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HISTOPATHOLOGICAL EVALUATION OF 114 OSTEOSARCOMA CASES

Dr. Hüseyin ÜSTÜN*, Dr. Salim GÜNGÖR**

* İnönü Üniversitesi Tıp Fakültesi Patoloji Anabilim Dalı, ** S.Ü.T.F. Patoloji Anabilim Dalı

SUMMARY

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

Key Words: Osteosarcoma, histopathology, epidemiology

ÖZET

114 Osteosarkoma Vak'asının Histopatolojik Yönden Değerlendirilmesi

Ankara Üniversitesi Tıp Fakültesine 1070 ile 1990 tarihleri arasında 114 osteosarkom hastası müracaat etmiştir. Bunların 75'i erkek, 39'u kadındır (Erkek/Kadın oranı 1.9/1'dir). Hastaların yaşları 5-75 yaş arasında değişmekte olup ortalama yaş 27'dir. Hasta dokularının histopatolojik verileri istatistiki olarak değerlendirilmiştir. Osteosarkomayı oluşturan olgular arasında osteoblastik olgulara, fibrioblastik veya telangiektatik olgulardan daha sıklıkla rastlanılmıştır.

Anahtar Kelimeler: Osteosarkoma, histopatoloji, epidemiyoloji

INTRODUCTION

Next to multiple myeloma, osteosarcoma is the most common primary malignant tumor of bone in which the malignantly proliferating spindle cells produce osteoid or immature bone (1, 2, 3, 4, 5, 6). Males are affected more frequently in the lung and bone (1, 4, 5, 6, 7, 8). The radiographic appearence of osteosarcoma is characterized by periosteal new bone formation (Codman's triangle), calcification, bone production and osteolysis (6, 8, 9).

Histopathological evaluation of osteosarcoma has been made on the basis of predominant tissue produced in the tumor as osteoblastic, fibroblastic and chondroblastic subtypes (1, 2, 3, 5, 7, 8, 10). Some lesions may contain considerably mineralized osteoid which may show maturation to readly recognized bony trabeculae. These are called as osteoblastic osteosarcomas. About one-fourth of osteosarcomas show predominant chondroid differentiation and called as chondroblastic osteosarcomas. The other subtype is fibroblastic osteosarcoma which resembles predominantly fibrosarcoma except for areas of osteoid production (1, 2).

In this study our aim is to point out that how important to make correct and differential diagnosis.

MATERYAL AND METHODS

All pathological and clinical records of pathology department of Ankara University Medical School patients with the diagnosis of osteosarcoma were reviewed retrospectly from 1970 to 1990. These cases were evaluated statistically. Histological materials were both biopsy and amputation specimens. On the basis of the availability of histological material 114 cases were included and those who have insufficient or unavailable histological materials are excluded from this study.

Histopathologic subclasification was done according to the abundance of cell type as suggested by Dahlin classification (2); the osteogenic tumors as osteoblastic, fibroblastic, chondroblastic and telangiectatic osteosarcomas. The numbers and percentages of subtypes were also calculated and presented in tables.

RESULTS

There were 75 (65 %) male and 39 (35 %) female patients in this study ranging in age from 5 to 75 years. The median age was 27 years. Adolescants

Haberleşme Adresi: Dr. Salim GÜNGÖR, S.Ü.T.F. Patoloji Anabilim Dalı, KONYA

in the second decade of life represented the majority of the patients. Especially those in the age range of 12-16 years. The youngest patient was a 5 years old boy and the oldest one was a 75 years old female. Approximately 64 % of the patients were in the second and third decade (Table 1).

Males were affected more frequently than females, the ratio was 1.9. The most common region which is involved was the knee where 58 % of the patients having the tumor. The most common sites for osteosarcomas were distal femur (40.4 %), proximal tibia (17.5 %), and proximal femur (10.6 %) (Table 2).

After classifying according to subtypes, it was clearly demonstrated that the osteoblastic subtype was most commonly encountered in 70.2 % of cases. Followed by fibroblastic subtype 15.8 %, chondroblastic subtype 10.5 %, and telangiectatic subtype 3.5 % (Table 3).

