Virchows Archiv (1995) 426:235–242

ORIGINAL ARTICLE

Michael Amling · Mathias Werner · Martin Pösl
Rainer Maas · Ulrich Korn · Günter Delling

Calcifying solitary bone cyst: morphological aspects and differential diagnosis of sclerotic bone tumours

Received: 21 November 1994 / Accepted: 22 December 1994

Abstract Fourteen solitary bone cysts (SBC) with large areas of calcification (7 in the femur, 4 in the humerus, and 1 each in the pelvis, the tibia and the scapula) and 402 SBC from the Hamburg Bone Tumour Registry were reviewed in a retrospective study. The analysis was done with emphasis on the clinical, radiological and histological appearances. SBC are well known lesions, but calcifying SBC (CSBC) or extensive extragnathic cement-like bone productions are rare. The clinical and radiological differential diagnosis includes fibrous dysplasia, chondroma, low-grade chondrosarcoma and osteosarcoma. Bits of this cement-like matrix are detectable within the wall of approximately 70% (278 of 402) of SBC from the registry. CSBC are changed SBC. The intraoperative confirmation of the diagnosis on a frozen section by the bone pathologist leads to curettage which is currently the most common therapy in this benign lesion.

Key words Calcifying solitary bone cyst · Bone tumour · Cementoma

Introduction

In addition to the 12 previously reported cases of extragnathic cementomas [1, 6, 8, 11, 21], 14 calcifying solitary bone cysts (CSBC) from the Hamburg Bone Tumour Registry were reviewed in a retrospective study (Table 1). These 14 cases consist of 7 cases in the femur, 4 cases in the humerus, 1 case in the tibia, and the first published cases in the pelvis and in the scapula.

M. Amling · M. Werner · M. Pösl · G. Delling (✉)
Department of Bone Pathology, University Hospital of Hamburg, Martinistrasse 52, D-20246 Hamburg, Germany

R. Maas
Department of Radiology, University Hospital of Hamburg, Martinistrasse 52, D-20246 Hamburg, Germany

U. Korn
Department of Orthopaedics, University Hospital of Hamburg, Martinistrasse 52, D-20246 Hamburg, Germany

In 1969 Friedman and Goldman [6] studied two cementomas of long bones and described these as a new tumour entity. In 1978 Mirra et al. [11] suggested their own three cases to be an uncommon form of a SBC, with cementum-like material. In 1982 Horn et al. [8] attempted to disproved this; they considered their own two cases to be cementoma-like bone fibromas and a true tumour entity.

There is no unique histological classification and the differentiation of CSBC from malignant bone tumours is of great importance for clinical treatment. The aim of this study is to show, on the background of 402 SBC of the Hamburg Bone Tumour Registry, why we concur with Mirra and consider cementomas to be changed SBC and why we prefer the term CSBC. The consequences for diagnosis and treatment will be discussed.

Materials and methods

Fourteen cases of CSBC were reviewed in a retrospective study. The histological characteristics were compared with the radiological findings. The patients were comprised 3 women and 11 men, aged between 7 and 57 years (diagnosis was confirmed at an average age of 37 years). Diagnosis of 11 cases was obtained from consultatory work of the Bone Tumour Registry and 3 cases from material of the University Hospital Hamburg-Eppendorf. These cases were compared with the 402 histologically proven SBC (162 women, 240 men; aged between 2 and 77 years, average age 26 years) from the Hamburg Bone Tumour Registry. The histological characterization was done on undecalcified material, embedded in methylmethacrylate, as well as conventional decalcified material embedded in paraffin. Histological evaluation was made with standard stainings (von Kossa, Goldner, Giemsa, toluidin blue, Movat, Berlin blue reaction). Immunohistological evaluation was performed on paraffin embedded material with the alkaline phosphatase-antialkaline phosphatase-technique according to Cordell et al. [5]. Histological and radiographical findings were compiled for each patient by each participant and were forwarded to one of us (G.D.) for compilation and analysis.

Table 1 Localization and distribution of the reported "extragnathic cementomas"

	Authors					
	Friedman et al. [6]	Mirra et al. [11]	Stelling et al. [21]	Horn et al. [8]	Adler [1]	Amling et al. (this study)
Number of cases	2	3	1	2	4	14
Femur	1	3	–	–	4	7
Humerus	1	–	1	–	–	4
Pelvis	–	–	–	–	–	1
Scapula	–	–	–	–	–	1
Tibia	–	–	–	1	–	1
Metacarpals	–	–	–	1	–	–

