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ORIGINAL PAPER

Treatment options for recurrent giant cell tumors of bone

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Abstract
Background Although the recurrence rate of giant cell tumors of bone (GCTB) is relatively high exact data on treatment options for the recurrent cases is lacking. The possible surgical procedures range from repeated intralesional curettage to wide resection.
Methods Two hundred and fourteen patients with histologically certified GCTB have been treated at the authors department from 1980 to 2007. Sixty-seven patients with at least one local recurrence were included in this study. The mean follow-up was 77.3 months. The data was evaluated according the re-recurrence rate with regard to the surgical procedure for the recurrence.
Results The mean time until the first local recurrence was 22.0 months; the mean number of recurrences per patient was 1.4. The recurrence occurred in 69.7% (46 out of 66 patients) within the first 2 years. If after intralesional procedures (curettage or intralesional resection) no adjunct was used the re-recurrence rate was 58.8% (10 out of 17 patients) and decreased to 21.7% (5 out of 23 patients) if a combination of all adjuncts (PMMA + burring) was used. The likelihood of re-recurrence was reduced by the factor 5.508 which was clearly significant ($P = 0.016$). In case of wide resection no re-recurrence occurred. Seven patients (10.5%) developed pulmonary metastases. Fourteen patients (20.9%) finally received an endoprosthesis; 12 due to tumor recurrence, 2 due to secondary arthritis.
Conclusion Recurrent GCTB can be treated by further curettage with additional burring and cementing with an acceptable re-recurrence rate of 21.7%. The rate of patients finally needing an endoprosthesis is 20.9%. Due to the high rate of pulmonary metastases recurrent GCTB may be considered as a severe disease.

Keywords Giant cell tumor · Bone tumor · Recurrence · Bone cement · Tumorprosthesis

Introduction

Giant cell tumor of bone (GCTB) is a rare primary bone tumor that typically occurs in the meta-epiphyseal region of long bones, predominantly around the knee joint (Campanacci et al. 1987; Freyschmidt et al. 1998). Usually of benign character, it arises after skeletal maturity with a peak incidence in the third and fourth decade of life and a slight female predilection (Balke et al. 2008; Campanacci 1990; Carrasco and Murray 1989; Freyschmidt et al. 1998; Larsson et al. 1975; Salzer-Kuntschik 1998; Schwartz 1998).

The biological behavior of GCTB varies from indolent and static tumors to locally aggressive lesions with extensive bony destruction, penetration/destruction of the cortex and extensive soft-tissue expansion (Enneking 1986). In standard X-rays GCTB present as lucent lesions without matrix calcifications eccentrically located within the meta-epiphyseal region of the bone (Freyschmidt et al. 1998)

Ethical Board Review statement: Each author certifies that his or her institution has approved or waived approval for the human protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

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usually stage II or III according to the three stage classification system of Campanacci (Campanacci 1990; Campanacci et al. 1987) and Enneking (Enneking 1983).

After intralesional procedures the local recurrence rate varies from 10 to 40% (Blackley et al. 1999; Campanacci et al. 1987; Goldenberg et al. 1970; Lausten et al. 1996; Malek et al. 2006). The treatment of choice is intralesional curettage, additional burring with a high-speed air drill and bone cement (polymethyl methacrylate—PMMA) packing; if applicable a chemical adjunct such as hydrogen peroxide (H_2O_2) or phenol can be used. With this combination the recurrence rate can be reduced by the factor 28 compared to curettage without adjunct (Balke et al. 2008). Local recurrence is accompanied by an increased risk of so called "benign" pulmonary metastases (Balke et al. 2008; Bertoni et al. 1985, 1988; Campanacci et al. 1987; Cheng and Johnston 1997; Dominkus et al. 2006; Goldenberg et al. 1970; Kay et al. 1994; Maloney et al. 1989; McDonald et al. 1986; Osaka et al. 1997; Rock et al. 1984; Sanjay and Kadhi 1998; Siebenrock et al. 1998; Tubbs et al. 1992). As recently published the recurrence rate varies by anatomical localization with the highest recurrence rate in the distal radius, followed by distal tibia and proximal femur (Balke et al. 2008).

Although the recurrence rate of GCTB is relatively high exact data on how to treat the recurrent cases is lacking. The possible surgical procedures range from repeated intralesional curettage to wide resection. This paper focuses on the treatment of 67 patients with recurrent GCTB treated from 1980 to 2007 at the authors institution and gives advices about the sufficiency of the above mentioned treatment options.

Patients and methods

This is a level II retrospective comparative study based on revision of surgical protocols and patient records. The last follow up was done via personal contact or phone call.

Two hundred and fourteen patients with histologically certified GCTB were treated at the authors department from 1980 to 2007. Sixty-seven patients with at least one local recurrence have been included in this study. Twenty-five of these patients received their first surgical treatment at our hospital, 42 were referred from other hospitals due to local recurrence. Thirty-two patients were male, 35 were female. The mean age at first diagnosis was 29.6 (15.5–63.1) years. The mean follow-up was 77.3 (13.2–267.2) months. The mean time until first local recurrence was 22.0 (1.6–172.2) months, the mean amount of recurrences per patient was 1.4 (1.0–4.0). Forty-six patients showed one local recurrence, 14 patients had two, 4 patients had three and 2 patients had four recurrences. In one patient the exact number of recurrences is not documented. The mean follow up after the most recent operation was 45.3 (1.4–208.6) months.

The vast majority (50.8%) of recurrent GCTB was localized around the knee joint (20 × distal femur, 11 × proximal tibia, 2 × proximal fibula, 1 × patella), followed by distal radius ($n = 8$). The other 25 tumors were distributed as indicated in Fig. 1.

At first diagnosis nine patients presented with a stage II, 33 with a stage III, and none with a stage I lesion according to Campanacci and Enneking (Campanacci et al. 1987; Enneking 1983). In 25 patients the radiological findings were not available. Thirty-three patients presented with a soft-tissue component at first diagnosis and 20 without. In 14 patients information on soft-tissue extension was lacking.

