168

COMBINED CHEMOTHERAPY IN PLEURECTOMIZED MALIGNANT PLEURAL MESOTHELIOMA PATIENTS

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In malignant pleural mesothelioma (MPM) patients, a better prognosis was reported with combined modalities of chemotherapy and palliative surgery. We planned a study in which a scheme of mitomycin (M) 10mg/m² IV, cisplatin (C) 50 mg/m² IV, α-interferon (I) 20 mIU would be administered to our pleurectomized MPM patients. Mean chemotherapy cycles was 4.5(range: 2-6). 20 MPM patients were given MCI protocol after being pleurectomized. There was neither complete nor partial response with this therapy. 15 patients were stable during the treatment course and a progressive disease status was observed in 5 patients. The median response duration of stable patients was 6 months (range:3-15) and the median survival was 15 months (range:4-31). In our progressive patients, the median survival was 5 months(range:3-13).The overall survival was calculated with Kaplan-Meier survival analysis method. The overall survival rate was 69%(95% confidence limit, 47-90%) in the first year and 33%(95% confidence limit, 9-56%) in the second year. A tolerable toxicity was observed with MCI protocol. In our interm analysis, we concluded that our two modal therapy was not superior to single modal therapy.

169

HYPERFRACTIONATED RADIATION THERAPY (HFX RT) WITH AND WITHOUT CONCURRENT CHEMOTHERAPY (CT) FOR STAGE III NON-SMALL CELL LUNG CANCER (NSCLC)

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In order to improve poor survival figures obtained with RT alone,169 pts with Stage III NSCLC underwent : group I-HFX RT to a total tumor dose (TD) of 64.80 Gy(61 pts); group II-HFX RT to the same TD with 100 mg of CBDCA,days 1 and 2 and 100 mg of VP 16,days 1-3,given every week during the RT course(52 pts),and group III-HFX RT to the same TD with 200 mg of CBDCA,days 1 and 2 and 100 mg of VP 16,days 1-5,given during the first,third and fifth weeks of RT course(56 pts).Pts in group II had significantly longer MST(18 months) and 1-,3-,and 5-year survival(73%,23%,and 21%,respectively) than those in group I(8 months,39%,6.6%,and 4.9%,respectively;p=0.0027) but not significantly different from those in group III (13 months,50%,16%,and 16%,respectively;p=0.06089), and with no difference between groups I and III(p=0.3313). Pts in groups II and III experienced higher incidence of both acute and late high grade toxicity,but no patient died of treatment-related toxicity.This study showed acceptable toxicity and substantially increased survival in pts treated with HFX RT and more continuous CT.

170

ALTERATIONS OF PARENCHYMAL α1-ADRENERGIC RECEPTORS IN HUMAN LUNG ADENOCARCINOMA

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The adrenergic part of the autonomic nervous system is involved in the pathogenesis of lung diseases; however, this was not investigated in lung cancer. In the present study α1-adrenergic receptors have been investigated in human lung parenchyma, obtained at the resection of tuberculoma patients within the normal tissues limits and the resection of adenocarcinoma patients. The Scatchard analysis indicated that α1-adrenergic sites markedly increased in the cancer lung-membrane preparation (control- Bmax= 270±85 fmol/mg; cancer-Bmax=1049±117 fmol/mg), including membranes of bronchioli, alveoli as well as blood vessels. The increase of α1-adrenoceptors activity may lead to a strong vascular smooth muscle contraction in lung cancer parenchyma and may result in a prevention of metastasis from a primary growth. The results suggest cancer-induced enhancement in parenchymal α1-adrenergic activity involved in the regulation of metastasis.

