

Clinical Significance of Genetic Imbalances Revealed by Comparative Genomic Hybridization in Chondrosarcomas

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DNA copy number changes were studied by comparative genomic hybridization (CGH) in 50 chondrosarcoma samples from 45 patients. Mean number of genetic aberrations in primary tumors was 4.8 ± 1.8 . The most frequently gained regions were 20q12-qter (37%), 20q (32%), 8q24.1-qter (27%), 20p (24%), and 14q24-qter (24%). Losses were 5.5 times less frequent than gains and observed mainly at Xcen-q21, 6cen-q22, and 18cen-q11.2 (11% each). Recurrent and metastatic tumors showed a mean of 4.0 ± 2.2 aberrations per sample. The most frequently gained regions were chromosome 7 (4 cases), 5q14-q32 (4 cases), 6p (3 cases), and 12q (3 cases). Losses of DNA sequences were 3.4 times less frequent than gains. Histological tumor grade was significantly associated with metastasis-free survival ($P = .002$) and overall survival ($P = .003$), being the strongest prognostic factor tested. A statistically significant correlation was found

Chondrosarcoma (CS) represents the second largest group of primary malignant bone tumors, accounting for nearly 10% of all bone tumors. CS is characterized by slow growth with late metastasis, with a peak incidence between 50 and 75 years of age.¹ Less than

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between gain at 8q24.1-qter and shorter overall survival ($P = .01$) but not with local recurrence or metastasis-free survival. Gain at 14q24-qter was associated with a trend to shorter overall survival ($P = .05$) but neither with an increased risk for local recurrence nor with metastasis-free survival. In a multivariate analysis, only the tumor grade associated with overall survival ($P = .02$). In a multivariate analysis together with the tumor grade, gain at 8q24.1-qter did not retain its significance ($P = .44$), indicating that this imbalance is not an independent prognostic factor. HUM PATHOL 30:1247-1253. Copyright © 1999 by W.B. Saunders Company *Key words:* comparative genomic hybridization, chondrosarcoma, chromosomal changes.

Abbreviations: CS, chondrosarcoma; CGH, comparative genomic hybridization.

one fourth of CS arise from osteochondromas, typically in patients with hereditary multiple exostoses syndrome, and 3% of CS originate from an enchondroma in patients with Ollier's disease (skeletal multiple enchondromatosis).² After radical resection of CS, the prognosis is based mainly on tumor grade, because it correlates with the tumor's ability to metastasize.³ Metastases are rarely observed in grade I CS, whereas grade III CS is metastatic in 60% to 70% of the patients.^{3,4}

Cytogenetic studies of CS are rare.⁵ Reports of chromosome banding analyses of fewer than 80 tumors show that most of the tumors are characterized by complex karyotypic changes. It has seldom been possible to completely characterize all chromosome aberrations in CS, and the value of cytogenetic analysis for assessing their prognostic significance is still unknown.

Genomic imbalances in tumors can be studied by comparative genomic hybridization (CGH),⁶⁻¹¹ which may solve some of the problems encountered using standard cytogenetics. Unlike chromosome banding analysis, no cell cultures or mitotic cells are required for CGH. Information on DNA copy number changes, including high-level amplification, can be obtained even in cases with poor chromosome morphology or complex marker chromosomes.⁶

In our previous study, CGH showed that CS is characterized by extensive genetic imbalances, mainly gains of whole chromosomes or whole chromosome arms, whereas losses of DNA sequences as well as high-level amplifications are rare.⁷ Because only 23

tumors were included in the previous study, the clinical significance of the changes was not evaluated. In the current study, 45 CS were analyzed by CGH, and the results were evaluated for their prognostic value.