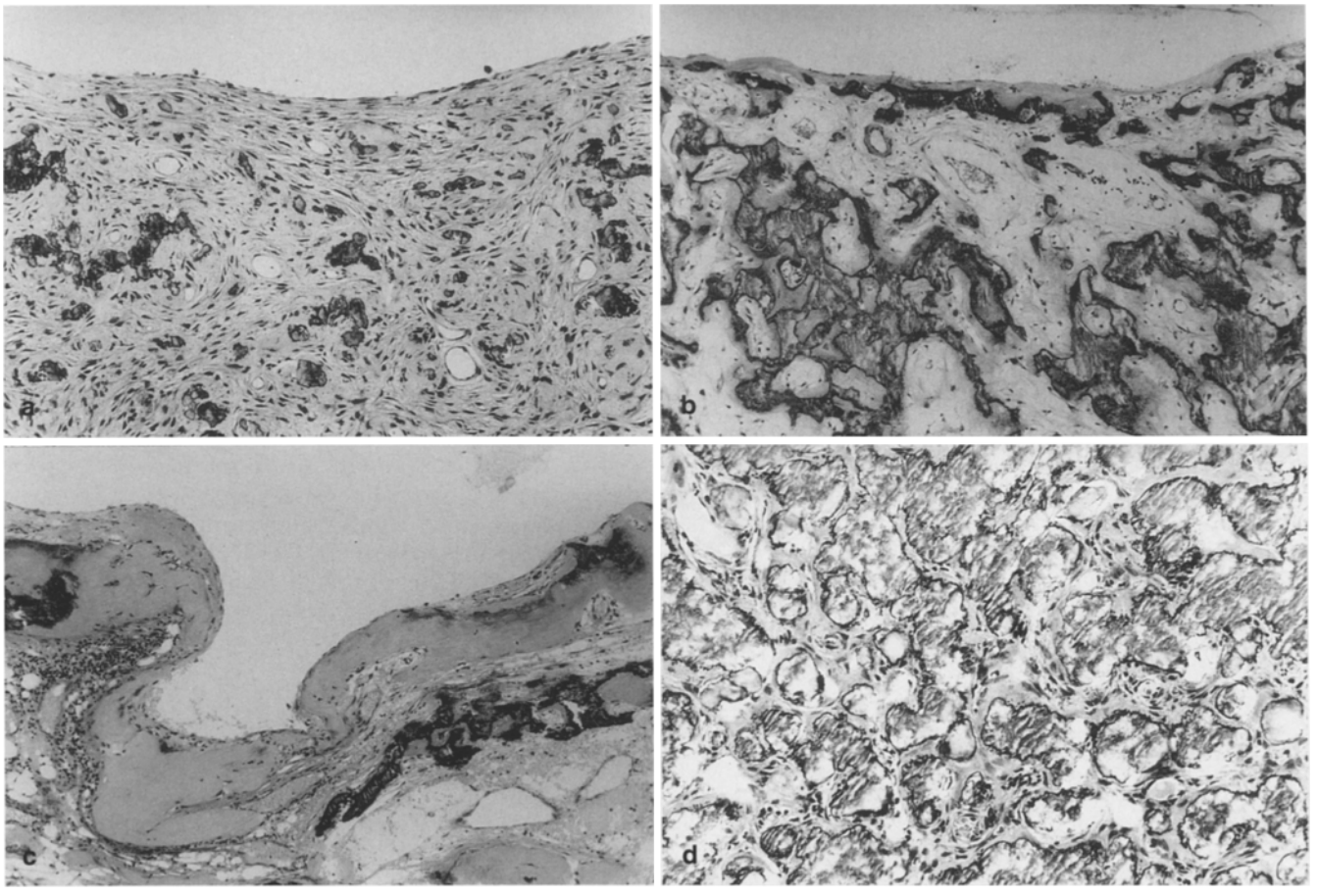

Fig. 1a–d Histology of calcifying solitary bone cysts. The wall, indistinguishable from that of a solitary bone cyst, is lined by a layer of flattened or plumper cells. The wall contains two major components of tissue: areas of loose fibrous tissue, with well-differentiated fibrocytes and fibroblasts, containing primarily vascular structures and also dense hypocellular matrix with large areas of mineralization, resembling odontogenic cementum. **a** Bits of cementum-like material in a highly cellular fibrous tissue area of the wall, which is lined by flattened cells. Case number 8 (93/3574) compare to the X-rays in Figures 3 and 4. (Undecalcified preparation, toluidin blue stain, magnification ×175). **b** Irregularly mineralized material in a hypocellular fibrous tissue area of the wall. Case number 8 (93/3574); compare to the X-rays in Figures 3 and 4. (Undecalcified preparation, toluidin blue stain, magnification ×85). **c** The wall contains a densely-structured, homogeneous and hypocellular osteoid-like matrix with areas of mineralization. Case number 9 (93/4099); compare to the X-ray in Figure 5. (Undecalcified preparation, von Kossa stain, magnification ×85). **d** Sclerotic, cement-like material from the centre representing most parts of the lesion. Case number 9 (93/4099); compare to the X-ray in Figure 5. (Undecalcified preparation, toluidin blue stain, magnification ×175)

