Virchows Archiv A Pathol Anat (1991) 418:419–425

Virchows Archiv A
Pathological Anatomy and Histopathology

Morphological typing of chondrosarcoma: a study of 94 cases*

Heike Welkerling, Thomas Dreyer, and Günter Delling

Department of Bone Pathology, Institute of Pathology, University of Hamburg, Martinistrasse 52, W-2000 Hamburg 20, Federal Republic of Germany

Received November 27, 1990 / Accepted January 23, 1991

Summary. Ninety-four chondrosarcomas of the Hamburg Bone Tumour Registry were reviewed in a retrospective study. The purpose of this study was to examine the morphological characteristics of different types of chondrosarcomas and to describe distinctive features of location, the age distribution and the male to female ratio. Central chondrosarcomas can be divided into classical chondrosarcomas, dedifferentiated chondrosarcomas, mesenchymal chondrosarcomas and clear-cell chondrosarcomas. Five periosteal chondrosarcomas were represented. Classical chondrosarcomas and clear-cell chondrosarcomas show a significant predominance of males; no sex predilection was seen in dedifferentiated and mesenchymal chondrosarcomas. Nearly 60% of classical and mesenchymal chondrosarcomas occur in the trunk. Eighty-five percent of dedifferentiated chondrosarcomas are located in the long bones of the limbs. Clear-cell chondrosarcomas arise in the proximal part of the femur. There is a marked predilection for mesenchymal chondrosarcomas in the second and third decades of life. The average age of patients with classical chondrosarcomas was 54 years, but clear-cell chondrosarcomas occur 10 years earlier and dedifferentiated chondrosarcomas 10 years later. Characteristically, classical chondrosarcomas produce a pure chondroid matrix with variable differentiation of tumour chondrocytes. The most important histological feature of the defifferentiated chondrosarcoma is the close association of two different cellular components. One of these consists of cartilage, which is generally well differentiated. In most of our cases the second component showed features of osteosarcoma (50%). Mesenchymal chondrosarcoma is characterized by concentric infiltration of cartilage islands by small tumour cells. Clear-cell chondrosarcomas show regions of cartilaginous tumour and areas of closely packed, glycogen-rich, large tumour cells with distinct boundaries. Osteoid formation and multinucleated giant cells are present in clear-cell areas. Knowledge of this group of tumours is indispensable for correct histological diagnosis and typing and is important in the design of surgical therapy and the prediction of biological behaviour.

Key words: Chondrosarcoma – Cartilaginous tumours – Dedifferentiated chondrosarcoma – Mesenchymal chondrosarcoma – Clear-cell chondrosarcoma

Introduction

Chondrosarcomas are the second largest group of primary malignant bone tumours and are characterized by slow growth, with late metastasis. There is a marked predilection for the trunk and proximal parts of the humerus and femur (Fig. 1). We distinguish four types of centrally located chondrosarcoma with variable cellular differentiation and production of matrix: classical chondrosarcomas, dedifferentiated chondrosarcomas, mesenchymal chondrosarcomas and clear-cell chondrosarcomas (Fig. 2). The number of special types is high (30%) in our material. The objectives of this report are to describe the morphological characterization and typing of chondrosarcomas in the Hamburg Bone Tumour Registry, with details of location, age and sex distribution. Accurate morphological typing is critical in surgical therapy and prognosis.

Materials and methods

Eighty-nine central and 5 periosteal chondrosarcomas identified between 1974 and 1989 were investigated. We used 6-μm-thick plastic and paraffin sections stained with haematoxylin and eosin (H&E), Masson-Goldner, astra-blue, periodic acid-Schiff (PAS) and toluidine blue. In addition, large-area sections of gross specimens were included in our examination. Furthermore, macromorphology of gross specimens, radiographs as well as radiographs of gross specimens were examined.

Results

Sixty-seven percent ($n=60$) of the central chondrosarcomas were classical chondrosarcomas. The mean age was

* Dedicated to Professor D. Seifert on the occasion of his 70th birthday.