The recurrences were detected by standard X-rays (Fig. 2a) and magnetic resonance imaging (MRI) (Fig. 3) and confirmed by fresh frozen sections during surgery.

The most common primary treatment had been intralesional curettage without any adjunct ($n = 30$), followed by curettage and PMMA packing ($n = 18$), and curettage plus

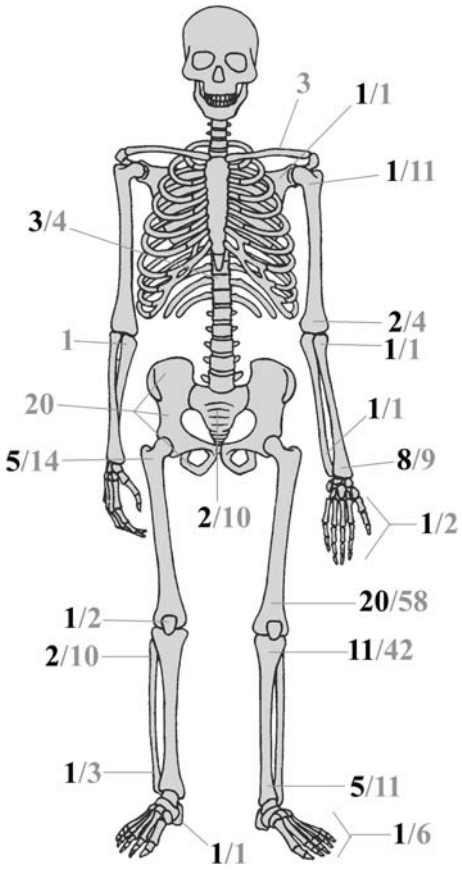

Fig. 1 Distribution of local recurrences according to anatomical site. The *black numbers* indicate the numbers of the recurrent cases ($n = 67$), the *gray numbers* the overall appearance at this localization of our whole patient collective ($n = 214$)

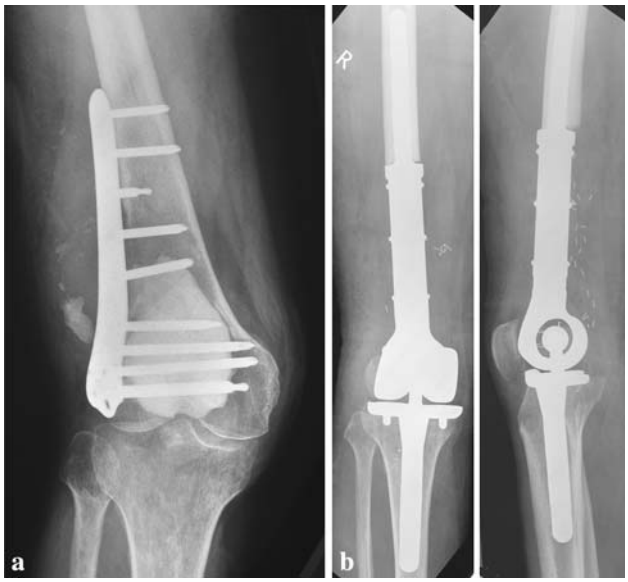

Fig. 2 Recurrent giant cell tumor of bone treated with a tumorprosthesis of the distal femur. Plain radiograph showing local recurrence after cementation and plate fixation (**a**) treated by wide resection and implantation of a Mutars® tumorprosthesis of the right distal femur (**b**) due to the massive bony destruction and soft tissue extension

PMMA plus burring ($n = 13$). Three patients had been treated with intralesional tumor resection, two with curettage plus burring without PMMA (Table 1).

The most common surgical procedure for the recurrence was curettage plus PMMA plus burring ($n = 23$), followed by curettage plus PMMA without burring ($n = 14$), wide resection ($n = 11$), curettage without adjunct ($n = 9$) and intralesional resection ($n = 8$). One patient received curettage plus burring without PMMA. In one patient the surgical procedure of the local recurrence was not documented. If cementation had been performed in the primary treatment the cement was totally removed before further curettage.

The re-recurrence rate was evaluated with regard to the recurrence operation, the anatomical localization and the outcome at final follow-up.

All statistical analysis was performed using chi-square tests for the likelihood ratio and ANOVA for determining the statistical significance (significance level $P < 0.05$, 95% confidence interval).

Results

Forty-five and a half percentage (30 out of 66 patients) of local recurrences occurred within the first year, 69.7% (46 out of 66 patients) within the first 2 years. From the third to fifth year, 27.3% (18 out of 66 patients) developed local recurrence and two patients developed local recurrence after more than 10 years. Ninety-seven percentage (64 out of 66 patients) of recurrences occurred within the first 5 years. In one patient the exact date of the recurrence was not documented.

If after intralesional procedures (curettage or intralesional resection) no adjunct had been used, the re-recurrence rate was 58.8% (10 out of 17 patients) and decreased