Results

Histologic features

The morphology of SBC consists of a thin fibrous membrane lined by a layer of flattened to slightly plumper cells, which show moderate expression for vimentin in immunohistochemistry. Sometimes the cyst is divided by septa into two or more compartments. Components of the membrane half-moon formed lumps of osteoid, as well as some osteoclast-like giant cells, and some haemosiderin may be found. In approximately 70% (278 of 402 cases) of SBC, localized small areas of a hypocellular, cementum-like substance within the membrane can be detected.

Histological examination of CSBC shows a cyst wall lined by a layer of flattened to enlarged cells. These walls may contain loose fibrous tissue, with well differ-

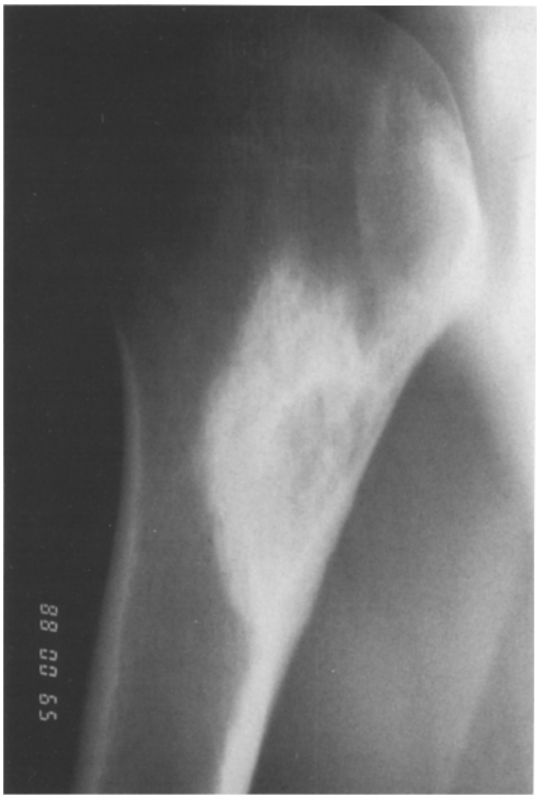

Fig. 2 The calcifying solitary bone cyst within the upper humerus of a 40-year-old male is almost completely filled by the mineralized component as demonstrated on the conventional tomography. (Case number 10)

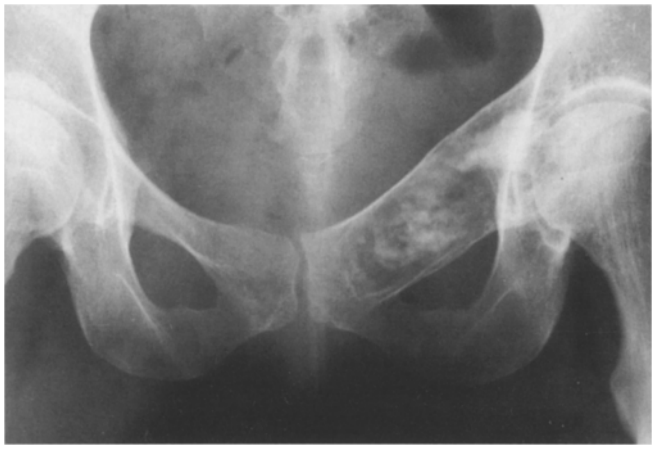

Fig. 3 X-ray of the pelvis of a 39-year-old female, demonstrating enlargement of the left superior pubic ramus. The cortex does not seem to be affected and there is no periosteal reaction visible. The spongiosa is replaced by calcified areas which are cloud-shaped in the middle and of homogeneous density towards the acetabulum. The histology of this case is also seen in Figure 1a and b. (Case number 8)

entiated fibrocytes and fibroblasts, numerous giant cells and a hyaline substance, which may be identified as osteoid. The second component of the tissue consists of a densely-structured, homogeneous, and hypocellular matrix with large areas of mineralization. Although Sharpey's fibres were absent, this material otherwise resembles odontogenic cementum. Within this cement-like substance isolated areas of fibrous tissue which contained capillaries with well differentiated endothelium may be seen (Fig. 1a–d).

