Proffered Papers

Lung cancer

1027 ORAL

Distinct patterns of chromosomal imbalances in adenocarcinoma and squamous cell carcinoma of the lung

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Purpose: To detect chromosomal imbalances that are associated with tumor differentiation in non-small cell lung carcinomas.

Methods: Comparative Genomic Hybridization (CGH) was used to screen 25 adenocarcinomas and 25 squamous cell carcinomas (SCC). For the first time, the differences between both tumor groups was visualized by a histogram and evaluated for statistical significance by Chi square test.

Results: DNA copy number decreases common to both entities and detectable in more than 50% of cases were observed on chromosomes 1p, 3p, 4q, 5q, 6q, 8p, 9p, 13q, 18q and 21q. Similarly, DNA gains were observed for chromosomes 5p, 8q, 11q13, 16p, 17q and 19q. Adenocarcinomas showed more frequently overrepresentations of chromosome 1q and DNA losses on chromosomes 3q, 9q, 10p and 19 whereas SCC were characterized by increased overrepresentations of chromosome 3q and 12p as well as deletions of 2q. The difference histogram of both entities and the statistical analysis indicated that the overrepresentation of the chromosomal band 1q23 and the deletions at 3q27–28, 9q22, 9q32–33, 9q34, 10p13, 19p13.3 and 19q13.2 were significantly associated with adenoid differentiation. Accordingly, the DNA loss of chromosomal band 2q36–37 and the overrepresentations at 3q21–22, 3q24-qter were statistically significant markers for the squamous cell type.

Conclusion: The study strengthen the notion that distinct patterns of chromosomal changes are prevalent in different tumor subtypes which will help in the development of a genetic grading and classification system of lung carcinomas.

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Lung cancer – Prognosis and classification

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Purpose: In lung cancer anatomical tumor spreading is an important prognostic factor and is classified by the worldwide uniform TNM classification. The data of 5,155 patients were analysed prospectively to examine the prognostic impact of the new 5th edition (1997).

Methods: These 5,155 patients entered the Thoraxklinik Heidelberg between January 1, 1988 and December 31, 1994 (date of last follow-up: December 31, 1996).

Results: The new substages IA and IB of the 5th edition could be validated referring to the clinical and the pathological staging ($p = 0.003$), $p = 0.001$), but no significant difference revealed after comparing the new stages IB and IIA. The prognosis of the new substages IIA and IIB was of significant difference in the clinical ($p = 0.049$), but not in the pathological classification ($p = 0.114$). All other comparisons of the new stages (IIB vs. IIIA, IIIA vs. IIIB and IIIB vs. IVB) were significant.

Conclusions: The the new 5th edition did satisfy most but not all requirements for an optimal prognosis-relevant classification. Some proposals for improvements are made.

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Detection of disseminated tumor cells in bone marrow of patients with resectable non-small cell lung cancer (NSCLC) – Long term results after 5 years of follow-up

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Introduction: By using immunocytochemical analysis an early dissemination of tumor cells into the bone marrow has been described in patients with apparently resectable NSCLC. However, the significance of this finding for the long term prognosis of patients with NSCLC is not known.

Methods: At primary surgery disseminated tumor cells in the bone marrow were detected immunocytochemically in 139 patients with NSCLC using a monoclonal antibody against the cytokeratin No. 18. After a median follow up of 60 months the influence of disseminated tumor cells in the bone marrow on disease-free and overall survival was analyzed.

Results: Cytokeratin positive cells were detected in 83 of 139 (59.7%) patients with no significant differences with respect to standard clinico-pathological parameters. In contrast to patients with lymph node involvement, in patients with early tumor stages (pN0) the detection of disseminated tumor cells in bone marrow was a strong and independent predictor of a shortened disease free ($p = 0.005$) and overall survival ($p = 0.018$).

Conclusions: In patients with apparently localized NSCLC the detection of disseminated tumor cells in bone marrow might be a useful indicator for the requirement of an adjuvant therapy.

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Possible negative impact on survival of too short an interval between surgery and postoperative radiotherapy in NSCLC

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Purpose: To evaluate the influence of prognostic factors in postoperative radiotherapy of NSCLC with special emphasis on the time interval between surgery (SX) and start of radiotherapy (RT).

Methods: A retrospective analysis of 340 cases with a median time interval between SX and RT of 36 days was performed. 230 patients (68%) had N2-disease; 228 patients were completely resected (R0).

Results: Patients with a long interval (37 to 84 days) had higher 5 year survival rates (26%) and median survival time (MST: 21.9 months, 95% C.I. 17.2 to 28.6 mo.) than patients with a short interval (18 to 36 days: 15%; 14.9 mo., 13 to 19.9 mo.; $p = 0.013$). A subgroup analysis revealed significant higher survival rates in patients with a long interval in N0/1 disease ($p = 0.011$) and incompletely resected NSCLC ($p = 0.012$). In multivariate analysis, time interval had a P-value of 0.009 (nodal disease: $p = 0.0083$; KPI: $p = 0.0037$; gender: $p = 0.035$).

Conclusion: Shortening the time interval between SX and RT to less than 6 weeks is not necessary and might even be deleterious.

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Long-term survival after complete response to chemotherapy in small cell lung cancer depends on cytokine secretion capacity at diagnosis

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Purpose: Suppression of Interleukin-2 (IL-2) secretion is mediated by Transforming growth factor (TGF) β1 secreted by small cell lung cancer