Cytogenetic heterogeneity and clonal evolution in bone and soft tissue tumors

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Cytogenetic clonal evolution in tumors, i.e., the sequential acquisition of chromosome aberrations, can be evidenced through analysis of samples from relapses of a tumor. Also the simultaneous existence of two or more clones in a tumor sample demostrates clonal evolution, and analysis of multiple samples from different arears of the same tumor not only increases the possibillity to detect different subclones, but also the possibility to identfy primary aberrations.

Cytogenetic heterogeneity was ealuated in bone and soft tissue tumors (BSTT) large enough to allow chromosomal analysis from more than one sample, and in recurrent tumors where samples from more than one occasion or location could be investigated.

Chromosomal aberrations were found in 136 samples from 50 BSTT. Cytogenetic heterogeneity was detected as more than one clone in the same tissue specimen in 36 of 136 samples (fraction 0.3), and as different clones in different samples from the same lesion in 23 of 29 informative tumors (fraction 0.8). The different clones were related in all but 5 of the 50 cases. Evolution in relapsing tumors could be evaluated in 12 cases, 10 of which were heterogeneous.

Thus, cytogenetic intratumor heterogeneity is more common than homogeneity in BSTT, and intersample heterogeneity is more frequent than intrasample heterogeneity.The abundance of intersample heterogeneity has implications for the interpretation of results obtained at cytogenetic analysis. It was also shown that increased karyotypic complexity parallels clinical and histiopathologic tumor progression. Ring chromosomes seem to characterize a subgroup of borderline or low malignant BSTT of different histiotypes, and probably represent early events in the development of malignant fibrous hisitiocytoma and pleomorphic liposarcoma. Loss of chromosome 13 and rearrangement of chromosome band 5q13 are candidate primary changes in chondrosarcomas. Cytogenetic analysis was also used to investigate the chronological relationship between cell population in primary tumors, local recurrences, and distant metastases. The findings indicate that cells from metastatic lesions may be the source of new metastases.