MATERIAL AND METHODS

Tumor Specimens

The material consisted of 50 CS samples obtained from 45 patients. The samples were obtained from the Department of Orthopedics and Traumatology, Helsinki University Central Hospital in Finland, and from the Departments of

Orthopedics, Lund University Hospital and Karolinska Hospital, Stockholm, Sweden. With the exception of patient no. 36, none of the patients had received chemotherapy or radiation therapy before surgery. Table 1 shows the histopathologic and clinical characteristics of the tumors. The material consisted of 38 samples from primary tumors, 11 samples from local recurrences, and 1 sample from a metastatic tumor. The primary tumors were histologically graded according to the system described by Huvos.¹² This 3-grade classification is used in all sarcoma centers in Scandinavia, and the samples were evaluated and reviewed by the pathologist in charge of sarcomas at each institution (J.V., T.B., and M.Å.). The primary tumors included 10 grade I CS, 16 grade II CS, and 12

TABLE 1. Clinical Characteristics of the 45 Chondrosarcoma Patients

Tumor No.	Code	Sex	Age (yr)	Tumor Type	Grade	Location	Size (cm)	Follow-up (years)
1*	890696	F	25	Primary	I	Ulna	8	8.4 A
2*	900190	M	44	Primary	I	Pelvis	14	7.9 A
3	900315	F	46	Primary	I	Femur	NA	7.9 A
4*	920485	F	44	Primary	I	Sacrum	NA	5.7 A
5	950506	M	39	Primary	I	Talus	4	2.6 A
6	1758-91	M	50	Primary	I	Tibia	7	6.6 A
7	2714-87	F	38	Primary	I	Rib III	9	Missing
8	910178	F	36	Primary	I	Femur	6	6.7 A
9	940974	F	72	Primary	I	Pelvis	6	3.3 A
10	2763-89	M	47	Primary	I	Pelvis	20	Missing
11	XP8713101	M	32	Primary	II	Pelvis	NA	1.0 D
12	901141	F	39	Primary	II	Pelvis	NA	6.9 D
13	921093	M	63	Primary	II	Tibia	NA	5.3 D
14	921121	M	37	Primary	II	Tibia	6	5.1 A
15	930402	M	78	Primary	II	Rib VIII	20	5.0 D
16	940163	F	34	Primary	II	Femur	15	3.9 A
17	950091	M	73	Primary	II	Humerus	11	3.1 A
18*	951015	M	52	Primary	II	Pelvis	8	2.0 A
19	585-90	M	70	Primary	II	Rib I-III	13	7.9 A
20	1203-90	M	79	Primary	II	Rib	10	2.9 A
21	270-90	M	66	Primary	II	Spine	12	5.9 A
22a	900643	M	39	Primary	II	Scapula	10	7.8 A
22b	910115		40	Recurrence	II	Scapula	NA	Missing
23a	900652	M	63	Primary	II	Femur	NA	7.9 A
23b	910788		64	Recurrence	II	Soft tissue	15	Missing
24a	1946-88	M	51	Primary	II	Rib X	10	6.4 D
24b	2280-92		55	Recurrence	?	Rib X	NA	Missing
25a	1273-93	M	36	Primary	II	Pelvis	8	4.7 A
25b	909-94		37	Recurrence	II	Pelvis	11	Missing
26	3003-88	F	46	Recurrence	II	Ulna	7	11.8 A
27	2349-91	M	80	Recurrence	II	Femur	6	5.6 D
28	940315	F	43	Primary	II	Tibia	7	0.7 D
29	910461	M	51	Primary	III	Femur	NA	0.9 D
30	920185	M	24	Primary	III	Clavicle	5	4.1 AD
31	920346	M	27	Primary	III	Femur	5	5.8 A
32	1164-94	M	71	Primary	III	Femur	19	0.2 D
33	2539-95	M	43	Primary	III	Humerus	18	2.1 D
34	422-87	M	38	Primary	III	Rib	NA	3.6 A
35	388-95	M	47	Primary	III	Sternum, Rib IV-VI	6	2.9 A
36†	1310-88	M	80	Primary	III	Femur	7	0.6 D
37	1479-91	F	45	Primary	III	Pelvis	15	6.4 A
38	1508-95	F	72	Primary	III	Scapula	7	0.8 D
39	1763-90	F	56	Primary	III	Humerus	14	3.7 D
40	920593	M	53	Primary	III	Soft tissue	9	0.3 D
41	1526-87	F	74	Recurrence	III	Femur	10	1.4 D
42	45-93	M	67	Recurrence	III	Sternum	10	0.9 D
43	2708-93	M	85	Recurrence	III	Femur	21	Missing
44a	388-89	M	71	Recurrence	III	Femur	10	Missing
44b	2362-91		74	Recurrence	III	Femur	27	Missing
45	890719	M	58	Metastasis	III	Gluteal muscle	NA	Missing

Abbreviations: A, alive; D, dead.