Table 1. Age and sex distribution of the osteosarcoma cases.

Age group	Male	Female	The Sum	Percent (%) of 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 2. Primary localization of osteosarcomas.

Localization	# of cases (n)	Percent of total (%)
Right distal femur	25	22.9
Left distal femur	20	17.5
Right proximal tibia	12	10.5
Left proximal femur	6	5.3
Right 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	0.9
Total	114	100.0

Table 3. Subclassifications of osteosarcomas

Type	# of cases (n)	Percent of total (9)
Osteoblastic	80	70.2
Fibroblastic	18	15.8
Chondroblastic	12	10.5
Telangiectatic	4	3.5
Total	114	100.0

Microscopically, production of osteoid by malignant cells even in 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 a part of homogenous eosinophilic osteoid tissue. In these cases a compact, richly vascularized mass of tumor cells which show prominent atypism with hyperchromatic often bizzare nucleus, prominent nucleolus and many atypical mitosis were observed (Figure 2).

Tumor cells with several pleomorphic bizzare nuclei and multinucleated giant cells of osteoclast type which have more numerous and typical nuclei were observed (Figure 3). This feature was found in 15 (18.8 %) osteoblastic osteosarcoma cases. Eighteen (15.8 %) cases were evaluated as fibroblastic osteosarcoma. They predominantly resembled to fibrosarcoma except for osteoid production areas (Figure 4). In chondroblastic cases, there were predominant chondroid diffrentiation in random samples of the tumors. Sometimes osteoid tissue were rather small foci that the matrix substance showed the finer ramification and deeper red staining with Hemotoxylin and Eosin. These areas showed deeper red staining with von Gieson stain (Figure 5). Telangiectatic osteosarcoma cases were containing prominent blood-filled spaces (Figure 6). It contained fairly numerous benign giant cells an sparse osteoid tissues. Parosteal osteosarcoma comprised about 3.5 percent of the total tumors in thes series. Microscopically, they were well differentiated osteosarcoma which were highly resembled to grade I fibrosarcoma (Figure 7).

