GENETIC IMBALANCES REVEALED BY COMPARATIVE GENOMIC HYBRIDIZATION IN EWING TUMORS

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** Backgrounds ** Ewing tumors (ETs) are characterized by reciprocal translocations involving the EWS gene on 22q12 fused to ETS transcription-factor family member. Little is known about further aberrations contributing to tumor development and progression.

** Methods ** Sixty-two frozen tumors with known EWS rearrangements (52 primary tumors, 10 relapses) of ET patients registered in the EICESS protocol were analyzed by comparative genomic hybridization (CGH).

** Results ** Average number of changes in 52 primary cases and 10 relapsed cases was 3.6 and 4.7 per tumor (p=0.153). Frequent gains of chromosomes included 8, 12, 20, and 1q and losses of 16q and 19q (Fig. 1). Neither number nor type of aberration was associated with histology, tumor size, disease stage, tumor localization, or histological effect. In 52 primary tumors, 26 tumors with type I fusion (EWS exon 7 to FLI1 exon 6) and 26 tumors with other fusion type had an average 2.4 and 4.8 aberrations per tumor, respectively (p=0.031) (Fig. 2). Combination of gains of 8 and 12 (7 cases), losses of 16q and 17p (7 cases), and gains of 8q and 20 (7 cases) frequently occurred. The cumulative overall survival (OAS) was different between 35 patients with aberrations <5 and 13 patients with aberrations ≥5 (p=0.006) (Fig. 3).

Univariate analysis showed those patients with gains of 1, 2q, 3q, 6, or 15q or losses of 10, 11p, 13q, 16, 17 had significantly lower OAS than those without aberrations. By multivariate analysis, losses of 16q (p=0.002) and 11p (p=0.002) were independent prognostic factors.

** Conclusions ** The number of genetic imbalances correlates with OAS in ETs. Furthermore, EWS/FLI-1 type-I tumors carry significantly lower numbers of aberrations. Our results underline the biological impact of the 22q12 rearrangement in the development of ETs.

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**Fig. 1** Chromosomal aberrations of ETs by comparative genomic hybridization. Complete lines means the primary cases and dotted lined lines means the relapsed cases.

**Fig. 2** Number of chromosomal aberrations in 26 cases with type I fusion gene transcript and 26 cases with type II fusion gene transcript.

**Fig. 3** Overall survival according to the number of aberrations (<5 or ≥5)