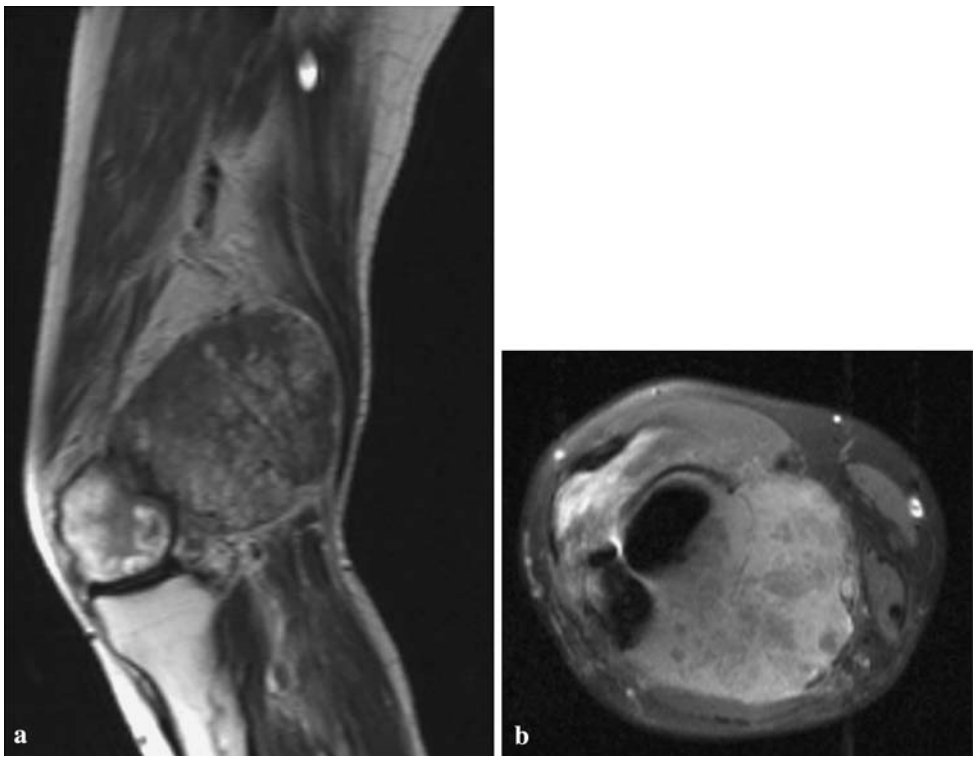

Fig. 3 Magnetic resonance imaging of recurrent GCTB with massive soft-tissue component Sagittal T2 (**a**) and transversal fat-saturated T1 (**b**) sequences of a recurrent GCTB after cementation and plate fixation with massive bony destruction and soft tissue extension. For X-ray see Fig. 2a

Table 1 Re-recurrence rate according to surgical procedure

Surgical procedure	Number of patients ($n = 67$)	Number of re-recurrence ($n = 20$)	%
Intralesional procedure w/o adjunct	17	10	58.8
Curettage ± bone graft	9	6	66.7
Intralesional resection	8	4	50.0
Curettage + adjunct	38	10	26.3
Curettage + PMMA ± H_2O_2	14	5	35.7
Curettage + PMMA + H_2O_2	3	0	0.0
Curettage + PMMA − H_2O_2	11	5	45.5
Curettage + PMMA + burring ± H_2O_2	23	5	21.7
Curettage + PMMA + burring + H_2O_2	10	3	30.0
Curettage + PMMA + burring − H_2O_2	13	2	15.4
Curettage + burring	1	0	0.0
Wide resection	11	0	0.0

The use of adjuncts reduces the re-recurrence rate from 58.8 to 26.3%

PMMA polymethylmetacrylate/bone cement, H_2O_2 hydrogen peroxide

to 26.3% (10 out of 38 patients) if at least one adjunct (PMMA, burring or both) was used (Table 1). The likelihood of re-recurrence was reduced by the factor 5.257 which was statistically significant ($P = 0.020$) (Table 2). The use of PMMA alone reduces the re-recurrence rate to 35.7% (5 out of 14 patients) by the factor 1.695 but without reaching statistical significance ($P = 0.213$). The best results of the intralesional procedures concerning re-recurrence were achieved by a combination of all adjuncts (PMMA + burring) with a reduction to 21.7% (5 out of 23 patients) (Table 1). Compared to intralesional procedures without adjuncts the likelihood of re-recurrence was reduced by the factor 5.508 which was clearly significant ($P = 0.016$) (Table 2). The groups with hydrogen peroxide or burring alone were too small so that statistical analysis was not possible (Table 1). In case of wide resection no re-recurrence occurred.

The re-recurrence rate according to the localization of the tumor (Fig. 1) was highest in the distal radius (8 out of 9 patients), followed by distal tibia (5 out of 11 patients), proximal femur (5 out of 14 patients), distal femur (20 out of 58 patients), and proximal tibia (11 out of 42 patients).

In GCTB of the distal radius major surgical procedures commonly became necessary. One resulted in allograft-reconstruction with an external orthosis, one in transposition of the ulna to the radius, one in tumor prosthesis, three in arthrodeses. Only two could be treated by repeated curettage, PMMA packing and subchondral bone graft, one with an additional intralesional resection of a soft tissue recurrence (Table 3). The worst outcome was in recurrent GCTB of the spine; two out of three patients suffered from incomplete paraplegia and one died due to excessive bleeding (Table 3).

Twenty out of 67 patients (29.9%) suffered from a second recurrence. Three were treated with curettage and cementing (no re-recurrence), three with curettage plus burring and cementing (two re-recurrences), eight with intralesional resection (three re-recurrences) and five with wide resection (no re-recurrence). In one case the treatment was not documented. Out of the six patients (9.0%) who suffered from a third local recurrence two were treated with curettage plus burring and cementing (no re-recurrence) and two with wide resection (no re-recurrence). Two patients (3.0%) experienced a fourth local recurrence, one after intralesional resection, in the second patient the surgical procedure was not documented. The first was finally cured by wide resection.

Seven patients (10.5%) developed pulmonary metastases. Five of them associated with the first local recurrence, one after the second and one after the third recurrence.