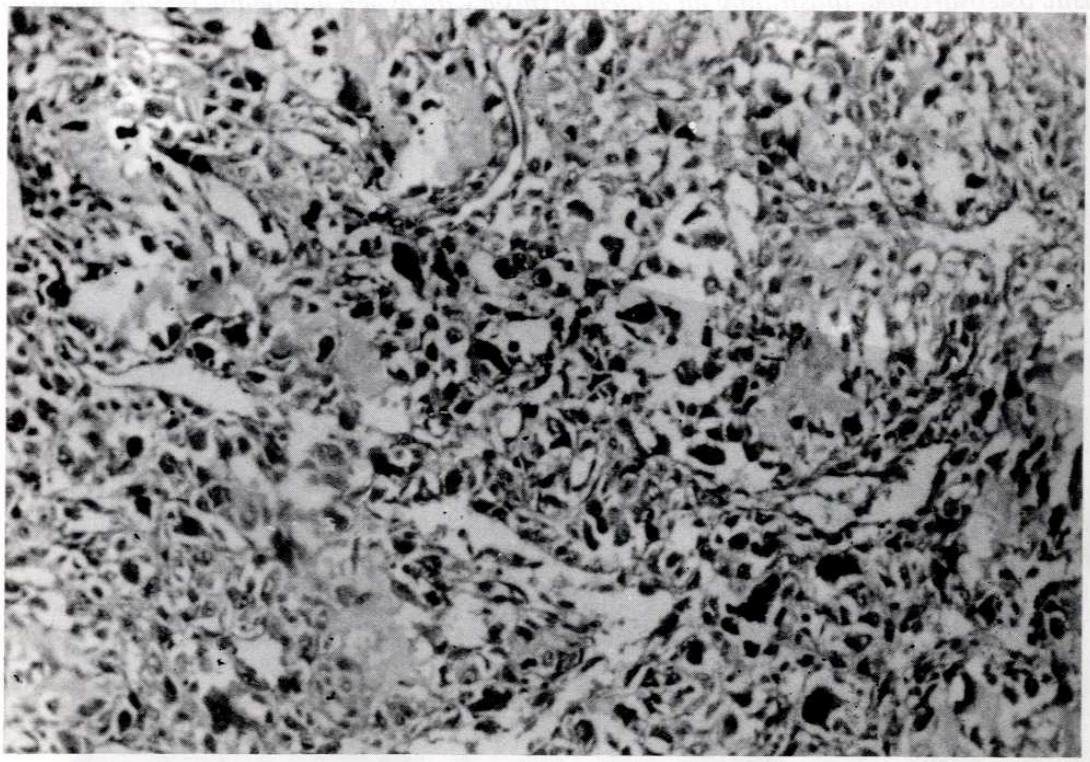

Figure 1. Osteoblastic osteosarcoma. Abundant osteoid areas with a background of atypical osteoblastic proliferation. (Hematoxylin - Eosin, X100).

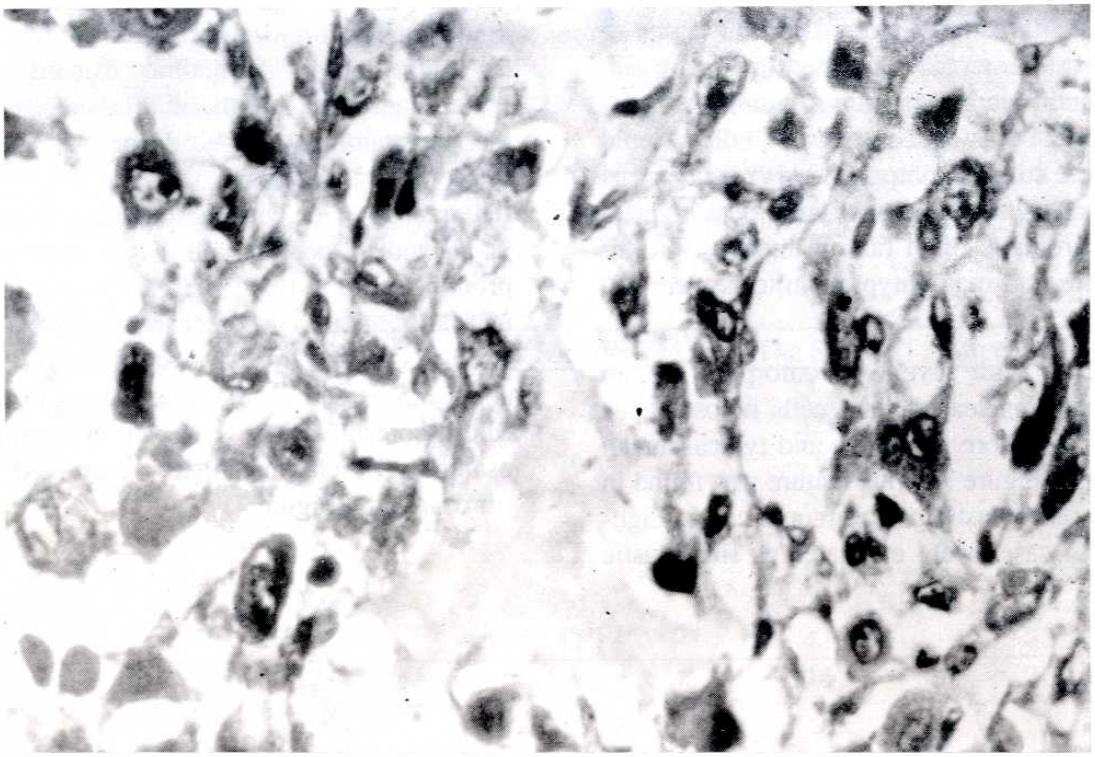

Figure 2. Osteoblastic osteosarcoma, illustrating an evident atypism with hyperchoramatic bizzare nuclei and prominent nucleoli and many atypical mitoses. (Hematoxylin- Eosin, x400).