Offprint requests to: G. Delling

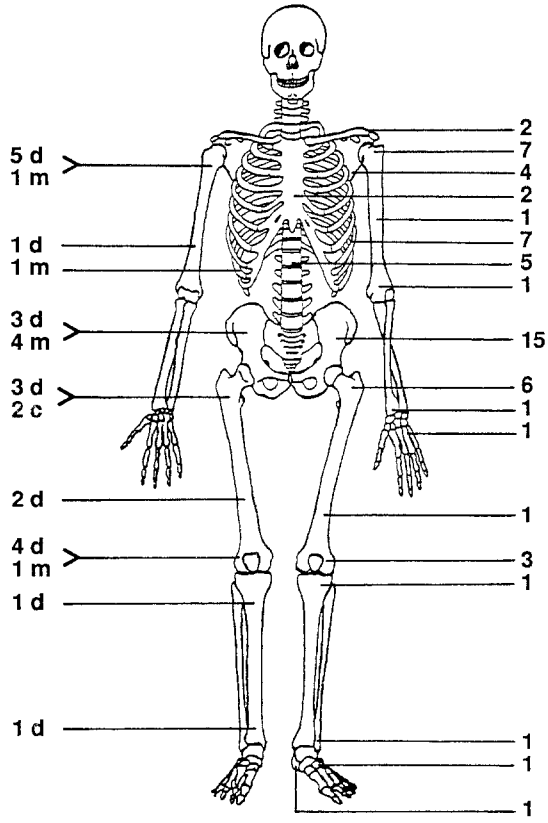


Fig. 1. Skeletal distribution of classical chondrosarcomas (right) and different types of chondrosarcomas. *d* Dedifferentiated chondrosarcoma; *m* mesenchymal chondrosarcoma; *c* clear-cell chondrosarcoma

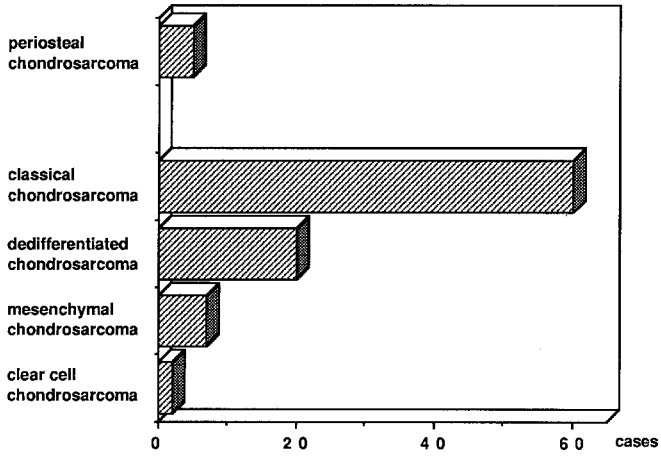


Fig. 2. Distribution of chondrosarcoma types

54 years and the youngest patient was 19. Most patients presented between the fifth and seventh decades. Sixty-two percent of the patients were more than 50 years old. The classical chondrosarcoma showed a significant predominance of males (3:2). Eighty percent were located in the trunk (58%) and in the upper ends of the femora and humeri (22%). Nearly 50% of chondrosarcomas located in the trunk occurred in the innominate bone. There was no significant predilection for the upper or lower extremities in tumours of the proximal femur and humerus.

Macroscopically chondrosarcomas are characterized by multilobulated and nodular structure (Fig. 7). The tumour permeates marrow spaces and is circumscribed in most cases. Thickening of the cortex may be produced by slow tumour infiltration or reactive bone formation. If rapid destruction or cortical erosion is observed, the cortex is narrowed. Normally, necrotic foci of varying size, bleeding and cystic alterations are found in the tumour tissue. Freckled and spotted calcification are characteristic features of classical chondrosarcomas. The tumour tissue is white-grey, semi-translucent and has a firm elastic consistency.

Microscopically classical chondrosarcomas are characterized by lobulated hyalin cartilage formation. The tumour is marked by variable differentiation of tumour chondrocytes with pure chondroid matrix production (Fig. 3). Nuclear size and nuclear polymorphism help to separate the group of classical chondrosarcoma into three grades (Welkerling et al. 1989). In 48% we had diagnosed grade 1 chondrosarcomas. Forty-five percent of our cases were grade 2 chondrosarcomas. The tumour is marked by eccentric infiltration of marrow spaces with embedding of the trabecular bone. In microscopic sections this growth pattern appears to represent isolated tumour areas.

Twenty-three percent ($n=20$) of our central chondrosarcomas belong to the group of dedifferentiated chondrosarcomas. The mean age was 64 years. These tumours thus occur 10 years later than classical chondrosarcomas. With the exception of two cases, the patients were more than 50 years old. We observed a predominance of patients in the seventh and eighth decades of life. No sex predilection was noted. In contrast with classical chondrosarcomas the most common location was the long bones of the limbs (85%). Nearly 50% arose in the proximal parts of femur and humerus. All tumours of the trunk were situated in the innominate bone.

