Involvement of Chromosome 12 in Well-Differentiated Liposarcoma

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1 Introduction

It is well known that "accurate classification of a given tumor is often not easy, so much that acknowledged international experts are still unable to pin a label on about 10% of sarcomas" (Fletcher 1990). In this context, the characterization of new tumor markers is of paramount interest for the diagnosis, prognosis, and classification of soft tissue tumors (Sandberg and Turc-Carel 1987; Molenaar et al. 1989; Fletcher et al. 1991).

Next to malignant fibrous histiocytoma, liposarcoma is the most common soft tissue sarcoma of adult life (Enzinger and Weiss 1988). Adipose tissue tumors are the soft tissue tumors which are most extensively studied by cancer cytogeneticists. Cytogenetic data have been accumulated that correlate very well with histopathological forms. Specific reciprocal translocations (or less frequently other chromosomal changes) involving two different regions on chromosome 12 characterize myxoid liposarcoma with the t(12;16)(q13;p11) and lipoma with translocations at 12q13–14 (Sandberg 1990). A more distal breakpoint of the 12q13–15 region has also been found in subsets of tumors of different histological background, such as pleomorphic adenomas of the parotid gland (Bullerdiek et al. 1987; Mark et al. 1988), uterine leiomyomas (Heim et al. 1988; Turc-Carel et al. 1988; Vanni and Lecca 1988), chondromas (Mandahl et al. 1993). In contrast to the benign tumors with specific chromosomal aberrations at 12q13–15, the breakpoint for the malignant liposarcomas is located more proximally. As recently shown by Aman et al. (1992), myxoid liposarcomas have a rearrangement of the CHOP gene that is thought to be an essential step for tumorigenesis of the myxoid liposarcomas. In contrast to myxoid liposarcoma, the highly malignant pleomorphic liposarcoma is distinctively

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characterized by very high chromosome number counts (70–200), multiple, complex structural rearrangements, and translocated segments which, on most chromosomes, could not be identified (see references in Sreekantaiah et al. 1992).

Although no individual characteristic chromosome changes, either numerical or structural, have been found in well-differentiated liposarcoma (WDLPS), recurrent cytogenetic profiles distinguish them clearly from the other types of malignant or benign lipomatous tumors. Whereas the chromosome number is usually near-diploid, the most striking cytogenetic features are ring chromosomes (one to five copies), large markers with homogeneously stained regions or abnormal, banded regions known to represent cytologic pictures of DNA sequence amplifications, and random telomeric associations which give rise to apparently multicentric giant markers. These abnormalities can be seen together within a single metaphase, in addition to more classical structural chromosome abnormalities. By contrast, other cases show a very simple karyotype with only supernumerary large marker(s) or ring chromosome(s) in an otherwise normal metaphase (Karakousis et al. 1987; Sreekantaiah et al. 1992; Stephenson et al. 1992). In none of these cytogenetically studied WDLPS were the chromosomes at the origin of the rings or large markers identified, due to the difficulty in ascertaining the nature of complex changes by standard cytogenetic banding techniques. We have used fluorescent in situ hybridization (FISH) techniques with centromeric and whole chromosome painting (WCP) probes to tentatively characterize such markers in two cases of WDLPS as an example.

2 Material and Methods

2.1 Investigated Tumors

The tumor T131 was a large retroperitoneal mass (33 × 28 × 60 cm) surgically excised in November 1991 in a 60-year-old woman. The histology of this primary tumor was WDLPS from the lipoma-like subtype with dedifferentiated areas.

The tumor T132 was a local recurrence of a retroperitoneal mass originally diagnosed to be a WDLPS in April 1989. The recurrence excised in November 1991 (14 × 8 cm in size) was from the sclerosing subtype.

2.2 Standard Cytogenetic Analysis

The surgically removed specimens were processed according to Limon et al. (1986). After mechanical and enzymatic dissociation (collagenase Sigma