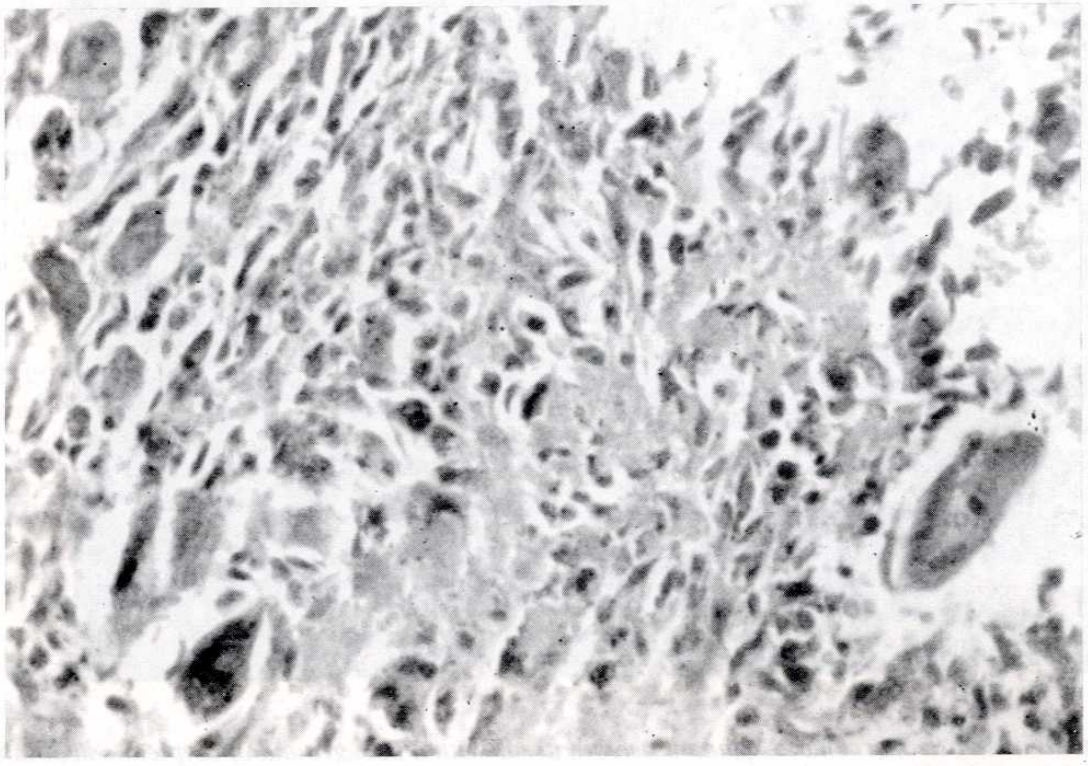

Figure 3. Photomicrography of osteosarcoma illustrating the peresence of osteoid production and typical multi-nucleated giant cells of osteoclast type. (Hematoxylin- Eosin, X200).