*Multiple hereditary exostoses.

†Radiation therapy before surgery.

grade III CS. DNA was extracted from 47 frozen tumor samples following standard procedures and from 3 paraffin-embedded tissue sections as described by Miller et al.¹³

Comparative Genomic Hybridization

Comparative genomic hybridization (CGH) was performed using direct fluorochrome-conjugated DNA for all samples according to previously described methods, with minor modifications.^{14,16} Briefly, tumor DNA and reference DNA (genomic DNA from peripheral blood lymphocytes from a normal donor) were labeled with fluorescein isothiocyanate-conjugated deoxycytidine triphosphate (dCTP) and deoxyuridine triphosphate (dUTP) (DuPont, Boston, MA) and Texas-red-conjugated dCTP and dUTP (DuPont) by nick translation to obtain fragments ranging from 600 to 2,000 base pairs, as reported previously.¹⁵ The hybridization mixture consisted of 400 ng tumor DNA, 400 ng reference DNA, and 10 mg unlabeled Cot-1 DNA (Gibco BRL, Life Technologies, Gaithersburg, MD) dissolved in 10 μ L hybridization buffer (50% formamide, 10% dextran sulfate, 2 \times SSC). The hybridization mixture was denatured at 75°C for 5 minutes and hybridized to a slide with normal metaphase spreads denatured in 70% formamide/2 \times SSC (pH 7) at 68°C for 2 minutes. Hybridization was performed at 37°C for 48 hours. The slides were washed 3 times in 50% formamide/2 \times SSC (pH 7), twice in 2 \times SSC, and once in 0.1 \times SSC at 45°C, followed by 2 \times SSC, 0.1 mol/L NaH₂PO₄·0.1 mol/L Na₂HPO₄·0.1% Nonidet P-40 (pH 8), and distilled water at room temperature, for 10 minutes each. After air-drying, the slides were counterstained with 4',6-diamidino-2-phenyl-indole-dihydrochloride (DAPI; Sigma Chemical Co., St. Louis, MO) and mounted with an anti-fading medium (Vectashield; Vector Laboratories, Burlingame, CA).

Digital Image Analysis

The hybridizations were analyzed using an Olympus fluorescence microscope and the ISIS digital image analysis system (MetaSystems, Altussheim, Germany) based on an integrated high-sensitivity monochrome charge-coupled device camera and automated CGH analysis software. Three-color images (red for reference DNA, green for tumor DNA, and blue for counterstaining) were acquired from 8 to 12 metaphases per sample. Chromosomal regions were interpreted as overrepresented when the corresponding ratio exceeded 1.17 (gains) or 1.5 (high-level amplification), and underrepresented (losses) when the ratio was less than 0.85. All results were confirmed using a 99% confidence interval. Briefly, intraexperiment standard deviations for all positions on the CGH ratio profile were calculated from the variation of the ratio values of all homologous chromosomes within the experiment. Confidence intervals for the ratio profiles were then computed by combining them with an empirical interexperiment standard deviation and by estimating the error probability based on the *t*-distribution. In each CGH experiment, a negative (peripheral blood DNA from normal controls) and a positive (tumor DNA with known copy number changes) control were included and run simultaneously with the tumor samples.

Statistical Analysis

Correlation between the most frequent CGH aberrations and clinical features was analyzed in 38 patients with primary tumors. The median follow-up time was 60 months (range, 4 months to 8.4 years). During the follow-up, 11 patients

developed local recurrences, 13 patients developed metastases, and 13 patients died because of the tumor. The association between CGH aberrations and clinical features (tumor grade, tumor size, age at diagnosis, and sex) was tested using the χ^2 test for dichotomous variables and the Mann-Whitney test with correction for ties for the other variables.

