Secondary chondrosarcoma in osteochondromas

Medullary extension in 15 of 45 cases

Paul I J M Wuisman[1], Paul C Jutte[1] and Toshifumi Ozaki[2]

We reviewed 45 secondary chondrosarcomas: 16 arising in solitary osteochondromas and 29 in 27 patients with multiple osteochondromas. Less than radical or wide primary surgery resulted in local recurrence in 8 of 14 lesions: 2 of 2 intralesional excisions, 5 of 11 marginal excisions, and in one case with radiotherapy alone. No local recurrence was found after a primary wide surgical procedure in 30 lesions and a radical procedure in 1 lesion after a mean of 8 (0.2–22) years' follow-up. 5 patients had died: 3 of pulmonary metastases (2 stage IB, 1 stage IIB), and 2 of local tumor invasion, both in the spine.

Medullary invasion occurred in 15 of 45 lesions, this was oftener than reported in secondary chondrosarcoma. Medullary invasion was not always detected preoperatively, even when MR or CT examinations had been performed. Therefore, we recommend that a secondary chondrosarcoma should be removed with a wide surgical resection, including a part of the underlying bone, to keep the local recurrence risk low. There were no clinical or prognostic differences between tumors that had arisen from solitary or from multiple osteochondromas.

Departments of Orthopaedic Surgery, [1]Academisch Ziekenhuis Vrije Universiteit, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands. Tel +31 0 2044-2355. Fax -357. E-mail: ortsecr@azvu.nl; [2]Okayama University Medical School, Okayama, Japan
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Secondary chondrosarcomas develop in 1–2 % of patients with solitary osteochondromas and in 1–25 % of patients with multiple osteochondromas (Jaffe 1958, Lichtenstein 1972, Solomon 1974, Ochsner 1978, Dahlin and Unni 1986, Peterson 1989). Repeated surgical excisions following local recurrences may result in malignant transformation (Huvos 1991). Since the literature regarding secondary chondrosarcomas is relatively scanty, we report our series of 43 patients.

Patients and methods

Between 1972 and 1994, 43 patients with secondary chondrosarcomas (45 lesions) were treated: 16 patients had solitary osteochondromas and 27 patients (29 lesions) had multiple osteochondromas (Table). On their first visit, 36 patients reported a local swelling that had suddenly increased in size, 12 of them also reported pain, 4 patients had neurologic symptoms and 3 patients reported only pain.

Malignant change was manifested radiologically by fuzzy margins on the cartilage cap and by the presence of lucent zones in the lesion. During the study, new imaging techniques (e.g., CT, MRI, bone scintigraphy) were introduced. Therefore complete sets of comparable imaging techniques were not available in every case.

The histopathological diagnosis of chondrosarcoma, according to Mirra et al. (1985), should include increased cellularity, enlarged chondrocyte nuclei, double-nucleated cells and infiltrative, permeative growth of the lesion. Both macroscopic and detailed microscopic analyses were performed to evaluate possible medullary involvement of the tumor.

The mean follow-up period was 8 (0.2–26) years. The statistical significance of various clinical and surgical parameters was analyzed by the Kaplan-Meier method. Univariate log-rank analysis was used to compare the curves.

Results

Secondary chondrosarcomas occurred in 29 men and 14 women (Table). Patients with multiple osteochondromas were younger—on average 34 (19–74) years, than patients with solitary osteochondromas, 39 (20–62) years. Secondary chondrosarcomas occurred in the flat bones in 9 of 16 solitary osteochondromas, and in 18 of 29 multiple osteochondromas.