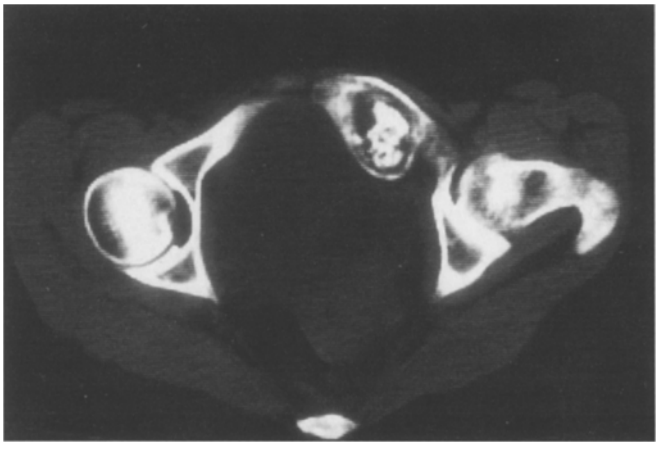

Fig. 4 Computed tomography at the level of the hip joints, showing in an axial view of the tumour in the left os pubis without superimposed structures. There is no soft tissue component detectable and the dense areas in the centre are surrounded by a zone of boneless material. Note the histology of this case in Figure 1a and b. (Case number 8)

In CSBS the cyst may be almost completely filled by the mineralized component. After curettage in these cases it may be difficult for the pathologist to identify a fibrous membrane at all. DNA-cytophotometry shows a DNA-diploid distribution in CSBC as well as in SBC.

Radiologic features

There is a wide range of radiographic findings in CSBC. The tumours occur as cystic, sclerotic lesions within the metaphysis. However, in some cases the cystic part may be undetectable due to extensive calcification (Fig. 2). Widening and deformation of the affected bone may be seen. Furthermore scalloping and extreme thinning of the cortex is also possible (Figs. 3, 4, 5). According to Lodwick lesions are classified as type 1b. Within the cysts appears a garland, cloudy, dense substance, reminiscent of the popcorn like pattern of enchondroma. In case 2 the conversion from a SBC to a CSBC within a few weeks, is impressively documented by a radiographic follow up over 1 year (Fig. 6a–c).

Computed tomography shows that the primary structure of cancellous bone is not detectable within these lesions. But an irregularly defined, mostly central calcification with often centripedal lighter zones is seen. After application of gadallinium-diethylenetriamine pentaacetic acid, magnetic resonance imaging may show slight enhancement in the peripheral zone structures. There is never a soft tissue component, joint involvement, nor indication of lymph node swelling.

Radiographic features and clinical appearances of the reviewed cases of calcifying solitary bone cysts are illustrated in Table 2.

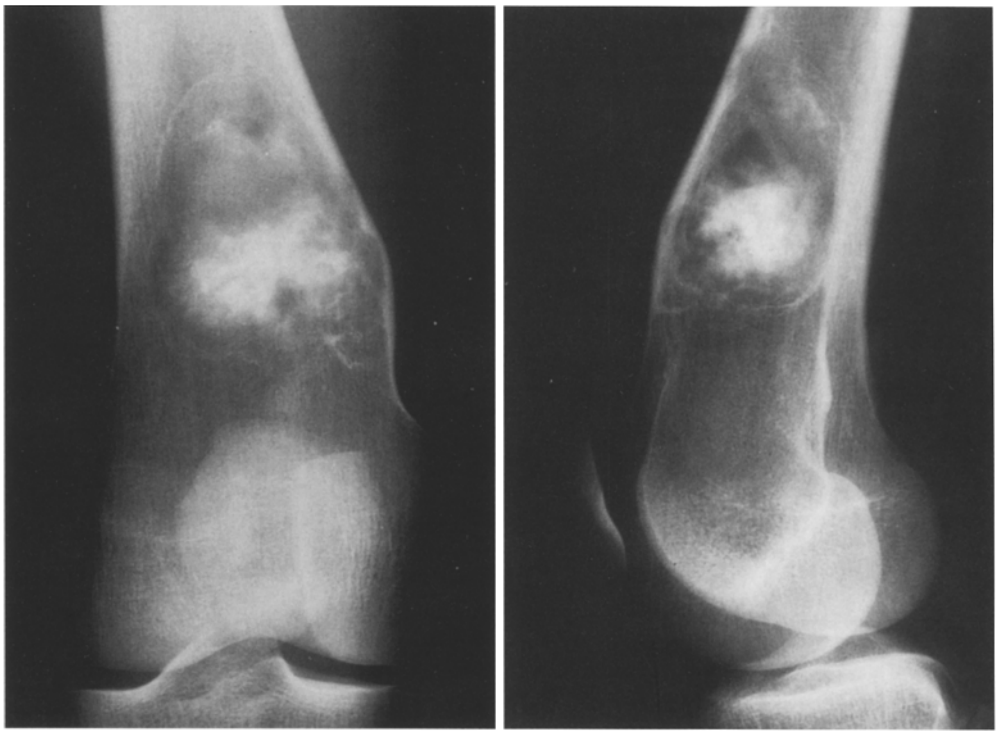

Fig. 5 X-ray of the distal femur of a 39-year-old male, demonstrating scalloping, thinning of the cortex, deformity and a 8×6×4 cm cystic lesion with sclerotic borders. The cloudy, dense material within the lesion leads to the clinical differential diagnosis of a giant cell tumour or fibrous dysplasia. Note the histology of this case in Figure 1c, d. (Case number 9)