Metastasis-free and overall survival rates were estimated using the Kaplan-Meier method.¹⁷ The most common aberrations were studied for their association with metastasis-free survival, overall survival, and local recurrence using the log-rank test.¹⁸ To avoid the problem with multiple comparisons, statistical testing was restricted to 7 of the most common aberrations (4 of the most frequent gains and 3 of the most frequent losses) and the presence of high-level amplifications irrespective of the location. The statistical significance level was set to 0.01 according to the methods of Bonferroni.¹⁹ The proportional hazards model was used to test for a linear association between the risk of death or relapse and the total number of aberrations (total number of aberrations, total number of gains, and total number of losses per tumor).

Four other factors (tumor grade, tumor size, age at diagnosis, and sex) were tested for association with local control, metastasis-free survival, and overall survival. Tumor size, tumor grade, and patient's age were tested as continuous variables, and sex as dichotomous. Factors that were significantly associated with the outcome were finally combined in a multivariate Cox analysis of overall survival.²⁰

RESULTS

DNA Sequence Copy Number Changes in Primary Tumors

Of the 38 tumors, 24 (63%) had changes with a mean value of 4.8 ± 1.8 aberrations per sample (range, 1 to 24). Fourteen (37%) samples did not show any aberrations. Gains were more frequent than losses (gains:losses = 5.5:1). Figure 1 shows all chromosomal regions with copy number changes.

Gains were observed to affect mostly entire chromosomes (48%) but less frequently chromosome arms (25%) or chromosome bands (27%) (Table 2, Fig 1). The most frequently gained chromosomes were 20 (24%), 21 (18%), 22 (18%), 7 (16%), and 17 (16%) (Table 3). The most frequently gained chromosome regions were 20q12-qter (37%), 20q (32%), 8q24.1-qter (27%), 20p (24%), and 14q24-qter (24%). Other less frequently gained regions are listed in Table 3.

High-level amplifications were rare and observed mainly at chromosomal bands 7p15, 12cen-q15, 12q24.1, and 18q21 (2 cases each) (Table 3).

Losses of entire chromosomes or chromosome arms occurred at similar frequencies and were twice as common as losses of chromosomal bands. Losses occurred most frequently at Xcen-q21, 6cen-q22, and 18cen-q11.2 (11% each).

DNA Sequence Copy Number Changes in Recurrent and Metastatic Tumors

Of the 12 tumors, 7 had changes with a mean value of 4.0 ± 2.2 aberrations per sample (range, 3 to 16). Five samples did not show any aberrations. Gains were more frequent than losses (gains:losses = 3.4:1). Figure