On plain radiographs and CT-scans, the demarcation towards the surrounding tissue was not sharp (Figure

Clinical data

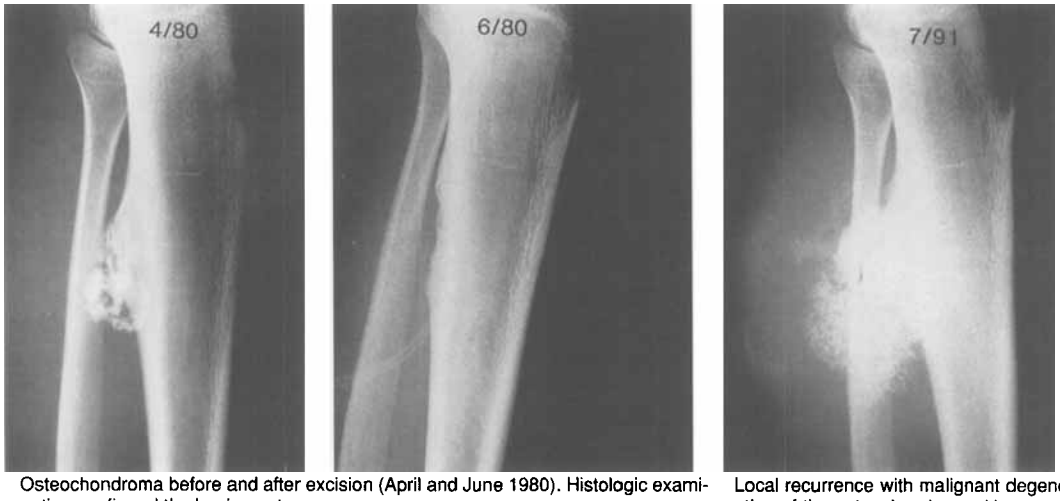
A	B	C	D	E	F	G	H	I	J	K	L
1	S	M	58	pubic bone	IB	LWE	I			33	NED
2	S	F	47	prox femur	IB	LWE	I			132	NED
3	S	F	20	cerv spine	IB	LME	II	174	II	259	Death, LR
4	S	F	62	prox humerus	IIB	MDA	III	3	III	85	Death, MD
5	S	M	23	prox tibia	IB	LWE	I			135	NED
6	S	M	40	prox tibia	IB	LWE	I			107	NED
7	S	F	32	pubic bone	IB	LME	I			76	NED
8	S	M	59	thor spine	IB	LIE	II	23	II	31	Death, MD
9	S	M	44	ischium	IB	LWE	I			144	NED
10	S	F	34	ilium	IA	LWE	I			35	NED
11	S	F	24	scapula	IB	LME	I	38	I	57	NED
12	S	M	32	dist femur	IB	LWE	II			205	NED
13	S	M	31	ischium	IB	LWE	I			144	NED
14	S	M	50	pubic bone	IB	LME	II			51	NED
15	S	M	28	ilium	IA	LWE	I			38	NED
16	S	F	38	ilium	IA	LWE	I			35	NED
17	M	F	23	cerv spine	IB	LIE	II	78	II	100	Death, LR
18	M	M	23	cerv spine	IB	LWE	I			91	NED
19	M	M	21	ilium	IA	LWE	I			143	NED
20	M	M	27	scapula	IB	LWE	II			58	NED
21	M	M	21	dist femur	IA	LME	I			172	NED
22	M	M	24	scapula	IB	LWE	I			84	NED
23	M	M	43	pubic bone	IB	LWE	I			74	NED
24	M	F	25	ilium	IB	MDA	I			46	NED
25	M	F	19	ilium	IB	LME	I	27	I	123	NED
26	M	M	28	prox femur	IB	LWE	I			58	NED
27	M	M	50	acetabulum	IB	LME	I			127	NED
28	M	M	27	ilium	IB	LWE	I			96	NED
29	M	F	36	prox femur	IB	LME	II			27	NED
30	M	M	19	scapula	IIB	RTH	III	83	III	117	LR
31	M	F	69	prox tibia	IB	RDA	I			23	NED
32	M	M	37	ilium	IB	LME	II	48	II	163	Death, MD
33	M	M	26	prox femur	IA	LWE	I			24	NED
34	M	M	45	ilium	IB	LWE	II			32	NED
35	M	M	24	ilium	IA	LWE	I			79	NED
36	M	M	30	scapula	IB	LWE	II			196	NED
37	M	M	49	prox femur	IB	LWE	II			200	NED
38	M	M	74	ischium	IB	LWE	II			2	NED
39	M	F	19	prox humerus	IA	LWE	I			128	NED
40	M	M	26	sacrum	IB	LWE	II			172	NED
41	M	M	51	scapula	IB	LWE	I			40	NED
42	M	F	37	prox humerus	IA	LWE	I			48	NED
				prox femur	IA	LWE	I				
43	M	M	63	sacrum	IB	LWE	I			102	NED
				ilium	IB	LWE	I				