Table 2 Statistical analysis of the different treatment regimen of GCTB

Surgical procedure	*P*	Likelihood ratio
Intralesional procedure w/o adjuncts versus curettage + adjunct	0.020	5.257
Intralesional procedure w/o adjuncts versus curettage + PMMA ± H_2O_2	0.213	1.695
Intralesional procedure w/o adjuncts versus curettage + PMMA + burring ± H_2O_2	0.016	5.508

Comparison of the likelihood ratio of intralesional procedures without adjuncts with curettage plus different adjuncts. The use of local adjuncts significantly ($P = 0.020$) reduces the likelihood of re-recurrence by the factor 5.257

Chi-square tests for likelihood ratio and ANOVA with significance level $P < 0.05$, 95% confidence interval

PMMA polymethylmetacrylate/bone cement, H_2O_2 hydrogen peroxide

Table 3 Overview of the whole patient collective

Patient number	Age at first diagnosis (years)/gender		Localization	Number of recurrences	Time to first recurrence (months)	Follow-up (months)	Status follow-up	First surgical procedure	Comment/final surgical procedure
1	21.9	F	Femur dist.	1	15.5	42.0	CR	C, P	**Tumorprosthesis** after wide resection
2	26.9	M	Femur dist.	2	12.0	66.3	CR	C, S	Arthrodesis with intramedullary nail and fibula allograft after wide resection
3	18.8	F	Femur dist.	1	26.9	85.0	CR	C, B, P	Again C, B and P
4	39.3	M	Femur dist.	3	10.1	61.8	CR	C, B, P	Joint instability and stabilization with external orthosis after C, B and P
5	63.1	M	Femur dist.	1	12.3	26.9	SD	C, B, P and subchondral S	**Tumorprosthesis** after wide resection, pulmonary metasases
6	28.6	M	Femur dist.	1	24.1	74.3	CR	C, P and subchondral S	Again C, B, P plus subchondral S
7	27.5	F	Femur dist.	1	4.1	84.8	CR	C, P	**Tumorprosthesis** after wide resection
8	34.2	M	Femur dist.	1	25.1	151.5	CR	C, B, P	**Endoprosthesis** due to secondary arthritis after C, B and P
9	41.5	F	Femur dist.	1	20.8	34.1	CR	C, S	Secondary arthritis after C, B, P and subchondral S
10	25.5	M	Femur dist.	1	25.8	58.6	CR	C, B, P	Removal of bone cement and S
11	35.6	M	Femur dist.	3	56.0	231.4	CR	C, P and subchondral S	Removal of bone cement and S after C, B, P
12	17.9	F	Femur dist.	1	14.0	22.8	CR	C, P	Secondary arthritis after C, B and P
13	20.2	F	Femur dist.	1	6.0	146.6	CR	C, S	C, B and P
14	26.8	F	Femur dist.	1	37.8	40.4	CR	C, S	Arthrodesis after C and P
15	28.8	M	Femur dist.	2	27.5	108.9	CR	C	Modified Juvara plasty after wide resection
16	22.3	F	Femur dist.	1	24.0	59.9	CR	C	**Tumorprosthesis** after wide resection
17	21.4	M	Femur dist.	2	4.6	109.2	CR	C, S	Corrective osteotomy in medial gonarthritis after C and P
18	17.6	M	Femur dist.	3	2.3	267.2	CR	C, S	Allograft with impaired knee-flexion after wide resection
19	46.4	F	Femur dist.	1	20.6	35.4	CR	C, S	C and S
20	36.2	M	Femur dist.	1	47.0	55.6	CR	C, S	C and P
21	26.5	F	Tibia prox.	2	6.0	44.6	CR	C, P	C, P and subchondral S
22	44.2	M	Tibia prox.	1	15.1	45.9	CR	C, S	C, B, P and subchondral S
23	43.7	M	Tibia prox.	1	59.2	93.8	CR	C, S	**Endoprosthesis** due to secondary arthritis after C, P and subchondral S
24	21.7	F	Tibia prox.	2	8.8	120.4	CR	C, S	C, B, P and subchondral S
25	20.2	M	Tibia prox.	1	22.5	33.9	CR	C, B, P and subchondral S	C, B, P and subchondral S
26	32.4	F	Tibia prox.	1	12.6	78.7	CR	C, S	**Tumorprosthesis** after wide resection
27	19.5	M	Tibia prox.	4	48.5	129.7	DD	C, B, P	Amputation, metastases to the lung, soft tissue of the upper arm, chest, tongue, brain and small intestine, finally death due to intestinal perforation

Table 3 continued

Patient number	Age at first diagnosis (years)/gender		Localization	Number of recurrences	Time to first recurrence (months)	Follow-up (months)	Status follow-up	First surgical procedure	Comment/final surgical procedure
28	34.1	M	Tibia prox.	1	30.2	32.0	CR	C, B, P and subchondral S	C, B, P and subchondral S
29	20.0	F	Tibia prox.	1	11.8	15.9	CR	C, S	C and S
30	53.9	F	Tibia prox.	1	6.5	15.9	CR	C, P	C, B, P and subchondral S
31	28.3	F	Tibia prox.	1	18.2	45.4	CR	C, S	C, B and P
32	23.5	M	Radius dist.	1	49.7	60.2	CR	C, B, S	C, P and subchondral S
33	20.2	M	Radius dist.	3	19.7	116.2	CR	C, S	Arthrodesis after wide resection
34	35.1	F	Radius dist.	2	11.0	26.3	CR	C, S	Intralesional resection of soft-tissue recurrence after C, P and subchondral S
35	43.0	M	Radius dist.	1	33.7	49.0	CR	C, P and subchondral S	**Tumorprosthesis** after wide resection
36	44.9	M	Radius dist.	1	10.1	56.2	CR	C, P	Arthrodesis due to secondary arthritis after C, B and P
37	34.7	F	Radius dist.	1	47.8	67.6	CR	C, B	Allograft and stabilization with external orthosis after intralesional resection
38	51.1	F	Radius dist.	1	10.8	22.7	CR	C, B, P	Transposition of the ulna after wide resection of distal radius and PMMA-spacer
39	29.4	F	Radius dist.	2	7.3	105.3	CR	C, P	Arthrodesis after intralesional resection
40	49.9	M	Radius prox.	2	21.8	76.3	SD	C, P	Wide resection of soft-tissue recurrence, pulmonary metastases
41	15.5	M	Femur prox.	1	5.4	46.8	SD	C, B, P	Synchronous multifocal (distal femur and proximal tibia), recurrence in proximal femur, **tumorprosthesis** after wide resection, pulmonary metastases
42	19.8	M	Femur prox.	2	6.0	46.5	SD	C, S	**Endoprosthesis** after intralesional resection, pulmonary metastases
43	28.7	M	Femur prox.	1	13.9	56.3	CR	C, S	**Endoprosthesis** with bipolar cup after intralesional resection
44	22.2	M	Femur prox.	1	30.5	32.8	CR	C, B, P and subchondral S	C, B, P and subchondral S
45	31.6	M	Femur prox.	1	15.4	36.4	CR	C, B, P	C, B and P
46	16.2	F	Tibia dist.	1	172.2	265.9	CR	C, S	C, P and subchondral S, removal of bone cement in second operation
47	27.7	F	Tibia dist.	1	8.7	19.8	CR	C, P and subchondral S	Infection/delayed healing after intralesional resection and implantation of a bone cement spacer, pulmonary metastases
48	27.3	F	Tibia dist.	1	6.5	14.6	CR	C	C, B and P, removal of bone cement in second operation
49	16.8	F	Tibia dist.	4	16.0	214.3	CR	C, S	Metachronous multifocal, therapy of recurrences not documented
50	26.9	F	Tibia dist.	1	41.4	253.6	CR	C, S	C, B and P, removal of bone cement in second operation
51	17.6	M	Thoracic spine	1	7.6	27.3	CR	C, S	Vertebral fusion T3-8 with incomplete paraplegia
52	23.0	F	Thoracic spine	1	11.3	43.6	SD	Intralesional resection	Vertebral fusion T8-L1, T10 spondylectomy with incomplete paraplegia, pulmonary metastases
53	25.9	F	Thoracic spine	2	6.5	20.8	DD	Intralesional resection	Death due to exsanguination after tumor resection