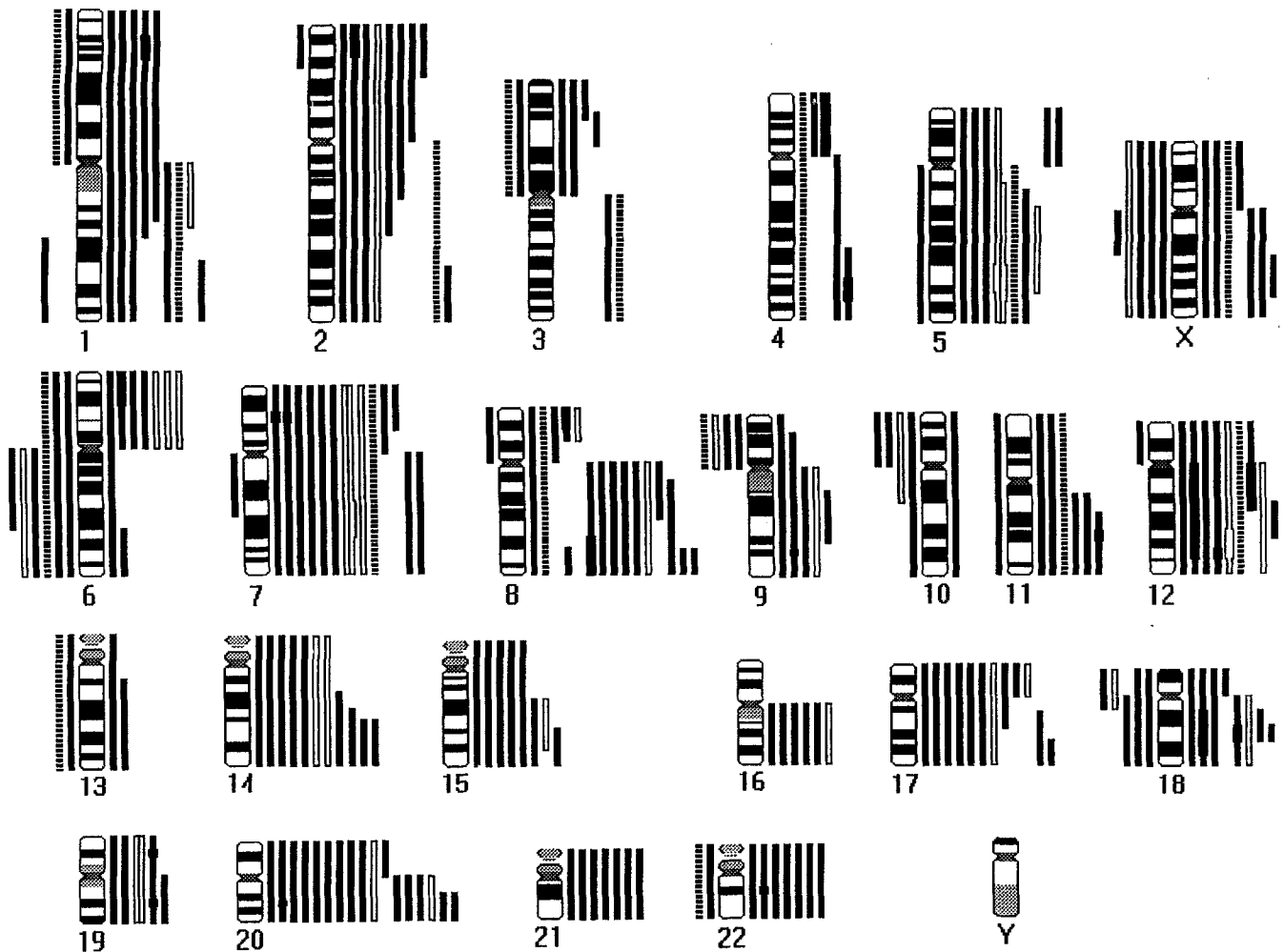


FIGURE 1. Summary of gains and losses of DNA sequence copy number in 45 chondrosarcomas analyzed by CGH. Losses are shown on the left and gains on the right of each chromosome. Each bar represents a genetic alteration seen in 1 tumor. High-level amplifications are marked with thick bars. Solid bars represent alterations observed in 38 primary tumors. Empty bar denotes changes in 11 recurrent tumors, and striped bars represent alterations found in 1 metastatic tumor.

1 shows all chromosomal regions with DNA sequence copy number changes.

Of the gains, 49% affected entire chromosomes, 38% chromosome arms, and 13% chromosome bands (Table 2, Fig 1). The most frequently gained chromosomes were 7 (4 cases), 14 (2 cases), and 19 (2 cases). The most frequently gained regions were chromosome 7 (4 cases), 5q14-q32 (4 cases), 6p (3 cases), and 12q (3 cases) (Table 3). High-level amplifications were rare, and no segment was involved in more than 1 patient (Table 2). Losses usually affected entire chromosomes (37%) or chromosome arms (45%) but less frequently chromosomal bands (18%).

Low-Grade CS (Grades I and II) Versus High-Grade CS (Grade III)

The mean numbers of DNA sequence copy number changes per tumor in low grade CS and high-grade CS were 3.3 ± 1.0 (range, 1 to 20) and 8.0 ± 2.2 (range, 1 to 24), respectively. In both categories, gains were more frequent than losses (low-grade CS, 78 gains and 8 losses; high-grade CS, 71 gains and 25 losses; $P = .07$).