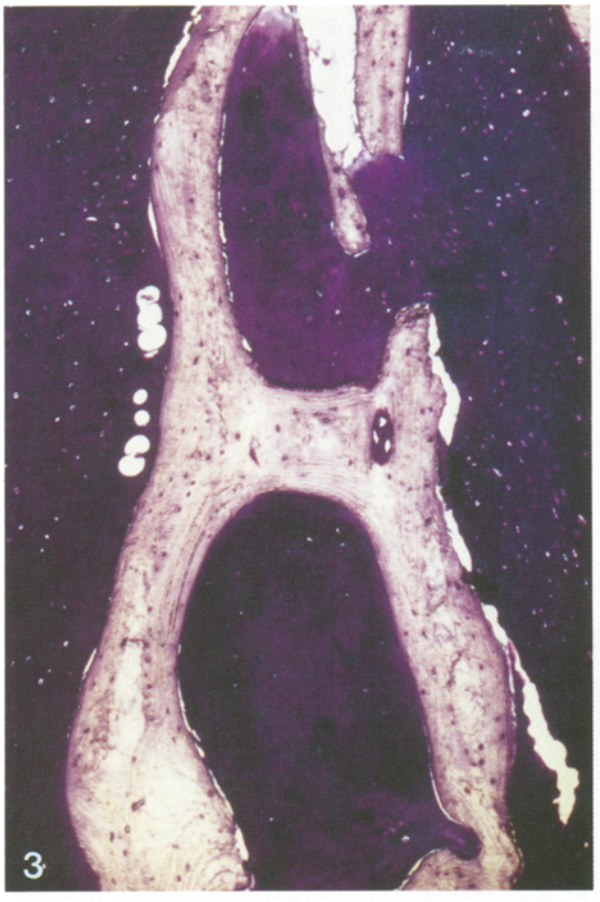
Macroscopically the gross appearance is in accordance with the features of classical chondrosarcoma. However, in many cases an expanded destruction of the cortex with distinct extraosseous tumour mass is present (Fig. 8). Grey tumour areas were variably separated from the cartilaginous tumour tissue. These lesions may

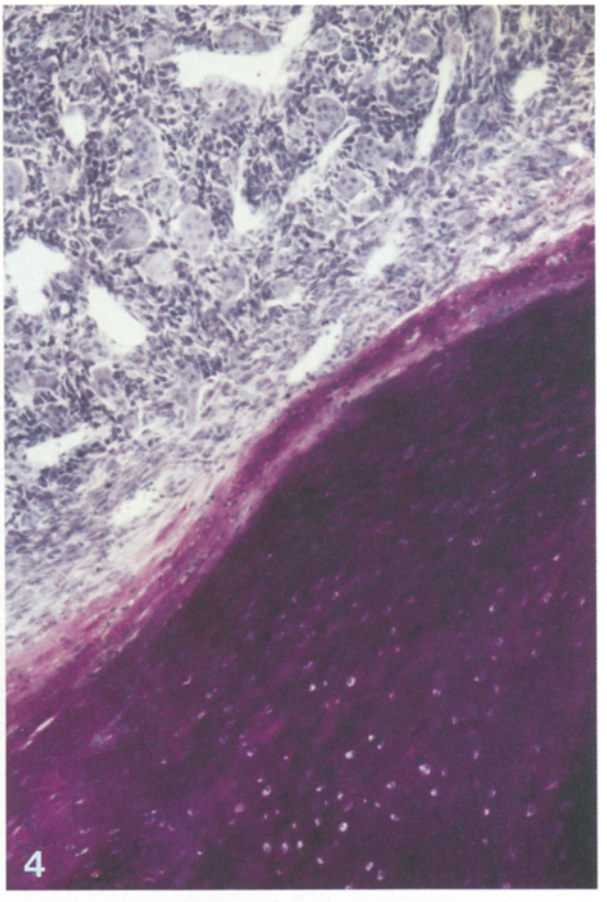
Fig. 3. Classical chondrosarcoma grade 1. Permeation of marrow spaces by cartilaginous tumour mass with invasion and embedding of trabecular bone. Toluidine blue ×63

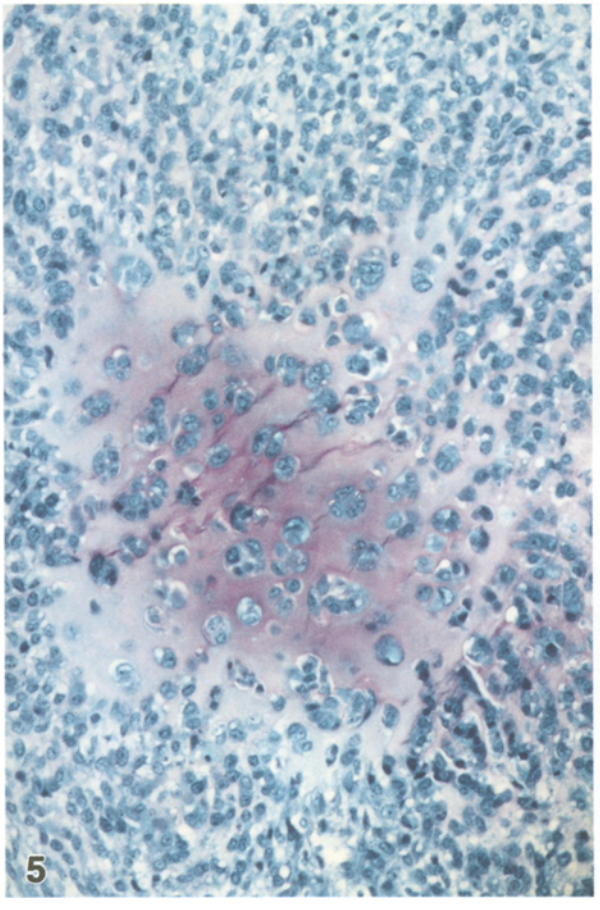
Fig. 4. Dedifferentiated chondrosarcoma with side-by-side association of cartilaginous tissue and undifferentiated areas with multinucleated giant cells. Toluidine blue ×63