A Patient number
B Type of osteochondroma
S Solitary
M Multiple
C Sex
D Age at diagnosis
E Location
F Stage at diagnosis (Enneking et al. 1980)
G Treatment
LWE Local wide excis.
LME Local marginal excision
LIE Local intralesional excision
MDA Marginal disarticulation
RDA Radical disartic.
RTH Radiotherapy
H Histology of the lesion (Mirra et al. 1985)
I Months to local recurrence
J Histology at recurrence
K Total follow-up time (months)
L Status at last follow-up
NED No evidence of disease
Death, LR Death due to local recurrence
Death, MD Death due to metastatic disease
LR Alive with local recurrence

1). MRI was correct in delineation towards the surrounding soft tissues, but no medullary involvement was found in 4 of 7 histologically proven cases (Figure 1). On gross pathologic examination, the surface of the thickened cartilage cap was irregular, its mean thickness was 4.6 (1–15) cm. Histologic examination showed 30 grade I, 13 grade II, and 2 grade III lesions and medullary involvement was noted in 15 of 45 lesions (Figure 1). Of these 15 lesions, 3 had a stalk with ingrowth at the edges, the other 12 were broad-based.

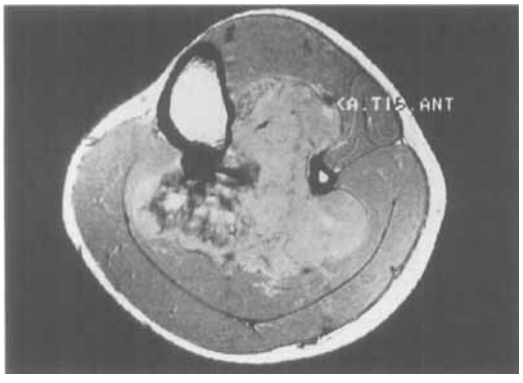
According to the Enneking system (1980), 35 lesions showed extracompartmental extension (stage

Figure 1. Case 31.



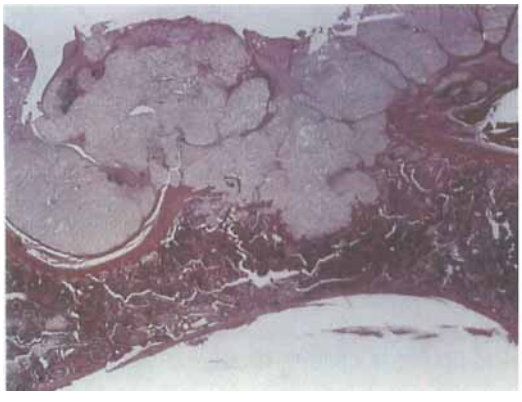
Osteochondroma before and after excision (April and June 1980). Histologic examination confirmed the benign nature.

Local recurrence with malignant degeneration of the osteochondroma 11 years after initial operation. The lesion is calcified. Note fuzzy margins of the cartilage cap.