Table 3 continued

Patient number	Age at first diagnosis (years)/gender		Localization	Number of recurrences	Time to first recurrence (months)	Follow-up (months)	Status follow-up	First surgical procedure	Comment/final surgical procedure
54	19.9	M	Fibula prox.	1	6.1	19.6	CR	C, P	Reconstruction of fibular collateral ligament with tensor fasciae latae ligament after wide resection
55	46.0	M	Fibula prox.	2	8.2	45.1	CR	Intralesional resection	Again intralesional resection
56	17.2	M	Fibula dist.	1	8.7	13.2	CR	C, S	C, B and P, removal of bone cement in second operation
57	27.0	F	Humerus dist.	2	8.7	45.1	CR	C, P	**Tumorprosthesis** after wide resection
58	24.0	F	Humerus dist.	1	36.0	190.7	CR	C, P	Again C and P
59	19.6	F	Humerus prox.	2	7.0	176.5	CR	C, S	Subprosthetic pathological fracture due to massive local recurrence after proximal humerus prosthesis resulting in wide resection and **tumorprosthesis** (total humerus) with Tikhoff–Limberg procedure
60	24.6	F	Sacrum	1	11.6	132.8	CR	C, P	Again C and P
61	23.9	F	Sacrum	?	?	164.3	CR	C, P	Further surgical procedures not documented
62	24.9	F	Calcaneus	1	1.6	105.5	CR	C, S	C, B and P
63	41.7	F	Midfoot	1	122.2	136.1	CR	C, S	Amputation of second metatarsus and toe
64	17.9	M	Midhand	1	16.8	72.9	CR	C, S	C and P, removal of bone cement in second operation
65	41.6	M	Patella	1	3.2	13.6	CR	C, P	**Tumorprosthesis** (extraarticular) after wide resection
66	38.0	F	Scapula	1	4.3	25.3	CR	C, P	Intralesional resection
67	38.6	F	Ulna dist.	2	7.6	46.5	CR	C, B, P	Intralesional resection of distal ulna and soft-tissue transposition

Information on anatomical site of the tumor, first surgical procedure and final surgical procedure. The endoprostheses/tumorprostheses are printed in bold

yrs years, *mths* months, *M* male, *F* female, *C* curettage, *B* burring, *P* PMMA/cementing, *S* sponge-bone, *CR* complete remission, *SD* stable disease, *DD* death due to disease

? exact number of recurrences/exact date of first recurrence is not documented

At last follow up after a mean of 77.3 (13.2–267.2) months, 60 patients were free of disease and five were alive with disease and stable pulmonary metastases. Despite high dose chemotherapy one male died due to intestinal perforation after developing multiple metastases (lung, soft tissue of upper arm, chest, tongue, brain and small intestine) after third recurrence. One female died in 1982 due to uncontrollable bleeding after resection of second recurrence of a GCTB of the thoracic spine.

Fourteen patients (20.9%) received an endoprosthesis after a mean of 71.1 (13.6–176.5) months (Fig. 2b), 12 due to tumor recurrence, 2 due to secondary arthritis after intralesional procedures, 6 and 7 years after the first surgery (Table 3). Five of these tumors were localized in the distal femur; four were reconstructed with a distal femur prosthesis after wide resection of the first local recurrence, one received a prosthesis due to secondary arthritis after curettage, burring and cementing (Table 3). Three of the tumors affected the proximal femur and were treated by a tumorprosthesis; once after wide (after first recurrence) and twice after intralesional resection (one after the first, one after the second recurrence). Two patients received a prosthesis of the proximal tibia, one after wide resection of the first recurrence, one due to secondary arthritis after curettage, cementing and subchondral bone grafting. The other tumors finally being treated by a tumorprosthesis were localized in the distal radius (wide resection of first recurrence), distal and proximal humerus (both after wide resection of second recurrence) and patella with extension into the joint after an insufficient intralesional procedure (Table 3).