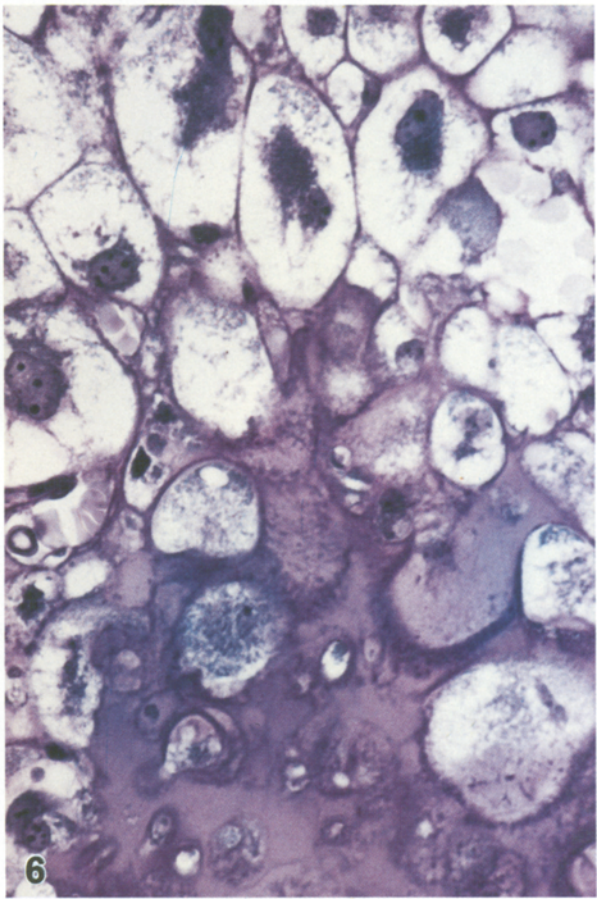
Fig. 5. Mesenchymal chondrosarcoma. Concentric infiltration of cartilage island by small, round tumour cells with high cellularity. Toluidine blue ×160

Fig. 6. Clear-cell chondrosarcoma. Besides closely packed, glycogen-rich large tumour cells with distinct boundaries a cartilaginous tumour area can be distinguished. Note the confluence of these two areas. Toluidine blue ×250