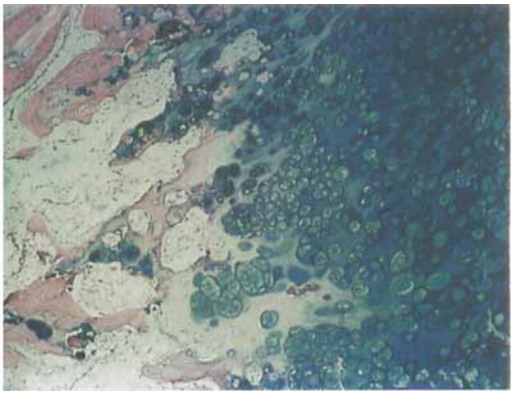


T2-weighted MR-image. Intramedullary infiltration of the tumor is not noted, but thinning and invasion of the cortical wall can be seen.

Gross specimen: infiltrative cartilaginous tumor.



Macrosection: local invasion of the chondrosarcoma into the tibia (HE, ×100).



Microsection: increased cellularity, enlarged chondrocyte nuclei, double-nucleated cells, and medullary invasion (HE, ×400).

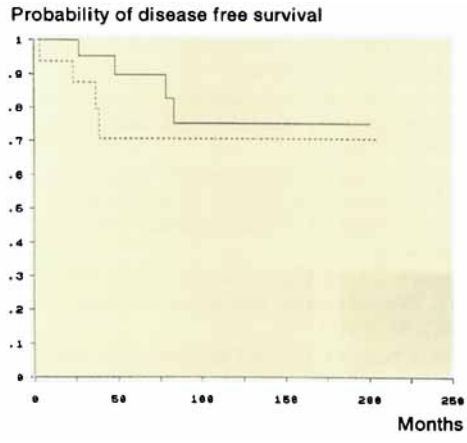


Figure 2. Disease-free survival after operation. —— solitary osteochondroma, - - - multiple osteochondromas.

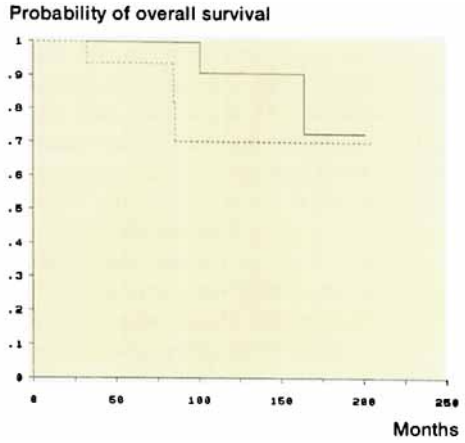


Figure 3. Overall survival after operation. —— solitary osteochondroma, - - - multiple osteochondromas.

IB: 33 lesions, stage IIB: 2 lesions). Only 10 lesions (stage IA) were confined to their compartment.

All cases were diagnosed by open biopsy. 44 lesions were primarily treated surgically, the margins were: 2 intralesional, 11 marginal, 1 radical, and 30 wide. A limb-saving procedure was performed in 41 lesions. 1 tumor was treated by radiation alone. The primary treatment resulted in a local recurrence in the 2 intralesional excisions, in 5 of 11 marginal excisions, and in the one given radiotherapy. Thus intralesional or marginal excision and radiotherapy proved inadequate in 8 of 14 cases. The local recurrences developed between 3 months and 14 years after initial treatment (Figure 2). No local recurrences were found after 30 wide resections and 1 radical. All local recurrences were treated surgically; histology did not show a higher degree of malignancy. In 2 subjects a rerecurrence was seen (both in the spine); both were judged to be inoperable and the patients died of local tumor extension.

The disease-free survival rate after operation in the group of solitary osteochondromas at 5 years was 0.9 and at 10 years 0.7, and in the group of multiple osteochondromas 0.7 at 5 and 10 years (Figures 2 and 3). Differences between solitary and multiple osteochondromas, as regards disease-free and overall survival, were not statistically significant.