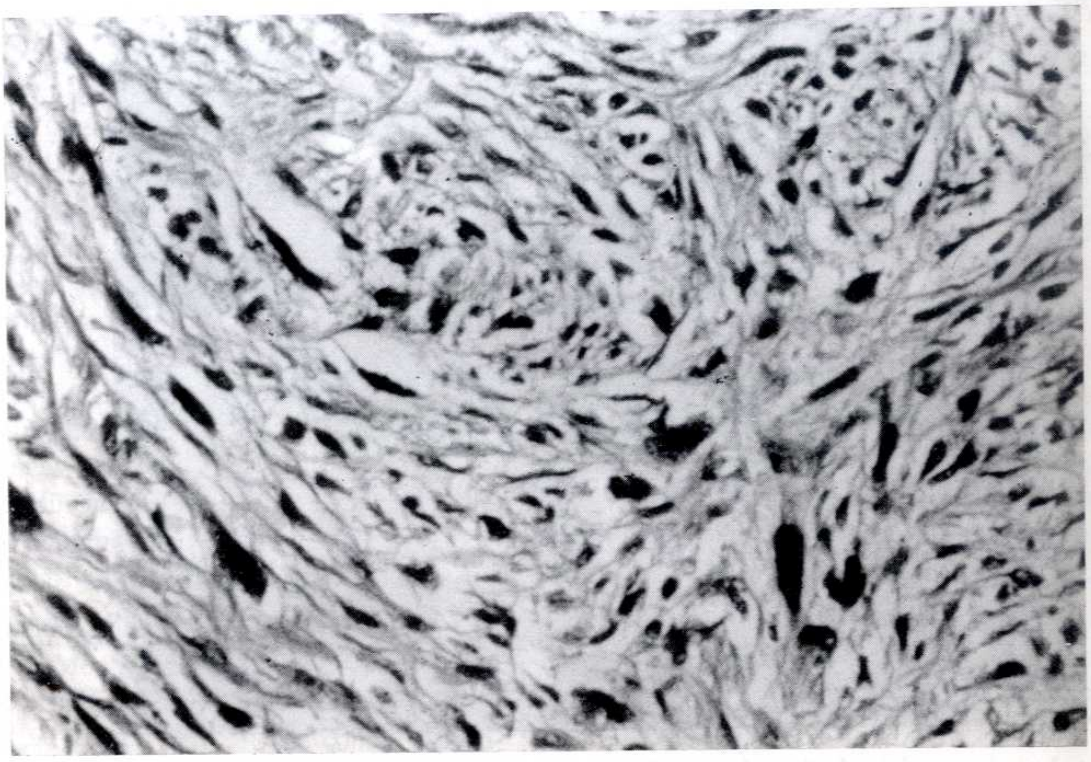

Figure 4. Photomicrograph of osteosarcoma, fibroblastic type. Rare osteoid trabeculae surrounded by spindle - cell tissue. (Hematoxylin- Eosin, X200).

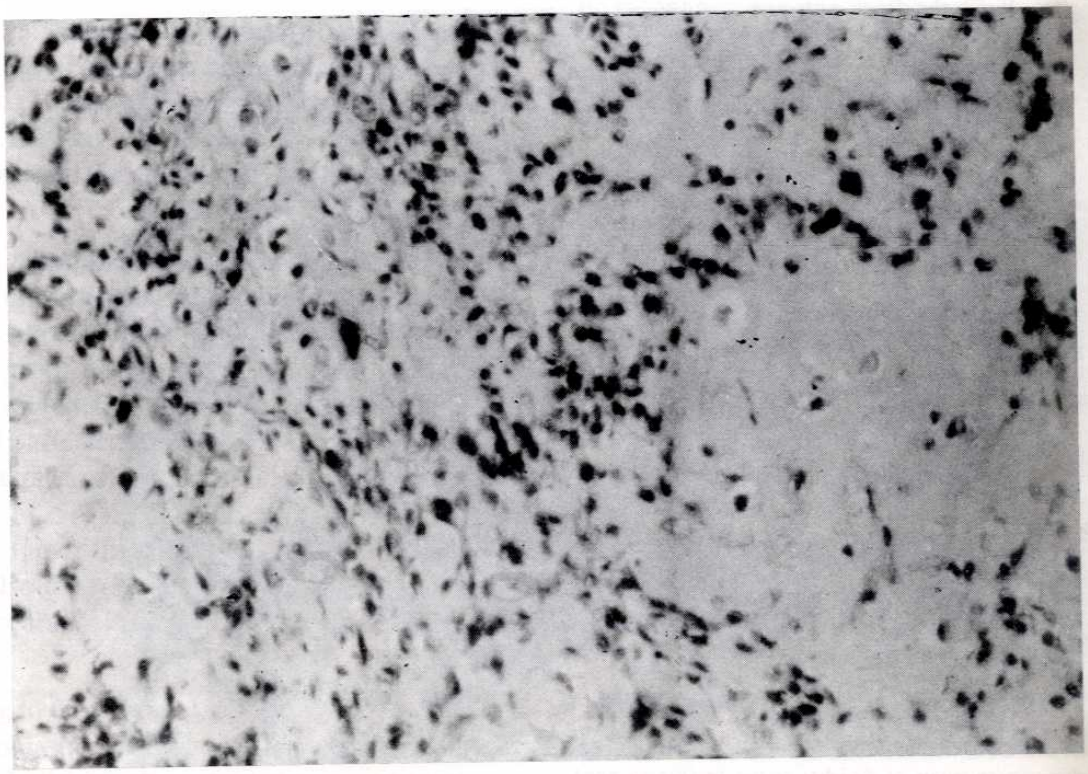

Figure 5. Chondroblastic osteosarcoma. Though there is prominent cartilaginous differentiation osteoid is prominent in the cellular foci, (Van Gieson, X100).