3


4


5


6

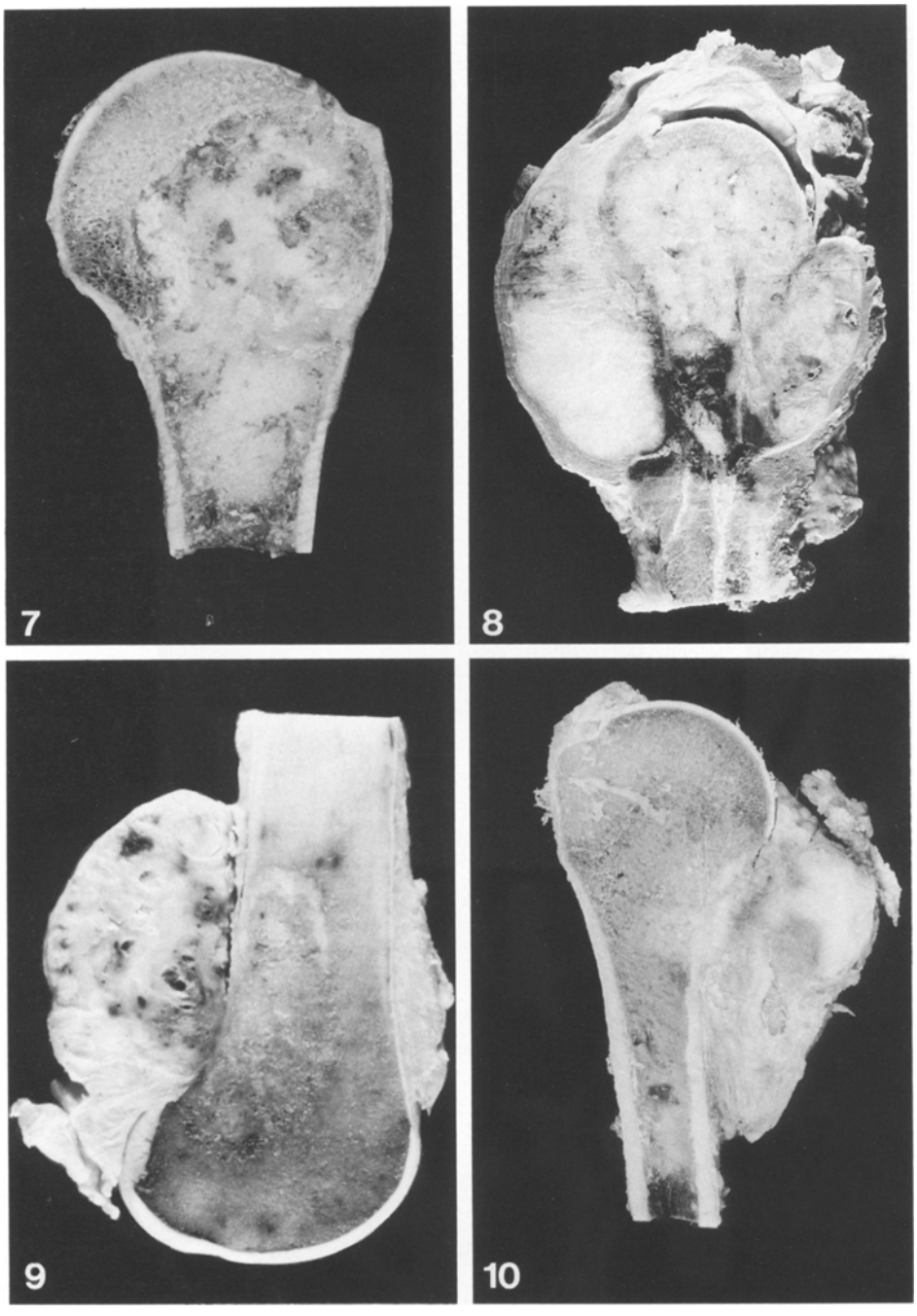


Fig. 7. Gross specimen showing classical chondrosarcoma of proximal humerus after en bloc resection. The tumour is lobulated and shows medullary expansion with rather sharply defined margins. On the right the cortex is very thin. The left tumour margin shows calification and necrosis

Fig. 8. Cut surface of dedifferentiated chondrosarcoma located in the proximal humerus after amputation. The gross specimen reveals infiltration of marrow spaces by cartilaginous tumour with extended cortical destruction and a large extraosseous tumour mass. The upper part of the tumour is haemorrhagic and necrotic with a pathological fracture. Dedifferentiated tumour areas cannot be distinguished from cartilaginous tumour mass

Fig. 9. Mesenchymal chondrosarcoma of the distal femur. The gross specimen after amputation shows fine lobulated tumour infiltrations with a large extraosseous tumour mass. The tumour shows calcification in varying patterns as well as necrotic foci

Fig. 10. Cut surface of periosteal chondrosarcoma after en bloc resection, showing a lobulated cartilaginous tumour. The cortex is infiltrated secondarily. Histologically, invasion of marrow spaces is lacking

have a soft consistency and represent the dedifferentiated component.

Microscopically the tumour contains two components. Cartilaginous areas and zones of osteosarcoma, fibrosarcoma or malignant fibrous histiocytoma component are present in varying amounts (Fig. 4). The zones are sharply delimited from cartilaginous tumour areas which are generally well differentiated. Approximately 50% showed features of osteosarcoma; 30% had dedifferentiated zones of malignant fibrous histiocytoma. The remaining cases showed combined components. In one case a "small cell", plasmacytoid component was present.

Seven of 89 centrally located chondrosarcomas (8%) belong to the group of mesenchymal chondrosarcomas. Five cases occurred in the trunk, mainly in the pelvis. In the present study only one female patient was observed. There is a marked predilection for the second and third decades of life in patients with mesenchymal chondrosarcoma. The median of our patients was 26 years.

Macroscopically, apart from cartilaginous areas with a fine lobulated structure, the tumour contains no obviously cartilaginous areas. On the cut surface the tumour tissue is grey or red-brown and varies in consistency. Foci of calcification are often present (Fig. 9).

Microscopically the mesenchymal chondrosarcoma is characterized by concentric infiltration of cartilage islands by small, round tumour cells with high cellularity (Fig. 5). At the margins of the tumour complexes there is pronounced vascularization. The cartilaginous component is present in varying amounts and in some cases it is almost absent. In other cases cartilaginous tissue predominates.

Clear-cell chondrosarcoma is a rare entity. Our study includes only two cases. Nearly 60% of the clear-cell chondrosarcomas which have been reported in the literature were located in the proximal femur. Typically these lesions arise in the epiphyses of long bones. The second common location was the upper end of the humerus. Clear-cell chondrosarcomas of the trunk are unusual.