Discussion

Bits of calcification are often seen in SBC and its recognition is thus helpful in the histological diagnosis. But CSBC and extensive extragnatic cementum-like bone production are rare and may lead to problems with differential [16]. Only 26 cases, including the 14 cases reported in this study, are documented in the literature. The lesion affects patients from the first to the sixth decade of life. In our cases the diagnosis of a CSBC was confirmed at an average age of 33 years, in contrast to the average age of 26 in SBC. The later manifestation of CSBC in comparison to the typical SBC is also documented in the literature [2, 3, 4, 7, 13, 14, 20]. This concurs with the conception that CSBC represents a changed SBC. The reported cases consist of 15 cases in the femur, 6 cases in the humerus, 2 cases in the tibia, and 1 case each in the scapula, pelvis, and the metacarpal bones in the hand. All CSBC of the long bones have occurred in the metaphysis. Thus, CSBC shows a skeletal distribution familiar to SBC. One half of the cases (7 of 14 in our group) were associated with symptoms such as swelling, deformation and pathological fracture, the other cases occurred as casual X-ray events.

The radiographic features of CSBC show a wide range, they are thus not solely pathognomonic. Fibrous dysplasia is known to have cementum-like ossicles. It is especially difficult to mark off CSBC against a chondroma, a chondrosarcoma or an osteosarcoma. The mineralized component of the CSBC could be misinterpreted as the confluing, popcorn-like pattern in chondromas. Widening of the affected bone, as well as thinning of the cortex and scalloping, can be found in all three entities. In contrast to malignancy a soft tissue component was observed in none of the cases.

Histological examination showed a cyst wall lined by a layer of flattened or enlarged cells. These walls may contain loose fibrous tissue, with well differentiated fibrocytes and fibroblasts, numerous giant cells and a hyaline substance, which may be identified as osteoid. The second component of the tissue consists of a densely-structured, homogeneous and hypocellular matrix, with large areas of mineralization. Although Sharpey's fibres were absent, this material otherwise resembled odontogenic cementum. However, in contrast to the cement of the tooth some osteocytes are detectable within the mineralized substance of CSBC. Within this cementum-like substance isolated areas of fibrous tissue could be seen which contained capillaries with well differentiated endothelium. A similar pattern of this basic substance may be found in some osteosarcomas.

In 1942 Jaffe and Lichtenstein [9], reported 19 cases of SBC, and mentioned that calcification within the cyst walls was observed frequently. They considered this substance to be calcifying fibrin and blood clot. In 1969 Friedman and Goldman [6] studied two cystic lesions of long bones in young boys which revealed extensive formation of calcified corpuscles resembling cementicles. They named these metaphyseal cysts "cementomas", taking them to be the result of extragnathic odontogenic differentiation. In 1978 electron microscopic studies of one of his own three cases prompted Mirra [10, 11] to suggest that the cementoma of the long bone is not a distinct entity, but a form of SBC associated with a peculiar, hypocellular form of bone which mimics tooth cementum. His main argument against an independent entity is the