Correlations Between Changes Detected by CGH and Clinical Features or Outcome

The estimated 5-year local control rate in the 38 patients studied for prognostic implication of genetic changes was 67%; the 5-year metastasis-free survival rate, 68%; and the 5-year overall survival rate, 70%.

No association was found between tumor grade, tumor size, age at diagnosis, sex, and local control. Histological grade was significantly associated with metastasis-free ($P = .002$) and overall survival ($P = .003$).

Neither the total number of aberrations, the total number of gains or losses per sample, nor the presence of high-level amplification had any prognostic impact on local control or metastasis-free or overall survival. The total number of gains was, however, associated with a trend to shorter metastasis-free survival ($P = .05$).

A statistically significant correlation was found between gain at 8q24.1-qter and shorter overall survival ($P = .01$) but not with local recurrence ($P = .10$) or metastasis-free survival ($P = .15$) (Table 4). The overall 5-year survival rates were 85% and 23%, in patients without and with gain at 8q24.1-qter, respectively (Fig

TABLE 2. DNA Sequence Copy Number Changes Detected in 45 Chondrosarcomas Analyzed by CGH*

Tumor No.	DNA Copy Number Changes
1	-X
2	+Xq22-q26
5	-18
6	+5, +7, +11q13-qter, +14, +20
8	-6, +16q, +17p, +18p, -18q, +20, +X
9	+4p , +7q, +8, +12, +14, +15, +17, +20, +Xq
11	+2pter-q24, +8q
14	+17, +20q, +21
15	+2, +5, +7, +8q, +14, +15, +16q, +17, +20, +21, +22
16	+1, +2, +6, +7q, -9p, +10, +12pter-q15 (12cen-q15), +16q, +17pter-q21, +20
17	-X
18	+1pter-q25 (1p33-p35), -1q31-qter, +2q33-qter, +3p, +6p, +7, +8p, +11, +12 (12cen-q24.1), +13q13-qter, +14q21-qter, +15, +16q, +18 (18q12-q22), +19 (19p13.2 , 19q13.2), +20 (20q13.1), +21, +22, +Xq
19	+1q32-qter
20	+12, +18q (18q21), +19, +20q
22b	+6p, +17p, +20
23b	+1cen-q24, +5q14-q32, +6p, -9p, +9q, +12q, +15q21-q25, +16q, +17, +20q
25b	+2, -6q, +7, +14, -18pter-q11.2, -X
27	+6p, +8q, +14
28	+2p, +6p, -6q, +14q23-qter, +15q23-qter, +16q, +17, +20q, +21, +22
29	-1p, +1q, +5, +7, +14, +18, +20, +21, +22, +X
30	+1, -2p22-pter, -3p, +3q, -5q, -6, +8q, -9p, +9q, -10, +11, -18, -22
31	+1pter-q23, +2 (2p23-pter), +3p22-pter, +4q, +5p, +6p (6p22-pter), -6cen-q22, +6q23-qter, +7p, -7cen-q22, -8p, +8cen-q21.3, -10p, -11, -12p, +13, +14q22-qter, +15q21-qter, +17, +18, +20p, +21, +22, +Xp
33	+4q28-qter (4q31.3-q33), +7 (7p15), +8p21-pter (8p22-pter), +8q24.1-qter, +9, -10p, +11q13-qter, -13, +14q24-qter, +17q23-qter, -18pter-q11.2, +18q21, +20q12-qter, -Xcen-q21
34	+8q24.1-qter
36	+2p21-pter, +3p21-p22, +7p14-pter, +8q13-qter, +11q14-qter (11q22)
37	+8q (8q23-qter), +15, +17q21-qter, +19q, +20q12-qter
39	+5q13-qter, +7 (7p15), +8q24.1-qter, +9p22-qter (9q33), +12 (12q24.1), +18q12-q21, +19, +20, +21, +22 (22q12), -X
40	+1, +2pter-q21, +3p, +4p, +5p, +8q, +9q13-q31, +12q15-q22, +14, +15, +17, +20, +22
44a	+5(5q31-q32), +7, +19
44b	+5q12-qter (5q31-q33), +7 (7q22-q31), +8p21-pter, -10pter-q21, +12 (12q22-q24.1), +18q, +19
45	-1p, +1q, +2q, -3p, +3q, +4, +5q, -6, +7, +8, -9p, +11, +12, -13, -22, +X

*Samples with no copy number changes excluded.