Macroscopically, in contrast to the chondrosarcomas described above, typical cartilaginous structures are lacking in most cases. In our own case the material obtained by curettage was red-brown and had a soft consistency. Cystic areas are typical.

Microscopically clear-cell chondrosarcoma is characterized by regions of chondroid tumour in varying amounts and areas of closely packed, glycogen-rich large tumour cells with distinct boundaries. Osteoid or bone formation and multinucleated giant cells are present in clear-cell areas, which may give the impression of being an osteoblastic bone tumour (Fig. 6).

In this series five periosteal chondrosarcomas have been investigated. The ages of the patients ranged from 21 to 55 years. With the exception of one case the tumours were all located in the trunk (pelvis, ribs). One lesion occurred in the proximal ulna.

Macroscopically periosteal chondrosarcomas develop within or under the periosteum. The tumour shows expansive growth or infiltrates soft tissue with secondary destruction of the cortex. Periosteal chondrosarcomas show a less lobulated structure. The tumour is white-grey with cystic areas and necrotic foci centrally (Fig. 10). Focal calcification of varying size and structure is abundant. The tumour has a firm elastic consistency.

Histologically periosteal chondrosarcomas cannot be distinguished from classical centrally located chondrosarcomas. Periosteal chondrosarcomas show a sub- or intraperiosteal expansion. In particular cases with progressive growth infiltration of the cortex can be observed. Three cases were considered to be grade 1 lesions; the remaining cases were grade 2.

Discussion

Nearly 60% of centrally located chondrosarcomas are classical chondrosarcomas. In addition, three types of central chondrosarcomas (dedifferentiated, mesenchymal and clear-cell chondrosarcomas) can be separated by their different cellular composition and production of matrix. In this study, more than 30% were special types; periosteal chondrosarcoma must be considered as a completely different group (5%). The different types of chondrosarcomas show distinctive morphological characteristics as well as notable differences in location, age distribution and male to female ratio. The distinction between different types is crucial for clinical behaviour and prognosis, and must be considered in the planning of therapy.

More than 50% of classical chondrosarcomas were located in the trunk; half of these cases occurred in the pelvis. These findings are in agreement with the observations of others (Evans et al. 1977; Kristensen et al. 1986). In contrast, 80% of the dedifferentiated chondrosarcomas and the clear-cell chondrosarcomas occur in the long bones of the limbs (Bjornsson et al. 1984; Capanna et al. 1988; Mac Carthy and Dorfman 1982; Weiss et al. 1988). In this location most of the tumours arise in the upper end of femur and humerus. In contrast to our results, more tumours were located in the trunk (57%) in other studies. Only 43% of the lesions were found in the long bones by Dahlin (1978). The most common location of mesenchymal chondrosarcomas is the trunk, especially the ribs. A large number of tumours located in the skull have been reported in the literature (Nakashima et al. 1986; Salvador et al. 1971) but a predominance of these lesions in long bones was observed by Huvos et al. (1983). None of the cases in the present study arose extraskeletally, whereas in other reports 30–34% were so located (Nakashima et al. 1986; Salvador et al. 1971). In comparison with the other types of chondrosarcoma clear-cell lesions show the most distinct predilection for a specific location. One hundred cases of clear-cell chondrosarcoma have been reported in the literature and almost 60% were situated in the proximal femur (Welkerling et al. 1990).

In agreement with other reports the mean age of patients with classical chondrosarcomas was 54 years (Rosenthal et al. 1984). Most of other studies noted, as we have, a predominance of patients in the fifth and sixth decades of life. Dedifferentiated chondrosarcomas occur nearly 10 years later than classical chondrosarcomas. We can confirm that the patients, with the exception of particular cases, were more than 50 years old (Mac Carthy and Dorfman 1982). This observation must be taken into account in the differential diagnosis of osteosarcoma. In contrast, mesenchymal chondrosarcomas have been observed in younger patients. The median of our patients was 26 years. The mean age of the patients documented in the literature ranges from 23 to 26 years (Harwood et al. 1981; Huvos et al. 1983; Salvador et al. 1971). Most patients were observed in the second and third decades of life (Pavon et al. 1971; Salvador et al. 1971; Steiner et al. 1973). Osteosarcomas show a similar age distribution. Therefore the preparation of complete tumour is an important aid in the differential diagnosis. There is a marked predilection of patients with clear-cell chondrosarcoma for the third and fourth decades. In comparison with classical chondrosarcomas clear-cell chondrosarcomas occur 10 years earlier (Bjornsson et al. 1984; Weiss and Dorfman 1988; Yamaguchi et al. 1986).

Classical chondrosarcoma has a significant predominance of male patients. Pritchard et al. (1980) noted, as we did, a male to female ratio of 3:2. In other studies the ratio was 2:1 (Evans et al. 1977; Kristensen et al.