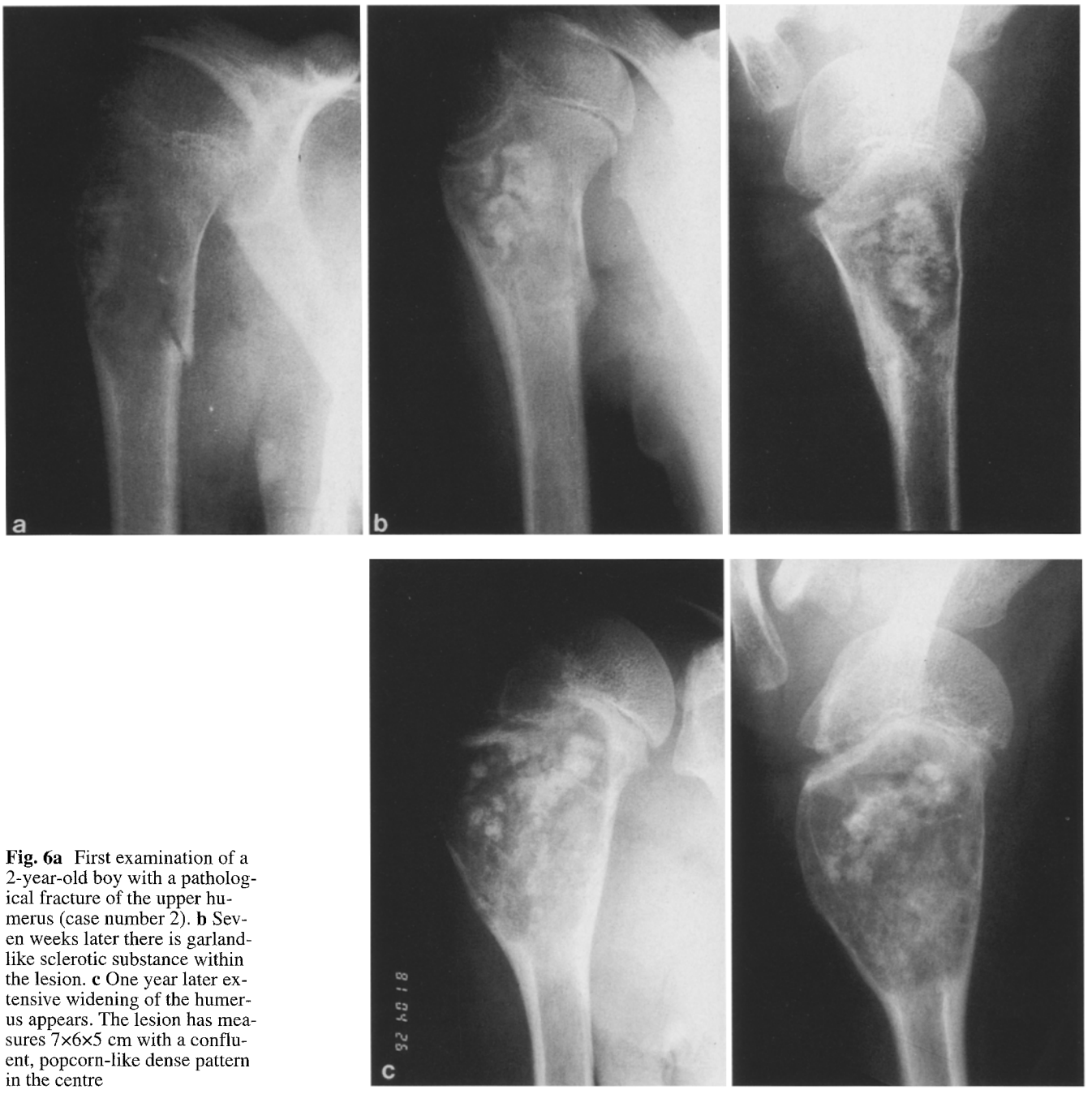

Fig. 6a First examination of a 2-year-old boy with a pathological fracture of the upper humerus (case number 2). **b** Seven weeks later there is garland-like sclerotic substance within the lesion. **c** One year later extensive widening of the humerus appears. The lesion has measures 7×6×5 cm with a confluent, popcorn-like dense pattern in the centre

observation of matrix vesicles which are a product of osteoblastic activity and are never found in odontogenic tumours of the jaw. These vesicles are the initial calcification loci, well known from calcified cartilage, woven bone and mantle dentin. One year later in 1979 Sanerkin [18] suggested that in SBC calcified fibrin coagula provide a scaffold on which osteoid followed by new bone is laid down. But in 1982 Horn and his colleagues [8] took a step back and considered extragnathic cementomas as a true tumour entity.

Much of the confusion that exists in the literature on the origin of so called extragnathic cementomas is due to the fact that the term cementoma has been used for two distinct lesions; the cement-like substance within the wall of SBC as first described by Jaffe [9] and for those rare examples of fibrous-osseous tumours which contain often extensive foci of cementicles within the fibrous stroma. These lesions have usually been described in the tibia, and the first recognized cases were written up by Sissons [19].

The origin of CSBC from a typical SBC is consistent with the histological findings. This is also confirmed by the radiographic long term follow up, as documented for case 2, with the final histological analysis. The SBC, which occurred in a pathological fracture, clearly show internal calcifications after 7 weeks. Thus, it is documented that a conversion of SBC into CSBC is possible within a few weeks. Furthermore, it is possible that mi-

Table 2 Calcifying solitary bone cysts of the Hamburg Bone Tumour Registry (*CT* computed tomography, *MRI* magnetic resonance image, *Gd-DTPA* gadallidium – diethylenetuamine pentaacetic acid)