+, DNA sequence gains; -, DNA sequence losses; high-level amplifications are printed in bold.

2). In the same patients, the corresponding rates of metastasis-free survival were 75% and 50%, and the rates of local control at 5 years were 79% and 34%. Gain at 14q24-qter was associated with a trend to shorter overall survival ($P = .05$) but not with an increased risk for local recurrence ($P = .23$) or metastasis-free survival ($P = .11$) (Table 4). The 5-year overall survival rates were 80% and 36% in patients without and with gain at 14q24-qter, respectively (Fig 3). The corresponding rates of metastasis-free survival were 72% and 56%, and the rates of local control at 5 years were 62% and 83%.

TABLE 3. The Most Frequent Gains, High-Level Amplifications, and Losses of DNA Sequence Copy Number Detected by CGH in 38 Primary and in 12 Recurrent/Metastatic (Bold Type) Chondrosarcomas

Gains		High-Level Amplifications		Losses	
Region	%	Region	%	Region	%
20q12-qter	37	5q31-32	17	Xcen-q21	11
5q14-q32	33	5q33	8	6cen-q22	11
7	33	7q22-q31	8	18cen-q11.2	11
20q	32	12q22-q24.1	8	X	8
8q24.1-qter	27	7p15	5	6q23-qter	8
6p	25	12cen-q15	5	10p	8
12q	25	12q24.1	5	18p	8
20p	24	18q21	5	18q12-qter	8
14q24-qter	24			6p	5
20	24			9p	5
7pter-p15	21				
7q	21				
8q13-q21.3	21				
17p	21				
17q21	21				
17q23-qter	21				
2p21-pter	18				
8q22-q23	18				
14q22-q23	18				
15q23-qter	18				
21	18				
22	18				

Gains at 20q12-qter, 20q, and 20p as well as losses at Xcen-q21, 6cen-q22, and 18cen-q11.2 did not have any impact on clinical outcome.

Table 5 shows the results of multivariate analysis on overall survival, including tumor grade and gains of DNA sequences at 8q24.1-qter and 14q24-qter. The only factor associated with overall survival in multivariate analysis was tumor grade ($P = .02$).

DISCUSSION

In the current study, gain of 8q24.1-qter emerged as a novel prognostic marker for human CS. It was associated with shorter survival ($P = .01$) but not with local recurrence or metastasis-free survival. It was not, however, an independent prognostic marker. In multivariate analysis, the strongest clinical prognostic parameter was tumor grade, which is in line with previous studies.²¹⁻²³

Copy number increases of chromosome 8 are frequent in most types of human malignancies.⁶ Among sarcomas, gains narrowed down to 8q have been de-

TABLE 4. Prognostic Significance of DNA Sequence Copy Number Gains at 8q24.1-qter and 14q24-qter in Chondrosarcoma

	Gain at 8q24.1-qter		Gain at 14q24-qter	
	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
Metastasis-free survival	2.76 (0.83-9.26)	0.15	2.95 (0.89-9.73)	0.11
Overall survival	3.96 (1.22-12.78)	0.01	3.00 (0.94-9.62)	0.05
Local control	2.78 (0.84-9.17)	0.08	0.31 (0.04-2.47)	0.24

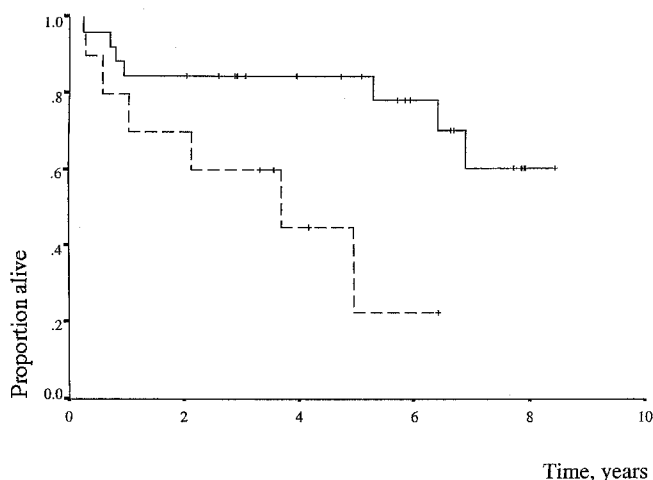


FIGURE 2. Overall survival in chondrosarcoma patients with (broken line) and without (solid line) gain at 8q24.1-qter.

