Sof 04

OSTEONECTIN IS AN IMMUNOCYTOCHEMICAL MARKER OF OSTEOSARCOMA CELLS.

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90% of the protein components of bone matrix are composed of collagen type I while the noncollagenous protein content is only 10%. Collagen type I is a protein that is not bone specific because it is present in the extracellular matrix of various connective tissues. Among noncollagenous components osteonectin (Termine, J.D. et al: Cell 26, 99-105, 1981) is a bone specific protein linking collagen and mineral together. Since this protein is suggested to be produced by osteoblasts we concluded that it might represent a reliable marker for osteoblastic tumor cells. We studied this problems by immunocytochemistry using two polyclonal antibodies against bovine & human osteonectin in different bone and soft tissue deriving tumors (see table). Immunocytochemistry was performed in tissue sections of formaldehyd fixed paraffin embedded material by the PAP-method:

Tumor	Osteoblasts/ Osteocytes	Osteoid	non osteogenic tumor cells
Callus	+	+	-
Osteoid-Osteoma	+	+	-
Osteosarcoma	+	(+)	-
Chondrosarcoma	-	-	-
Ewing sarcoma	-	-	-
Fibrosarcoma	-	-	-
Leiomyosarcoma	-	-	-
Rhabdomyosarcoma	-	-	-

The results showed a positive reaction of the cytoplasm of osteosarcoma cells and benign osteoid producing cells by both antibodies (table). A positive reaction occurred even in matrix free parts of the tumor tissue. No reaction could be observed in cartilagenous or soft tissue tumors. The bovine osteonectin antibody was cross reacting with human osteonectin.

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Sof 05

THE EVALUATION OF ALKALINE PHOSPHATASE ISOENZYMES AND CORRELATION WITH BONE TUMORS, MAINLY RESPECTING THE BONE FRACTION OF ALKALINE PHOSPHATASE₂

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500 patients with increased alkaline phosphatase (AP) were investigated by a specific method of evaluation of the bone fraction. In case of increased AP - bone fraction clinical diagnosis and radiological findings were compared. 31 patients with bone tumors were subdivided according to alkaline phosphatase isoenzyme grouping. Even, when total AP was not increased, a significant increase in AP bone fraction was present with a corresponding decrease in the other fractions of AP. Alkaline phosphatase can be divided into 5 isoenzymes using electrophoresis and a specific way of staining the samples. The isoenzymes may be divided as follows: hepatic fraction, bone fraction and placental fraction in last trimester of pregnancy. Each fraction occupies a distinct place along the electrophoretic strip. Densitometry then provides a quantitative evaluation of the isoenzyme. The bone fraction alone is heat labile and disappears from the densitometry tracing at 39,5° C or above in approximately 95 % of cases. The same result could be found when bone tumors were taken after surgery and homogenized.

In conclusion: AP - isoenzyme examination is a valid screening method together with radiology and nuclear medicine to detect bone lesions even when visualisation is not yet possible at the time of presentation.

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Sof 06

MORPHOLOGICAL CHANGES IN PATIENTS WITH OSTEOSARCOMA AFTER CHEMOTHERAPY (RESULTS OF COSS 80/82)

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Since 1977, patients with primary osteosarcoma were treated with high-dose chemotherapy prior to definitive surgery (COSS therapy protocol). Patients and methods: In 213 surgical specimens the effect of preoperative chemotherapy on the primary tumor was noted and assigned a value (grade I-VI) according to the extent of tumor destruction of one complete tumor area attributable to chemotherapy as defined previously by Salzer-Kuntschik. In a separate series quantitative analysis of ground substance formation was performed in 58 resection specimens and 23 biopsies. Before fixation imprint cytologies were prepared. Distribution of nuclear size was determined by an image analysis system (IBAS). Results: 77 tumors (36%) showed a good effect of preoperative chemotherapy. 136 tumors (64%) responded badly to the chemotherapy. In the regression grades I-III (responder) the mean chondroid ground substance amounted to 5% of the entire tumor area. On the other hand the regression grades IV-VI (non-responder) showed a mean chondroid ground substance of 20%. These results correlate well with the distribution of chondroid ground substance in primary biopsies (n=23). The determination of nuclear size and polymorphism indicated that less differentiated osteosarcomas showed a better effect of preoperative chemotherapy on the primary tumor than higher differentiated ones. Conclusions: 1. Osteosarcomas with marked formation of chondroid ground substance (more than 25% of the tumor area) show a bad effect of preoperative chemotherapy on the primary tumor. 2. Possibly the effect of chemotherapy on the primary tumor can be predicted in the biopsies on the basis of the grade of differentiation and extent of chondroid ground substance.

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Sof 07

THE PROGNOSTIC VALUE OF THE GRADING FOR SOFT TISSUE SARCOMAS

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The management of soft tissue sarcomas is usually dictated in great part by size and the location of the tumor. Other factors with prognostic value are important in deciding the optimal treatment for a given patient. It is well known that certain histological types or subtypes of sarcomas have a slow clinical course and low metastatic potential, whereas other types characteristically exhibit a very aggressive course. To assess the impact of histological patterns on the clinical course we estimated the grading of 62 patients with soft tissue sarcomas. Our study is based on the grading system described by HAJDU. In contrary to the grading system of the American Joint Committee for cancer staging it confines on two grading types: The clinical data are summarized in Tab. 1

	low grade (n=22)	high grade (n=40)
Primarily localized tu. (T _{1,2} N ₀ M ₀)	17 (77 %)	14* (38 %)
Primarily advanced tu. (T _{3,4} N ₀ M ₀)	6 (27 %)	23* (62 %)
Radical operation	8 (36 %)	11 (27 %)
Metastases (synchron.)	1 (45 %)	19* (51 %)
Metastases (total)	4 (18 %)	27* (73 %)
Alive patients	15 (68 %)	10 (25 %)
Dead patients	5 (23 %)	30 (75 %)
Median survival (24 mo.)	not yet reached	11 months

* only 37 pts evaluable

In our series we found a striking difference for the incidence of recurrences and the overall survival between the low grade and the high grade group. In summary HAJDU's grading system is clinically relevant, satisfactorily reproducible and allows a prognostic prediction. There are hints that high grade sarcomas benefit from postoperative adjuvant chemotherapy. Therefore the estimation of the grading should be a mandatory part of the histological diagnosis.