Case	Identity number	Age	Sex	Site	Clinical	X-ray	Clinical differential diagnosis
1	81/2154	7	male	Proximal femur	Fracture, no history of pain, No recurrence	Pathologic fracture through a 3.5×3-cm cystic lesion with sclerosis	1. Enchondroma 2. Solitary bone cyst 3. Osteosarcoma
2	81/0426	12	Male	Proximal humerus	Fracture, no history of pain, no recurrence	First examination: pathologic of fracture through a 4×3×3 cm cystic lesion. Seven weeks later: scalloping, sclerotic tissue within the lesion. One year later: extensive widening to a 7×6×5 cm cystic lesion with a confluent, popcorn like, dense structure	1. Osteosarcoma 2. Enchondroma 3. Chondrosarcoma
3	94/1408	14	Male	Proximal humerus	Fracture, no prior history of pain	Pathological fracture through a 6.5×3.5 cm cystic lesion with regions of internal calcification, widening of the upper humerus, scalloping and extremely thinned cortex	1. Aneurysmal bone cyst 2. Solitary bone cyst
4	87/1969 87/2036 88/1867 89/2656	15	Male	Proximal humerus	No fracture, history of pain, two recurrences in the following 2 years.	6×5.5 cm lesion with a 5.5×4 cm sclerotic area and a 5×2 cm cystic part. The cortex was extremely thinned in the cystic area No recurrence for 4 years	1. Enchondroma 2. Giant cell tumour 3. Osteosarcoma
5	93/2239 93/1829	22	Female	Proximal femur	No fracture, no history of pain	6×4 cm lesion of different density with a sclerotic proximal border	Unknown malignancy
6	91/1647	25	Male	Proximal femur	No fracture, pain in the upper left leg for 3 months	9×5 cm tumour, mostly sclerotic, with some up to 1.5 cm lytic areas between metaphysis and diaphysis, with a medial widening, thinning of the cortex. Lodwick 1b	1. Osteosarcoma 2. Osteomyelitis 3. Ewing sarcoma
7	94/0747	33	Male	Proximal femur	No fracture, no pain	4×3 cm sharply limited, oval, dense lesion	1. Osteoblastoma
8	92/3574	39	Female	Os pubis	No fracture,	4×4×9 cm cystic lesion with dense	1. Enchondroma

Table 2 continued

Case	Identity number	Age	Sex	Site	Clinical	X-ray	Clinical differential diagnosis
					1.5 year history of pain in the left the left inguinal region, limited hip movement	regions of calcification, widening of superior pubic ramus. CT: irregularly defined central calcification with centripedal lighter zones. MRI: no soft tissue component, after application of Gd-DTPA there was slight enhancement in the peripheral zone structures	2. Chondrosarcoma
9	93/3583 93/4099	39	Male	Distal femur	No fracture, no history of pain	8×6×4 cm cystic lesion with sclerotic borders, scalloping, widening of the distal femur; within this lesion a dense structure. This was macroscopically 53 g of solid material with a size of 7×6×3 cm	1 Giant cell tumour 2. Fibrous dysplasia
10	88/0065	40	Male	Proximal humerus	No fracture, no history of pain	5×3 cm sclerotic, dense lesion, with some lytic areas on CT Scintigraphically cool lesion	1. Chondroblastoma 2. Enchondroma
11	77/0762	50	Male	Proximal tibia	No fracture, no history of pain	5×4 cm cystic lesion with a sclerotic border, thinning of the cortex, scalloping, widening of the upper tibia, Lodwick 1b, with dense structure within the lesion	1. Giant cell tumour
12	93/2337	52	Male	Distal femur	No fracture, incidental finding at X-ray examination of a meniscopathy	Intercondylar 5×4.5 cm mixed cystic lesion with blurred, fragmented dense material within the lesion. Lodwick 1b	Unknown malignancy
13	93/4622	55	Male	Scapula	No fracture, no history of pain	Oval 4×2×2 cm cystic lesion within the spina of the scapula. CT shows a dense matrix within the lesion and the thinning of the cortex. Lodwick 1b. Scintigraphically a hot lesion.	1. Giant cell tumour 2. Enchondroma 3. Chondrosarcoma
14	78/0910	57	Female	Proximal humerus	No fracture, incidental finding at X-ray of a periarthritis lasting for approximately 10 years	4×3 cm mostly sclerotic, tumour with cystic areas up to 1.5 cm in diameter. Thinning of the cortex. Lodwick 1b	1. Enchondroma 2. Giant cell tumour

crofractures in cases without clinically manifest fractures are the starting point of the changes, leading to CSBC.

