

Estradiol-17 β Receptors in Cytosolic Fraction of Chondrosarcoma

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Estradiol-17 β receptors were detected in the cytosolic fraction of the majority of bone chondrosarcomas by protamine sulfate sedimentation of the hormone-receptor complex. The absolute number of receptors in tumors was higher in men than in women, but chondrosarcomas with estradiol-17 β receptors more often occurred in women. The highest level of receptors was revealed in highly differentiated chondrosarcomas. No relationships between tumor location, size, type of the process, and the number of receptors was detected. We can state with assurance that the absence of estradiol-17 β receptors in chondrosarcomas in women is a favorable prognostic sign with regard to metastases or local tumor relapses.

Key Words: *chondrosarcoma; estradiol-17 β receptors; prediction*

Chondrosarcoma (CS) is an extremely malignant and unpredictable tumor [3]. These neoplasms derive from cartilage islets retained since the period of embryonal or early postnatal bone development and from undifferentiated multipotent mesenchymal cells [2].

The incidence of CS among primary skeletal tumors is 10-38%. CS can develop as a primary malignant tumor or a secondary tumor due to malignization of a benign cartilaginous tumor or dysplastic process in the bone [1-3].

Published reports indicate the involvement of sex steroid hormones and polypeptide growth factors in the regulation of normal development and functioning of the bone system and in blastomogenesis in bones [2,6]. Direct effects of estradiol and testosterone on normal [7] and transformed [5,8] cartilaginous cells were detected.

We studied the incidence and levels of estradiol-17 β receptors (ER) in the cytosolic fraction of CS, the role of these factors in prediction of the disease course and outcome, and selection of patients for endocrine therapy.

MATERIALS AND METHODS

Patients with bone CS aged 10-70 years (mean age 38.3 years), 36 men and 25 women, were examined. The number of patients per decade of age was practically the same. In 43 patients tumors were detected in tubular bones, in 17 in flat bones, and in only 1 case in the laryngeal cartilage.

Histological analysis of CS showed typical variant of CS with different degree of differentiation (mainly I and II) to predominate in the majority of patients (Table 1).

Primary localized tumor process was diagnosed in 41 patients and primary generalized in 4. Sixteen patients were treated previously (surgery, polychemotherapy, radio- or combined therapy) and hospitalized again with relapses at Cancer Research Center.

Maximal size of CS was less than 8 cm in 12 patients, 8.1-15.0 cm in 21 patients, and more than 15 cm in 16 patients.

Surgical treatment predominated: sparing surgery were performed in 18 and mutilating surgery in 41 patients; 2 patients were treated conservatively.

Estrogen receptors were assayed by the method of Lippman and K. Huff (1976) based on protamine sul-

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TABLE 1. Incidence and Mean Levels of ER in CS of Different Histological Structure and Differentiation ($M \pm m$)

CS	Number of cases	ER ⁺ CS		Mean content, fmol/mg protein	Range of values
		abs.	%		
Differentiation degree I	17	10	58.8	125.5 \pm 41.7	21-396
II	23	13	56.5	77.0 \pm 27.9	22-376
III	6	3	50.0	20.0 \pm 1.5*	18-22
Mesenchymal	5	4	80.0	24.5 \pm 3.7	14-31
Dedifferentiated	10	7	70.0	25.6 \pm 3.2	15-34

Note. * $p=0.05$ vs. CS of the first degree of differentiation.

fate precipitation of the hormone-receptor complex from the cytosolic fraction. Total protein in the cytosol was measured by the method of Lowry.

RESULTS

Estrogen receptors in tumors were detected in 37 (60.7%) patients. The content of ER varied from 14 to 396 fmol/mg protein (69.2 ± 21.3 fmol/mg protein).

In men, ER were detected in 55.6% tumors. In women ER⁺ tumors were two times more incident than ER⁻ variants (68 and 32%, respectively).

The mean level of tumor ER in men (99.9 ± 27.9 fmol/mg protein) was higher than in women (35.1 ± 4.8 fmol/mg protein, $p=0.05$).

The content of ER in CS of each histological variant is shown in Table 1. ER were more often found in dedifferentiated CS compared to typical highly and moderately differentiated tumors.

Analysis of distribution of ER in CS of different histological structure and differentiation showed the following tendency: the higher the degree of differentiation, the higher the level of ER in tumor cytosolic fraction.

ER⁺ tumors were found in 55.8% tubular bones. In flat bones, ER⁺ CS were found in 70.6% cases, while ER⁻ tumors were almost twofold more rare (29.4%). The mean content of ER in CS in tubular and flat bones were 69.9 ± 21.2 and 73.9 ± 26.2 fmol/mg protein, respectively. These data indicate that the content of ER in CS does not depend on the type of involved bone. In 1 case with laryngeal cartilage involvement, CS contained 27 fmol/mg protein ER.

TABLE 2. Content of ER in CS of Different Size ($M \pm s$)

Tumor size, cm	ER ⁺ CS, %	Mean content, fmol/mg protein
<8	72.7	62.8 \pm 34.1
8.1-15.0	66.7	74.9 \pm 26.9
>15	56.2	98.3 \pm 41.3

In primary local process, ER were detected in 58.5% tumors (70.4 ± 19.1 fmol/mg protein). In 4 cases with generalized process the incidence of ER⁺ and ER⁻ tumors was the same (15-184 fmol/mg protein). ER were detected in 68.7% cases with relapses, their mean content being 64.0 ± 33.3 fmol/mg protein. The concentrations of ER in CS in patients with different types of tumor process were virtually the same.

Large CS were rarely ER-positive, and the level of ER in these tumors was higher (Table 2).

Delayed outcomes of treatment were analyzed in 58 patients with bone CS. There were no relationships between the incidence of metastases or relapses and the time of their manifestation in men and the presence of ER in tumors. ER were not detected in 14 patients. Metastases or relapses were detected in 57.1% of them over a period of up to 96 months. In patients with ER⁺ tumors this value was 60%.

Of 8 female patients with ER⁻ CS, metastases or relapses were detected in 37.5% patients over a period of up to 132 months. Of 10 patients with ER⁺ tumors, metastases or relapses occurred in 68.8%. The absence of ER in tumors in women is a favorable prognostic sign with regard to metastases or local relapses of CS.

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