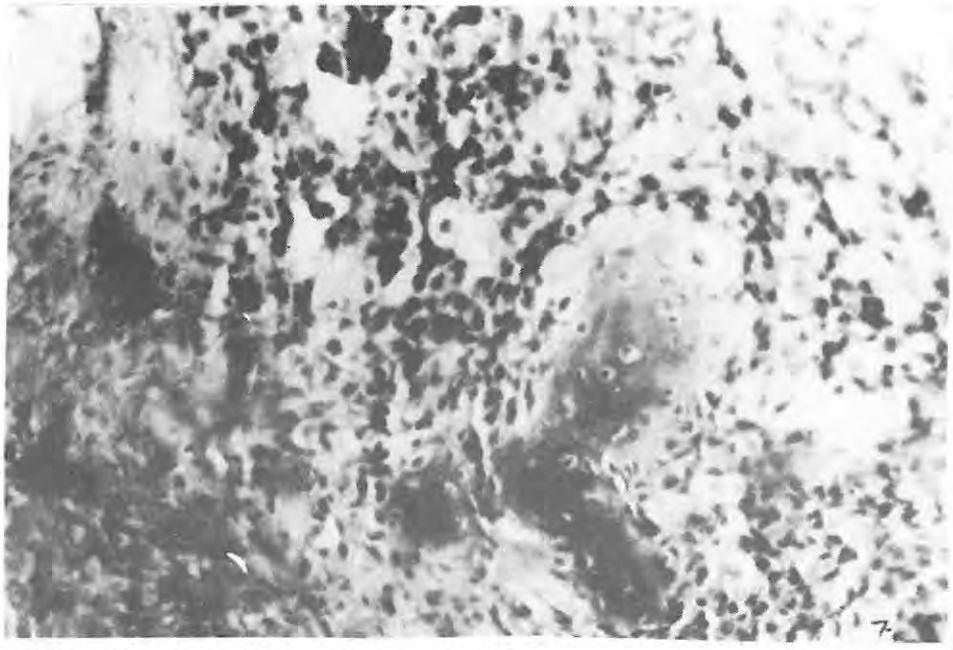

Figure 7: Parosteal osteosarcoma shows the bone trabeculae separated by a fibirous stroma, revealing some pleomorphism of the fibroblastic elements. (Hematoxylin-Eosin, X100).

Misdiagnosis in osteosarcoma is frequent and an important problem. Recently, a study revealed that the ratio of histopathological misdiagnosis of osteosarcomas was 8.2%. On the other hand, the ratio of radiological misdiagnosis was 27%. When two modalities of diagnosis were combined, the diagnostic inaccuracy decreases. For this reason, clinical, radiological and histopathological evaluation should be done together in a center which is experienced on this matter (20).

Changes and improvements in the methods of treating osteosarcomaparticularlyicohp diotherapy, and limb-preserving surgery have heigtened the responsibility of pathologists to accurately interpret material from these lesions. The hisitologic effects of chemotherapy on osteosarcoma are variable depending on the histologic type. The osteoblastic osteosarcoma has shown most significant response to treatment. But telangiectatic osteosarcoma responded poorly to treatment (18).

Developing of new technixues, such as CT scan, cytodiagnosis, have made diagnosing or staging of osteosarcomas easien and more reliable (2,7,8,11,15). The conception that chemotherapy has beneficially altered the course of osteosarcoma is generally accepted. Fiveyear disease-free survival rates at present are 65 to 85 percent. Prior to chemotherapeutic intervention, the expected 3 years survival was less than 25 percent (11,15,18).

The advent of per-and postoperative chemotherapy has significantly enhanced five-year disease-free survival rates that are now approaching 85%. Improved consepts of en bloc resection and better reconstructive techniques suggest that limb salvage proce-

dures are not only possible but can provide excellent functional results in the context of muscle loss. Patients presenting with thoracic lesions, although difficult to treat, can expect a 45% long-term survival following repetitive thoracotomies (8,10,11,18).

Some authors claimed a better prognosis for the fibroblastic subtype but the difference is so small as to be of no statistical significance (5,14). Parosteal osteosarcoma is associated with an improved prognosis (1,4,14).

Depending on which component predominates, osteosarcomas have been divided into osteoblastic, chondroblastic and fibroblastic types but there seems to be no prognostic significance to this division. The important fact to remember is that a malignant tumor should be designated as osteosarcoma whenever osteoid is seen unconnected with cartilage and is formed directly from the tumor cells, no matter how much neoplastic cartilage or fibrous tissue is present elsewhere, because the prognosis of osteosarcoma is worse than fibrosarcoma and chondrosarcoma of bone (5,6,11,14).

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