Discussion

Our data shows that almost 70% of local recurrences of GCTB occur within the first 2 years after treatment which is in accordance to the literature (Malek et al. 2006; Turcotte et al. 2002; Vult von Steyern et al. 2006). Therefore we recommend short term controls within this period, e.g. every 3 months. If the patient presents with newly occurred pain or swelling or the standard X-rays show any suspicious findings an MRI should be performed.

A previously published study by the "Scandinavian sarcoma group" with a total of 19 recurrent GCTB reports that recurrent tumors of the long bones can be successfully treated by further intralesional curettage and cementing (Vult von Steyern et al. 2006). An older study by O'Donnel et al. (O'Donnell et al. 1994) reported the treatment of 15 recurrent cases. Five were treated by further curettage and cementing and ten by resection. Because in both studies only a few patients with recurrent GCTB were included statistical analysis was not possible.

Due to the high patient count this is the first study that precisely analyzes the different treatment modalities and the statistical significances. Intralesional procedures without any adjuncts such as burring or PMMA result in an unacceptably high re-recurrence rate of about 58.8%. The additional use of at least one adjunct reduces this rate to 26.3%. The additional use of PMMA as single adjunct reduces the likelihood of re-recurrence by the factor 1.695–35.7% compared to intralesional procedures without adjuncts but did not reach statistical significance ($P = 0.213$). As recently proven for primary treatment (Balke et al. 2008) the best results concerning re-recurrence can be achieved by a combination of all adjuncts (PMMA + burring) with a recurrence rate of 11.9%. We proof here that even the recurrent cases further curettage, burring of the cavity with a high-speed air drill and cementing significantly reduces the likelihood of re-recurrence to 21.7% by the factor 5.508 ($P = 0.016$). This rate is an acceptable control rate for a recurrent, usually benign lesion. Unfortunately the groups treated with hydrogen peroxide were too small, so that significance could not be statistically analyzed.

In case of recurrence after cementing we generally removed the cement completely before further curettage. The removal of the cement is sometimes difficult and may cause further destruction of the bone and especially the cartilage. In early recurrences within the first 2 years the tumor often recurred in multiple localizations surrounding the cement and not just at the sites visible on the MRI. Thus we recommend this procedure although it might seem like an over treatment and evidence data is lacking.

Although in case of wide resection no re-recurrence occurred we do not recommend this treatment in general. As long as adjuncts are used the re-recurrences are in most cases sufficiently controllable with further intralesional curettage (Wang et al. 2005). In contrast to wide resection followed by arthrodesis or tumor prosthesis, curettage and cementing mostly result in almost normal function (Oda et al. 1998; Turcotte 2006; Vult von Steyern et al. 2006). With intralesional procedures the recurrence rate in the distal radius was very high in our patient collective which is in contrast to previous reports (Ozalp et al. 2006). It may be explained by insufficient primary treatment. Despite the aggressiveness of the tumors (all grade III, six with a soft tissue component) the initial procedure was intralesional curettage in all cases, bone cement packing was performed in five cases only. There is still no general recommendation for the treatment of GCTB at this special anatomical site (Bianchi et al. 2005; Cheng et al. 2001; Intuwongse 1998; Leung and Chan 1986; Sheth et al. 1995). Due to the high complication rate in recurrent giant cell tumors of the spine, a marginal or even wide primary surgery according to Enneking (Enneking et al. 1980) may be justified for this localization (Chen et al. 2004; Gille et al. 2005; Gruber

et al. 1999; Ozaki et al. 2002). Some authors recommend spondylectomy as an aggressive operative treatment to prevent local recurrences (Kawahara et al. 1998; Samartzis et al. 2008) especially because of the difficulty to use conventional treatment options with curettage and cementing in these localizations (Matsumoto et al. 2007). According to Fiedler (Fidler 2001) the en bloc approach is the safest technique. Nowadays we perform preoperative embolisation of giant cell tumors involving the spine and sacrum with the aim to decrease the rate of sometimes excessive bleeding and reduce complications.

There are no reliable numbers in the literature about the use of endoprostheses in recurrent GCTB. In our patient collective 14 out of 67 patients (20.9%) finally received an endoprosthesis which in our opinion is a relatively high rate for a benign skeletal lesion. Only two patients received the prosthesis due to secondary arthritis after 6 and 7 years. In both cases the tumor had been located around the knee and was formerly treated by curettage and cementing (distal femur) or curettage and bone grafting (proximal tibia). Giant cell tumors often reach very close to the articulating cartilage. Thus especially in the weight-bearing lower extremity secondary arthritis is often unpreventable. It is still not clear if the performance of a subchondral bone graft in combination with cementing is able to reduce cartilage destruction (Frassica et al. 1990; Suzuki et al. 2007; Szalay et al. 2006). As recently published there is no increased local recurrence rate caused by a subchondral bone graft (Balke et al. 2008). The other 12 patients received the tumorprosthesis due to the extensive local recurrence and were predominantly located in the lower extremities (four distal femur, three proximal femur, one proximal tibia, one patella due to massive invasion of the joint). Three were cited in the upper extremity (distal radius, proximal and distal humerus).

In contrast to the "Scandinavian sarcoma group" study (Vult von Steyern et al. 2006) in which at final follow-up all patients were free from disease and showed a good function, our study proofs that recurrent GCTB can become a severe disease. The rate of pulmonary metastases in GCTB is generally low with approximately 2–3% (Balke et al. 2008; Bertoni et al. 1985, 1988; Cheng and Johnston 1997; Goldenberg et al. 1970; Kay et al. 1994; Masui et al. 1998; Osaka et al. 1997; Rock et al. 1984; Sanjay and Kadhi 1998; Siebenrock et al. 1998; Tubbs et al. 1992), but the literature indicates that local recurrence is accompanied by an increased risk of pulmonary metastases (Bertoni et al. 1985; Cheng and Johnston 1997; Kay et al. 1994; Lausten et al. 1996; Masui et al. 1998; Rock et al. 1984; Sanjay and Kadhi 1998; Tubbs et al. 1992). In fact in our study 10% of recurrent GCTB developed possibly life-threatening metastases. Therefore every patient with a local recurrence of a GCTB should be examined with a CT-scan of the chest.