The average age at the time of diagnosis of our own 14 cases is 33 years. This is clearly higher than the three cases reported by Mirra [10, 11]. Another difference to Mirras' report is that only three cases are associated with a pathological fracture; 7 of 14 cases were randomly detected by X-ray examinations. As in SBC the cystic-sclerotic lesions involve mostly the entire width of the affected bone. All cases occurred in the metaphysis and the histology of the calcifyng solitary bone cyst concurs in substantial points with the findings in typical SBC [16, 17]. Of great importance is the evidence of bits of cementum-like matrix within the wall of approximately 70% (278 of 402 cases) of SBC from our registry. There is a different extent of this matrix and its degree of mineralization. The conversion of SBC to CSBC shows a smooth transition. In CSBC the dense structure is the leading component on X-rays and the histology shows the previously described homogeneous, hypocellular matrix, which is not circumscribed to single areas of the cyst membrane.

Because diagnosis derived from only clinical or radiological appearances is difficult, only the interdisciplinary cooperation of orthopaedic surgeon, radiologist and bone pathologist leads to the correct diagnosis. Exclusion of malignancy, an important aspect when differential diagnostic procedures are carried out, is crucial for the clinical treatment of this benign lesion. The intraoperative confirmation of the diagnosis on a frozen section by the bone pathologist, leads to appropriate treatment (curettage) [12, 13, 15].

Acknowledgements The authors would like to express their thanks to the contributors of the Hamburg Bone Tumour Registry for their trust in the register and excellent clinic information and Christiane Korn for assistance in correcting the manuscript.

References

1. Adler CP (1985) Tumour-like lesions in the femur with cementum-like material. Skeletal Radiol 14:26–37
2. Chigira M, Maehara S, Arita S, Udagawa E (1983) The aetiology and treatment of simple bone cysts. J Bone Joint Surg [Br] 65:633–637
3. Cohen J (1960) Simple bone cysts. Studies of cyst fluid in six cases with a theory of pathogenesis. J Bone Joint Surg [Am] 42:609–616
4. Cohen J (1970) Etiology of simple bone cyst. J Bone Joint Surg [Am] 52:1493–1497
5. Cordell J, Falini B, Erber W (1984) Immunoenzymatic labelling of monoclonal antibodies using immune complexes of alkaline phosphatase and monoclonal anti-alkaline phosphatase (APAAP) complexes. J Histochem Cytochem 32:219–229
6. Friedman NB, Goldman RL (1969) Cementoma of long bones. An extragnathic odontogenic tumor. Clin Orthop 67:243–248
7. Garceau GJ, Gregory CF (1954) Solitary unicameral bone cyst. J Bone Joint Surg [Am] 36:267–280
8. Horn V, Bozdech Z, Macek M, Foukal T, Kolar J, Zidkova H (1982) Cementoma-like tumours of bone. Arch Orthop Trauma Surg 100:267–272
9. Jaffe HL, Lichtenstein L (1942) Solitary unicameral bone cyst. Arch Surg 44:1004–1025
10. Mirra JM (1989) Bone tumors. Clinical, radiologic, and pathologic correlations. Lea and Febiger, Philadelphia, pp 1234–1261
11. Mirra JM, Bernard GW, Bullough PG, Johnston W, Mink G (1978) Cementum-like bone production in solitary bone cysts. So-called "cementoma" of long bone. Clin Orthop 135:295–307
12. Neer CS, Francis KC, Marcove RC, Terz J, Carbonara PN (1966) Treatment of unicameral bone cyst. J Bone Joint Surg [Am] 48:731–745
13. Neer CS, Francis KC, Johnston AD, Kiernan HA (1973) Current concepts on the treatment of solitary unicameral bone cyst. Clin Orthop 97:40–51
14. Porat S, Lowe J, Rousso M (1978) Solitary bone cyst in the infant radius. A case report. Clin Orthop 135:132–136
15. Resnick D, Niwayama G (1988) Diagnosis of bone and joint disorders, 2nd edn. WB Saunders, Philadelphia, p 3829
16. Saito Y, Hoshina Y, Nagamine T, Nakajima T, Suzuki M, Hayashi T (1992) Simple bone cyst. A clinical and histopathologic study of fifteen cases. Oral Surg Oral Med Oral Pathol 74 (4):487–491
17. Salzer-Kuntschik M (1972) Zysten im Knochen. Wien Klin Wochenschr 27–29:425–429
18. Sanerkin NG (1979) Old fibrin coagula and their ossification in simple bone cysts. J Bone Joint Surg [Br] 36:194–199
19. Sissons HA, Kancherla PL, Lehman WB (1983) Ossifying fibroma of bone. Report of two cases. Bull Hosp Jt Dis Orthop Inst 43:1–14
20. Smith RW, Smith CF (1974) Solitary unicameral bone cyst of calcaneus. A review of twenty cases. J Bone Joint Surg [Am] 65:49–56
21. Stelling CB, Martin W, Fechner RE, Alford BA, Strider DV (1981) Case report 150. Skeletal Radiol 6:213–215