1986; Rosenthal et al. 1984), whereas a sex predilection for dedifferentiated chondrosarcoma was not found (Capanna et al. 1988; Dahlin 1978; Dahlin and Beabout 1971; Mac Carthy and Dorfman 1982). With the exception of one case, all of our patients with mesenchymal chondrosarcomas were males (6/1). Extended studies have not confirmed our results. A sex predilection was not found to be present in other reports (Harwood et al. 1981; Nakashima et al. 1986; Salvador et al. 1971). Clear-cell chondrosarcomas show a significant predominance of males (2.7:1) (Weiss and Dorfman 1988).

Histological examination is crucial for correct diagnosis and typing of chondrosarcomas and has considerable influence for differential diagnosis of other lesions. The distinction between centrally located well-differentiated classical chondrosarcomas and enchondromas can be very difficult. Apart from the characteristic growth pattern (Freyschmidt and Ostertag 1988; Mirra et al. 1985) DNA measurements make it possible to differentiate chondrosarcomas and enchondromas (Dreyer and Delling 1989) and well-differentiated periosteal chondrosarcomas.

Several authors use the term juxtacortical chondrosarcoma instead of periosteal chondrosarcoma (Freyschmidt and Ostertag 1988; Nojima et al. 1985) for tumours which arise on the surface of the bone. We have observed a consistent sub- and intraperiosteal expansion in periosteal chondrosarcoma.

With regard to the therapy (chemotherapy), it is crucial to distinguish dedifferentiated chondrosarcomas from osteosarcomas, malignant fibrous histiocytomas or fibrosarcomas. The differential diagnosis of mesenchymal chondrosarcomas is mainly with Ewing's sarcoma, haemangiopericytoma or chondroblastic osteosarcoma (Dabska and Huvos 1983; Dahlin 1978; Goldmann 1967; Huvos et al. 1983; Nakashima et al. 1986; Salvador et al. 1971). If the biopsy only contains the cartilaginous component, the distinction between dedifferentiated and well-differentiated chondrosarcomas is not possible without inspecting the radiograph. In the diagnosis of bone tumours interdisciplinary co-operation between the orthopaedic surgeon, the radiologist and the pathologist is of great importance. In dedifferentiated chondrosarcomas a tendency for the production of a specific component is not seen. Half of our cases had dedifferentiated zones of osteosarcoma. In other studies 78% of the cases have shown features of malignant fibrous histiocytoma ($n=18$) as well as features of fibrosarcoma (in 66% of 33 cases; Dahlin and Beabout 1971; Mac Carthy and Dorfman 1982).

The mean mortality of classical chondrosarcomas varies with grade, as does that of clear-cell chondrosarcomas, ranging from 15% to 40% (Eriksson et al. 1980; Evans et al. 1977; Kumar et al. 1985; Le Charpentier et al. 1979; Unni et al. 1976; Volpe et al. 1983). The mortality of dedifferentiated chondrosarcomas varied from 72% (Mac Carthy and Dorfman 1982) to 93% (Capanna et al. 1988). The value of chemotherapy has been discussed by Capanna et al. (1988), but results of trials on the outcome of chemotherapy in large groups of patients are lacking. The mortality of mesenchymal chondrosarcoma ranges from 71% (Harwood et al. 1981) to 100% (Dowling 1964). One of our cases, treated by chemotherapy, did not respond. For mesenchymal as well as for dedifferentiated chondrosarcomas the management of choice is early radical surgical treatment (Dahlin and Beabout 1971; Dahlin and Henderson 1962; Harwood et al. 1981). The metastatic potential is very high (Capanna et al. 1988; Dowling 1964; Huvos et al. 1983; Nakashima et al. 1986). In comparison with classical chondrosarcomas the prognosis for mesenchymal and dedifferentiated chondrosarcomas is poor. En bloc resection with wide margins is the treatment of choice for classical and clear-cell chondrosarcomas.

Knowledge of the morphological features of different chondrosarcomas is important for the correct histological diagnosis and typing. It is crucial for adequate surgical therapy and for the prediction of clinical behaviour.

Acknowledgement. This work was supported by the Hamburger Krebsgesellschaft e.V.