Conclusion

Recurrent GCTB can be treated by further curettage with an acceptable re-recurrence rate as long as burring and cementing is used. Rate of the recurrent cases who finally end up in an implantation of an endoprosthesis is 20.9%, which is a remarkable rate for a benign skeletal lesion. In contrast to non-recurrent GCTB the rate of pulmonary metastases in the recurrent cases is high (10%). Thus recurrent GCTB has to be considered a severe disease. Although the outcome in recurrent GCTB of the long bones is generally good, this does not apply to giant cell tumors of the spine.

Conflict of interest statement Each author certifies that he or she has no commercial associations (e.g. consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted article.

References

Balke M, Schremper L, Gebert C, Ahrens H, Streitbuerger A, Koehler G, Hardes J, Gosheger G (2008) Giant cell tumor of bone: treatment and outcome of 214 cases. J Cancer Res Clin Oncol

Bertoni F, Present D, Enneking WF (1985) Giant-cell tumor of bone with pulmonary metastases. J Bone Joint Surg Am 67(6):890–900

Bertoni F, Present D, Sudanese A, Baldini N, Bacchini P, Campanacci M (1988) Giant-cell tumor of bone with pulmonary metastases. Six case reports and a review of the literature. Clin Orthop Relat Res 237:275–285

Bianchi G, Donati D, Staals EL, Mercuri M (2005) Osteoarticular allograft reconstruction of the distal radius after bone tumour resection. J Hand Surg [Br] 30(4):369–373. doi:10.1016/j.jhsb.2005.04.006

Blackley HR, Wunder JS, Davis AM, White LM, Kandel R, Bell RS (1999) Treatment of giant-cell tumors of long bones with curettage and bone-grafting. J Bone Joint Surg Am 81(6):811–820

Campanacci M (1990) Bone and soft tissue tumors. Springer, New York, pp 117–151

Campanacci M, Baldini N, Boriani S, Sudanese A (1987) Giant-cell tumor of bone. J Bone Joint Surg Am 69(1):106–114

Carrasco CH, Murray JA (1989) Giant cell tumors. Orthop Clin North Am 20(3):395–405

Chen LH, Niu CC, Lai PL, Fu TS, Chen WJ (2004) Recurrent giant cell tumor of the thoracic spine with bilateral pulmonary metastases. J Formos Med Assoc 103(12):957–961

Cheng JC, Johnston JO (1997) Giant cell tumor of bone. Prognosis and treatment of pulmonary metastases. Clin Orthop Relat Res 338:205–214. doi:10.1097/00003086-199705000-00027

Cheng CY, Shih HN, Hsu KY, Hsu RW (2001) Treatment of giant cell tumor of the distal radius. Clin Orthop Relat Res 383:221–228. doi:10.1097/00003086-200102000-00026

Dominkus M, Ruggieri P, Bertoni F, Briccoli A, Picci P, Rocca M et al (2006) Histologically verified lung metastases in benign giant cell tumours-14 cases from a single institution. Int Orthop 30(6):499–504. doi:10.1007/s00264-006-0204-x

Enneking WF (1983) Staging of musculoskeletal tumors. In: Enneking WF (ed) Musculoskeletal tumor surgery, vol 1. Churchill Livingstone, New York, pp 87–88

Enneking WF (1986) A system of staging musculoskeletal neoplasms. Clin Orthop Relat Res 204:9–24

Enneking WF, Spanier SS, Goodman MA (1980) A system for the surgical staging of musculoskeletal sarcoma. Clin Orthop Relat Res 153:106–120

Fidler MW (2001) Surgical treatment of giant cell tumours of the thoracic and lumbar spine: report of nine patients. Eur Spine J 10(1):69–77. doi:10.1007/s005860000206

Frassica FJ, Sim FH, Pritchard DJ, Chao EY (1990) Subchondral replacement: a comparative analysis of reconstruction with methyl methacrylate or autogenous bone graft. Chir Organi Mov 75(Suppl 1):189–190

Freyschmidt J, Ostertag H, Jundt G (1998) Knochentumoren. 2. Auflage. Springer, Berlin, pp 611–649

Gille O, Soderlund C, Berge J, Sacko O, Vital JM (2005) Triple total cervical vertebrectomy for a giant cell tumor: case report. Spine 30(10):E272–E275. doi:10.1097/01.brs.0000162931.80082.04

Goldenberg RR, Campbell CJ, Bonfiglio M (1970) Giant-cell tumor of bone. An analysis of two hundred and eighteen cases. J Bone Joint Surg Am 52(4):619–664

Gruber AW, Sabitzer RJ, Gorzer H, Hainfellner JA, Ungersbock K (1999) Acute symptom transverse laminectomy for a benign osteoclastoma of thethoracic spine–case report and review of the literature. Zentralbl Neurochir 60(2):93–99

Intuwongse CS (1998) Reconstruction following en bloc resection of a giant cell tumor of the distal radius using a vascularized pedicle graft of the ulna. J Hand Surg [Am] 23(4):742–747. doi:10.1016/S0363-5023(98)80064-6

Kawahara N, Tomita K, Matsumoto T, Fujita T (1998) Total en bloc spondylectomy for primary malignant vertebral tumors. Chir Organi Mov 83(1–2):73–86

Kay RM, Eckardt JJ, Seeger LL, Mirra JM, Hak DJ (1994) Pulmonary metastasis of benign giant cell tumor of bone. Six histologically confirmed cases, including one of spontaneous regression. Clin Orthop Relat Res 302:219–230

Larsson SE, Lorentzon R, Boquist L (1975) Giant-cell tumor of bone. A demographic, clinical, and histopathological study of all cases recorded in the Swedish Cancer Registry for the years 1958 through 1968. J Bone Joint Surg Am 57(2):167–173