5 of 43 patients died because of the tumor: 3 of them (2 stage IB and 1 stage IIB) had pulmonary metastases. In addition, the other 2 (both stage IB) died of a local tumor invasion.

Discussion

In our series of secondary chondrosarcomas, men predominated. The same was reported by Evans et al. (1977), Garrison et al. (1982), and Huvos (1991). The male preponderance might be partially due to the finding of a decreased expression in many involved women with multiple osteochondromas, resulting in fewer clinical manifestations (Wood et al. 1985). This is in accordance with our series, where the difference in sex distribution is especially due to a large group of men with multiple osteochondromas. The average age (36 years) of patients in our study is in accordance with other published series (Ochsner 1978, Garrison et al. 1982).

Although many bones may be affected, 9 of 16 secondary chondrosarcomas in patients with solitary osteochondromas and 18 of 29 secondary chondrosarcomas in patients with multiple osteochondromas occurred in the flat bones. Garrison et al. (1982) found equal distributions of sarcomatous degeneration in solitary osteochondromas between long and flat bones and an 80% predilection for flat bones in multiple osteochondromas. The commonest symptom was a mass lesion which suddenly increased in size, as in our series.

Increase in size after skeletal maturity or pain in a previously symptom-free osteochondroma suggests sarcoma (Coley and Higinbotham 1954, Garrison et al. 1982).

The malignant change in an osteochondroma is characterized by radiographic findings. According to Norman and Sissons (1984), the most reliable feature on plain radiographs is the presence of widespread calcifications in the cartilaginous portion of the lesions. Scintigraphy shows an increased uptake in nearly all chondrosarcomas, but also in osteochondromata before the epiphyses fuse, and in some osteochondromata in adults before the age of 30 (Hudson et al. 1983). Thickness of the cartilage cap is an important factor with respect to malignant degeneration.

Although Garrison et al. (1982) state that there is no thickness value specific to malignancy, this should be seriously suspected if the cartilage cap is thicker than 1 cm (Lichtenstein 1972, Huvos 1991, Merchan et al. 1993). In our series, the thickness of the cartilage caps varied from 1 to 15 cm on gross macroscopic examination and its shape was often irregular. MRI accurately separates cartilage from muscle density, cartilage generating a bright or light-grey signal (Lee et al. 1987). In our series, MRI was performed in 7 of 15 cases with histologically shown medullary involvement. In 4 of these, no medullary involvement was detected.

Histologic diagnosis of chondrosarcoma is difficult because of the borderline distinction between benign cartilage cells and low-grade malignancy (Pritchard et al. 1980). Mirra et al. (1985) described another criterion for malignancy—i.e., any sign of permeation or destructive invasion of medullary bone. Although Garrison et al. (1982) found no medullary involvement in any of 75 cases, we found medullary invasion in 15 of 45 cases. In case of invasion of the underlying bone, an adequate resection cannot be done by removing the tumor at the base. Only a segmental resection, including the underlying bone, is a safe procedure in these cases.

The rate of local recurrence is primarily dependent on the adequacy of surgical therapy rather than on histologic grade (Evans et al. 1977, Mankin et al. 1980, Gitelis et al. 1981). In 1982, Garrison et al. reported that inadequate surgical treatment (marginal or intralesional) may lead to a local recurrence in possibly up to 75% of patients. We found a local recurrence as a result of inadequate initial treatment in 8 of 14 lesions.

Henderson and Dahlin (1963) observed a tendency in some chondrosarcomas to be more anaplastic when they recur and Marcove and Huvos (1971) found a progression towards greater malignancy in at least 10% of locally recurrent cases. In our series, however, local recurrence did not change towards greater malignancy (Table). Metastasis is uncommon in secondary chondrosarcomas (Evans et al. 1977, Ochsner 1978, Dahlin and Unni 1986). Garrison et al. (1982) reported pulmonary metastases in 2 of 75 cases. In our series, 3 of 43 patients developed pulmonary metastases.

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