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

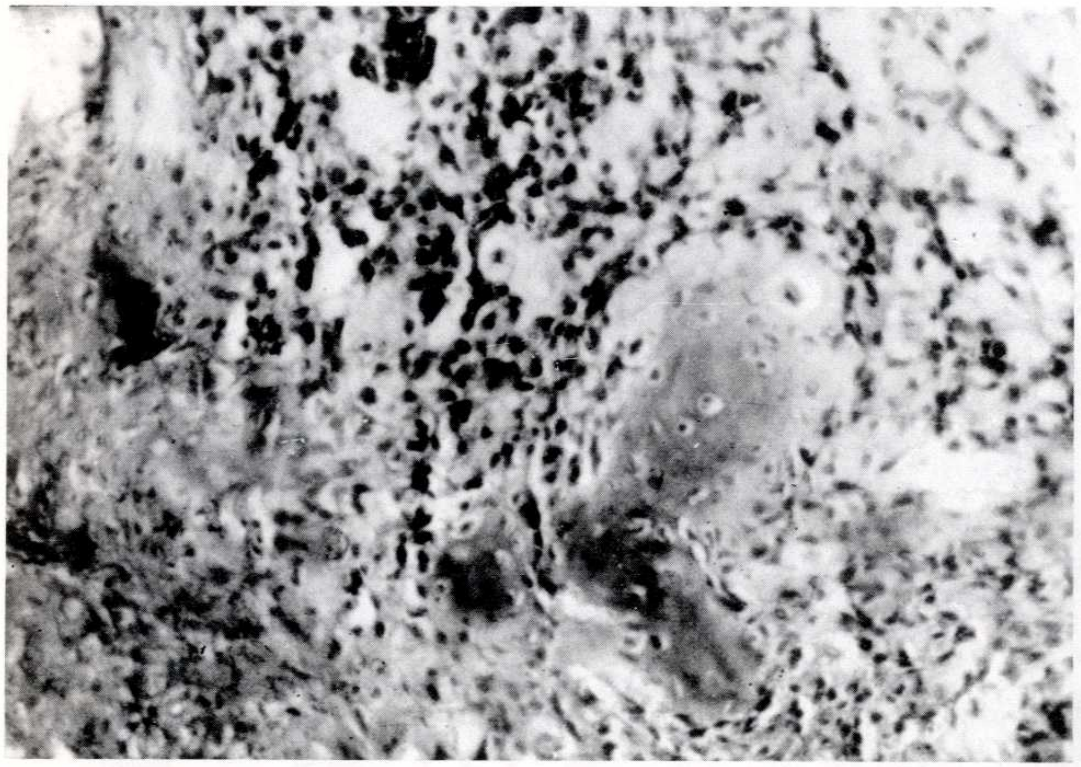

Figure 7. Parosteal osteosarcoma shows the bone trabeculae separated by a fibrous stroma, revealing some pleomorphism of the fibroblastic elements. (Hematoxylin- Eosin, X100).

DISCUSSION

The origins of osteosarcoma are as mysterious as those of all other forms of the tumor. However a number of interesting observations can be considered under the light of genetic make up and environmental constraints (4, 11).

Osteosarcoma comprises neoplastic bone and osteoid with cytologically malignant osteocytes and osteoblasts; these are accompained 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 aneurysmal areas, may have foci characteristic of malignant fibrous histiocytoma, and may have small round cells. A combination of these many histologic variations may be present (3, 7, 8, 12).

At the Pathology Department of Ankara University Faculty of Medicine, 237 osteoblastic bone tumors have been diagnosed between 1970 and 1990. In our study 48 % of cases were osteosarcomas. Approximately 64 % of the cases were in the second and third decades of life. This percantile is 55 % in the USA and 65 % in Denmark (6, 7, 13).