References

Bjornsson J, Unni KK, Dahlin DC, Beabout JW, Sim FH (1984) Clear cell chondrosarcoma of bone. Observation in 47 cases. Am J Surg Pathol 18:223–230

Capanna R, Bertoni F, Bettelli G, Picca P, Bacchini P, Present D, Giunti A, Campanacci M (1988) Dedifferentiated chondrosarcoma. J Bone Joint Surg [Am] 70:60–69

Dabska M, Huvos AG (1983) Mesenchymal chondrosarcoma in the young. Virchows Arch [A] 399:89–104

Dahlin DC (1978) Chondrosarcoma. Mesenchymal chondrosarcoma. Bone tumors, 3rd edn. Thomas, Springfield, pp 190–225

Dahlin DC, Beabout JW (1971) Dedifferentation of low grade chondrosarcoma. Cancer 28:461–466

Dahlin DC, Henderson ED (1962) Mesenchymal chondrosarcoma. Cancer 15:410–417

Dowling EA (1964) Mesenchymal chondrosarcoma. J Bone Joint Surg [Am] 46:747–754

Dreyer T, Delling G (1989) Fortschritte in der Knochentumordiagnostik bei Anwendung eines vollautomatischen Programms zur DNA-Analyse. Ber Pathol 108:488

Eriksson AI, Schiller A, Mankin HJ (1980) The management of chondrosarcoma of bone. Clin Orthop 153:44–66

Evans HL, Ayala AG, Romsdahl MM (1977) Prognostic factors in chondrosarcoma of bone. Cancer 40:818–831

Freyschmidt J, Ostertag H (1988) Knorpelbildende Tumoren. Chondrosarkom. Knochentumoren. Springer, Berlin Heidelberg New York, pp 321–365

Goldmann RL (1967) Mesenchymal chondrosarcoma, a rare malignant chondroid tumour usually primary in bone. Cancer 20:1494–1498

Harwood AR, Krajbich JJ, Fornasier VL (1981) Mesenchymal chondrosarcoma: a report of 17 cases. Clin Orthop Relat Res 158:144–148

Huvos AG, Rosen G, Dabska M, Marcove RG (1983) Mesenchymal chondrosarcoma. A clinicopathologic analysis of 35 patients with emphasis on treatment. Cancer 51:1230–1237

Kristensen IB, Sunde LM, Jensen OM (1986) Chondrosarcoma. Acta Pathol Microbiol Immunol Scand [A] 94:73–77

Kumar R, David R, Cierney G (1985) Clear cell chondrosarcoma. Radiology 154:45–48

Le Charpentier Y, Forest M, Postel M, Tomeno B, Abelanet R (1979) Clear-cell chondrosarcoma: a report of five cases including ultrastructural study. Cancer 44:622–629

Mac Carthy EF, Dorfman HD (1982) Chondrosarcoma of bone

with dedifferentiation: a study of eighteen cases. Hum Pathol 13:36–40
Mirra JM, Gold R, Downs J, Eckardt JJ (1985) A new histological approach to the differentiation of enchondroma and chondrosarcoma of the bones. Clin Orthop Relat Res 201:214–237
Nakashima Y, Inni KK, Shives TC, Swee RG, Dahlin DC (1986) Mesenchymal chondrosarcoma of bone and soft tissue. A review of 111 cases. Cancer 57:2444–2453
Nojima T, Unni KK, Mc Leod RA, Pritchard DJ (1985) Periosteal chondroma and periostal chondrosarcoma. Am J Surg Pathol 9:666–677
Pavon SJ, Bullough PG, Marcove RC (1971) Mesenchymal chondrosarcoma. NY State J Med 1:1662–1664
Pritchard DJ, Lunke RJ, Taylor WF, Dahlin DC, Medley BE (1980) Chondrosarcoma: a clinicopathologic and statistical analysis. Cancer 45:149–157
Rosenthal DJ, Schiller AL, Mankin HJ (1984) Chondrosarcoma: correlation of radiological and histological grade. Radiology 150:21–26
Salvador AH, Beabout JW, Dahlin DC (1971) Mesenchymal chondrosarcoma. Observations on 30 new cases. Cancer 28:605–615
Steiner GC, Mirra JM, Bullough PG (1973) Mesenchymal chondrosarcoma. Cancer 32:926–939
Unni KK, Dahlin DC, Beabout JW, Sim FH (1976) Chondrosarcoma: clear-cell variant. J Bone Joint Surg [Am] 58:676–683
Volpe R, Mazabraud A, Thiery JP (1983) Clear cell chondrosarcoma. Report of a new case and review of the literature. Pathologica 75:775–787
Weiss APC, Dorfman HD (1988) Clear-cell chondrosarcoma: a report of ten cases and review of the literature. Surg Pathol 1:123–129
Welkerling H, Dreyer T, Delling G (1989) Morphologie des Chondrosarkoms – eine retrospektive Studie zum histologischen Grading, der Lokalisation, Alters- und Geschlechtsverteilung. Verh Dtsch Ges Pathol 71:633
Welkerling H, Dreyer T, Delling G (1990) Das Klarzellchondrosarkom – klinisch-pathologischer Bericht eines weiteren Falles. Z Orthop 128:657–660
Yamaguchi H, Isu K, Ubayama Y, Yamawaki S, Gotoh M, Miyagawa A, Minami A, Matsuno T, Sasaki T, Nojima T (1986) Clear cell chondrosarcoma. A report of two cases and review of literature. Acta Pathol Jpn 36:1577–1585