scribed to be common in leiomyosarcoma of soft tissue,²⁴ chondrosarcoma,⁷ osteosarcoma,^{11,25} synovial sarcoma,²⁶ and Ewing tumors.²⁷ So far, these gains have been demonstrated to correlate with large tumor size in leiomyosarcoma²⁴ shorter overall survival in osteosarcoma,²⁸ and with a trend both to worse survival in the Ewing family of tumors²⁷ and increased risk for metastatic disease in synovial sarcoma.²⁹

The 8q24.1-qter segment includes the *MYC* locus at 8q24. This proto-oncogene has been suggested to be important for cellular growth in many types of sarcomas,³⁰ including CS.^{31,32} In the current series, most of the cases with 8q24.1-qter amplification had gained the entire long arm of chromosome 8. Thus, it is evident that, besides *MYC*, 8q also contains other genes that may have prognostic value in sarcomas. Previous studies have not indicated *MYC* amplification to be associated with such clinical or histological features of CS as histological subtype, tumor grade, surgical stage, or the ploidy level.³¹

Loss of heterozygosity has been reported for all 3 known loci for hereditary multiple exostoses in spo-

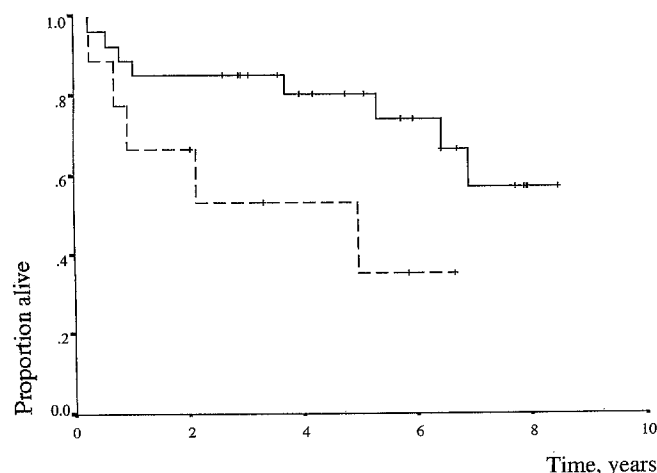


FIGURE 3. Overall survival in chondrosarcoma patients with (broken line) and without (solid line) gain at 14q24-qter.

TABLE 5. Effect of Tumor Grade and Gain of Sequences at 8q24.1-qter and 14q24-qter on Overall Survival in Patients With Chondrosarcoma

	Univariate Analysis		Multivariate Analysis	
	Hazard Ratio (95% CI)	P	Hazard Ratio (95% CI)	P
8q24.1-qter gain	3.96 (1.22-12.78)	.01	1.64 (0.46-5.81)	.44
14q24-qter gain	3.00 (0.94-9.62)	.05	2.46 (0.74-8.19)	.14
Tumor grade	4.57 (1.69-12.37)	.003	3.44 (1.22-9.70)	.02

radic and familial CS.³³⁻³⁵ In our series of 50 CS, we did not detect any recurrent losses at any of these loci (8q24.1, 11p11-13, and 19p). This does not, however, rule out the possibility of deletions that are too small to be detected by CGH.

In 24% of the primary tumors, a gain was seen at 14q24-qter. This imbalance was associated with a trend to shorter survival ($P = .05$). The target gene(s) for amplification at distal 14q remains unknown. Gains or high-level amplifications of DNA sequences at this location have been rare in other tumors.⁶

To conclude, we found that 8q gain indicates shorter survival in chondrosarcoma. Further studies are needed to characterize the target genes involved in the gain.

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