Males are affected more frequently than females, the ratio was 1.9. This ratio changes between 1.3 and 2.1 elsewhere (1, 3, 5, 6, 12, 13, 14). Higher incidences in males may be related to the longer period of skeletal growth and the additional volume of bone (6, 7).

The most common sites for osteosarcoma in our study were around the knee joint which are parallelled to published data (1, 3, 5, 6, 7, 8, 13, 14, 15). Until the cessation of groth period, the long bones are most frequently involved, but after this period all bones are almost equally affected (5, 7). The majority of the lesions are metaphysial, but occassionally extend into the epiphysis (4, 5, 7). Articular cartilage is very resistant to the tumor invasion (4, 6, 11). Most of the cases show also irregular borders, periosteal spicules (Sunburst appearance) and Codman's triangle (5, 6, 8, 14).

According to the subtypes, 70.2 % of cases shows that the osteoblastic subtype is the most commonly encountered similar to other reported series where the ratios changes from 44.5 % to 55 % 2, 3, 5). Fibroblastic subtype is estimated as 15.8 % and chondroblastic subtype is 10.5 %. Telangiectatic and parosteal osteosarcoma subtypes represent the lesser proportion of all osteosarcomas in our series (Table 3) and other reported series (7, 16, 17, 18).

The differential diagnosis of osteosarcoma enables differentiate remarkably high number of benign and malignant lesions, such as osteoblastoma, fibrosarcoma, chondrosarcoma, giant cell tumor, lymphoma and metastatic carcinoma versus to fibrous dysplasia, fracture callus and myositis ossificans (3, 4, 5, 6, 8, 10).

Misdiagnosis an osteosarcoma is not unusual and important problem. Recently, a study revealed that the ratio of histopathological misdiagnosis of osteosarcomas was 8.2% (14). On the other hand, the ratio of radiological misdiagnosis was 27% (14). When two modalities of diagnosis were combined, the diagnostic inaccuracy can be reduced considerably. For this reason, clinical, radeological and histopathological evaluation should be done concomitantly for a sound treatment (14).

Improved methods of diagnosis and staging have been mode possible by the computed tomography scan, cytodiagnosis and DNA analysis, and magnetic resonance imaging methods (7, 8, 19, 20, 21).

Changes and improvements in the methods of treating osteosarcoma -particularly in chemotherapy, radiotherapy, and limb- preserving surgery have heightened the responsibility of pathologists to accurately interpret material from these lesions. The response of osteosarcomas to chemoteraphy can be assessed by examing the histological changes during follow up. The osteoblastic osteosarcomas showed most significant response to treatment. But, telangiectatic osteosarcoma responded poorly to treatment (18).

Dramatic regression of osteosarcomas after receiving chemotherapy has significantly improved the condition of the patients. Five-year disease-free survival rate now is 65 to 85 percent. Prior to chemotherapeutic intervention, the expected survival for three years was less than 25 percent (8, 9, 21).

The advent of pre-and postoperative chemotherapy has significantly improved five-year disease-free survival rates which is now approaching 85%. Improved concepts of en bloc resection and better reconstructive techniques suggest that limb salvage

procedures are not the only possible choice but also can provide excellent functional results in the context of muscle loss. Patients having thoracic lesions, although difficult to treat, can expect a 45% long-term survival following repetitive thoracotomies (7, 8, 9, 13).

Although, some authors claimed a better prognosis for the fibroblastic subtype but the difference is statistically insignificant (1, 4). However, parosteal osteosarcoma has better prognosis (8, 17, 18).

Depending on which component predominates, osteosarcomas have been divided into three subtypes; osteoblastic, chondroblastic, and fibroblastic, but it seems this classification does not have prognostic significance,. However, it should be pointed out that a malignant tumor can be addressed as osteosarcoma when osteoid is unassociated with cartilage and originated directly from the tumor cells, no matter how much neoplastic cartilage or fibrous tissue is present elsewhere. Also it should the stressed that the prognosis of osteosarcoma is worse than fibrosarcoma and chondrosarcoma of bone (1, 2, 4, 8).

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