Lausten GS, Jensen PK, Schiodt T, Lund B (1996) Local recurrences in giant cell tumour of bone. Long-term follow up of 31 cases. Int Orthop 20(3):172–176. doi:10.1007/s002640050057

Leung PC, Chan KT (1986) Giant cell tumor of the distal end of the radius treated by the resection and free vascularized iliac crest graft. Clin Orthop Relat Res 202:232–236

Malek F, Krueger P, Hatmi ZN, Malayeri AA, Faezipour H, O'Donnell RJ (2006) Local control of long bone giant cell tumour using curettage, burring and bone grafting without adjuvant therapy. Int Orthop 30(6):495–498. doi:10.1007/s00264-006-0146-3

Maloney WJ, Vaughan LM, Jones HH, Ross J, Nagel DA (1989) Benign metastasizing giant-cell tumor of bone. Report of three cases and review of the literature. Clin Orthop Relat Res 243:208–215

Masui F, Ushigome S, Fujii K (1998) Giant cell tumor of bone: a clinicopathologic study of prognostic factors. Pathol Int 48(9):723–729

Matsumoto M, Ishii K, Takaishi H, Nakamura M, Morioka H, Chiba K et al (2007) Extensive total spondylectomy for recurrent giant cell tumor in the thoracic spine. Case report. J Neurosurg Spine 6(6):600–605. doi:10.3171/spi.2007.6.6.600

McDonald DJ, Sim FH, McLeod RA, Dahlin DC (1986) Giant-cell tumor of bone. J Bone Joint Surg Am 68(2):235–242

O'Donnell RJ, Springfield DS, Motwani HK, Ready JE, Gebhardt MC, Mankin HJ (1994) Recurrence of giant-cell tumors of the long bones after curettage and packing with cement. J Bone Joint Surg Am 76(12):1827–1833

Oda Y, Miura H, Tsuneyoshi M, Iwamoto Y (1998) Giant cell tumor of bone: oncological and functional results of long-term follow-up. Jpn J Clin Oncol 28(5):323–328. doi:10.1093/jjco/28.5.323

Osaka S, Toriyama M, Taira K, Sano S, Saotome K (1997) Analysis of giant cell tumor of bone with pulmonary metastases. Clin Orthop Relat Res 335:253–261

Ozaki T, Liljenqvist U, Halm H, Hillmann A, Gosheger G, Winkelmann W (2002) Giant cell tumor of the spine. Clin Orthop Relat Res 401:194–201. doi:10.1097/00003086-200208000-00022

Ozalp T, Yercan H, Okcu G, Ozdemir O, Coskunol E (2006) Giant cell tumor at the wrist: a review of 23 cases. Acta Orthop Traumatol Turc 40(2):144–150

Rock MG, Pritchard DJ, Unni KK (1984) Metastases from histologically benign giant-cell tumor of bone. J Bone Joint Surg Am 66(2):269–274

Salzer-Kuntschik M (1998) Differential diagnosis of giant cell tumor of bone. Verh Dtsch Ges Pathol 82:154–159

Samartzis D, Foster WC, Padgett D, Shen FH (2008) Giant cell tumor of the lumbar spine: operative management via spondylectomy and short-segment, 3-column reconstruction with pedicle recreation. Surg Neurol 69(2):138–141. doi:10.1016/j.surneu.2007.01.038 discussion 141–2

Sanjay BK, Kadhi SM (1998) Giant cell tumour of bone with pulmonary metastases. A report of three cases. Int Orthop 22(3):200–204. doi:10.1007/s002640050242

Schwartz HS (1998) Update on giant cell tumor of bone. Compr Ther 24(10):488–493

Sheth DS, Healey JH, Sobel M, Lane JM, Marcove RC (1995) Giant cell tumor of the distal radius. J Hand Surg [Am] 20(3):432–440. doi:10.1016/S0363-5023(05)80102-9

Siebenrock KA, Unni KK, Rock MG (1998) Giant-cell tumour of bone metastasising to the lungs. A long-term follow-up. J Bone Joint Surg Br 80(1):43–47. doi:10.1302/0301-620X.80B1.7875

Suzuki Y, Nishida Y, Yamada Y, Tsukushi S, Sugiura H, Nakashima H et al (2007) Re-operation results in osteoarthritic change of knee joints in patients with giant cell tumor of bone. Knee 14(5):369–374. doi:10.1016/j.knee.2007.05.008

Szalay K, Antal I, Kiss J, Szendroi M (2006) Comparison of the degenerative changes in weight-bearing joints following cementing or grafting techniques in giant cell tumour patients: medium-term results. Int Orthop 30(6):505–509. doi:10.1007/s00264-006-0190-z

Tubbs WS, Brown LR, Beabout JW, Rock MG, Unni KK (1992) Benign giant-cell tumor of bone with pulmonary metastases: clinical findings and radiologic appearance of metastases in 13 cases. AJR Am J Roentgenol 158(2):331–334

Turcotte RE (2006) Giant cell tumor of bone. Orthop Clin North Am 37(1):35–51. doi:10.1016/j.ocl.2005.08.005

Turcotte RE, Wunder JS, Isler MH, Bell RS, Schachar N, Masri BA et al (2002) Giant cell tumor of long bone: a Canadian Sarcoma Group study. Clin Orthop Relat Res 397:248–258. doi:10.1097/00003086-200204000-00029

Vult von Steyern F, Bauer HC, Trovik C, Kivioja A, Bergh P, Holmberg Jorgensen P et al (2006) Treatment of local recurrences of giant cell tumour in long bones after curettage and cementing. A Scandinavian Sarcoma Group study. J Bone Joint Surg Br 88(4):531–535. doi:10.1302/0301-620X.88B4.17407

Wang HC, Chien SH, Lin GT (2005) Management of grade III giant cell tumors of bones. J Surg Oncol 92(1):46–51. doi:10.1002/jso.20338