171

PROGNOSTIC FACTORS IN SMALL CELL LUNG CANCER

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The objective of this study was identify significant prognostic factors which can influence in overall survival of small cell lung cancer (SCLC) patients (pts). We reviewed 183 pts with SCLC between December 1981 and September 1992. Median age was 60.4 years (range 32-86). 174 men and 10 women. 81 pts (44.3%) had 0-1 ECOG performance status. 69 pts (37.7%) were limited stage disease (LSD) and 114 (62.3%) were extensive stage disease (ESD) at diagnosis. Central nervous system (CNS) infiltration was observed in 17 (9.3%). 21 were not treated, one underwent palliative radiotherapy, two pts with stage I (UICC) recieved surgery as first treatment and 161 underwent combination-chemotherapy regimens (in 101 the regimen included cisplatin).154 pts. were evaluable for response:33 (21.4%) achieved complete response (CR) and 48 (31.2%) partial response (PR). Stage disease response: LSD: 21 CR (36.2%); 15 PR (25.9%); ESD: 12 CR (12.5%), 33 PR (34.4%). The median survival was 34.5 weeks (w) (23.3 in ESD and 52.5 in LSD). 14 pts were alive after 2 years and there are 4 survivors at the end of the study for 294+, 307+,320+ and 468+ (all of them LSD: 1 treated with surgery initially, 3 recieved consolidation thoracic radiotherapy and all underwent prophylactic cranial irradition).Univariant analyses identified the following features with prognostic significance in relation with overall survival: age <65 vs>65 (p=0.05); ECOG: 0-1 vs 2-4 (p=0.0001); stage:LSD vs ESD (p=0.0001); first chemotherapy:regimens with CDDP vs no CDDP (p=0.0001); response:CR vs no CR (p=0.0001); serum albumin: normal vs low (p=0.002); LDH levels: normal vs high (p=0.0216). In the multivariable analysis using Cox's regression model, response to treatment, clinical stage and LDH level were proven to be significant prognostic factors for survival in the order of importance.

172

RADIATION THERAPY OF PROGRESSIVE BRONCHIAL CARCINOMA IN 1988 - 92

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Between 1988 and 1992 we treated 244 patients with non-squamous-cell bronchial carcinoma stage III and IV.
With single doses of 2 Gy a day we applied a total tumor dose of 60 Gy in 58% patients, in 27% the total dose ranged from 40 to 60 Gy. For patients with stage III tumors (n=170) the mean survival time was 7.5 months, with stage IV tumors (n=74) 5.2 months.
Most important survival parameters were the Karnofsky-index (p<0.0001), the amount of weight loss before therapy (p<0.0001), the value of LDH before therapy (p=0.0003), the total tumor dose (p<0.0001), the T-stage (p<0.0001) and the N-stage (p=0.004). There was only a slight influence of the proved presence of distant metastases on prognosis (p=0.04).
Surgical treatment of primary tumors in stage III appeared to have a favourable influence on prognosis (p<0.0001, 1-year-survival 50% vs. 18% in not operated cases). Most probably these figures are highly influenced by pre-operative selection of patients: the mean Karnofsky-index of the operated patients was 75% (vs. 68%) and there were clearly better T-stages among this group (44% vs. 18% stage T1/T2).
Comparing the non-operable Tumors stage III with stage IV tumors there was no significant difference in prognosis. We should consider these Patients incurable and treat them accordingly.

173

TUMOR MARKERS IN LUNG CANCER: SUPERIORITY OF CYFRA21-1 TO CEA AND SCC-Ag

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75 patients (pts) with operable non-small cell lung cancer (NSCLC) and 48 with pulmonary benign disease were tested for CYFRA 21-1 (IRMA-CIS bio), carcino-embryonic antigen - CEA and squamous cell carcinoma antigen - SCC-Ag (both MEIA- ABBOTT). Sensitivity and specificity were better for CYFRA 21-1 (57% and 96%), than for CEA (51% and 90%) and SCC-Ag (47% and 92%). Only CYRA 21-1 values related significantly to TNM stage. In 16 of 75 pts who survived complete resection, recurrence were subsequently detected. The percentage of recurrence in pts with normal postoperative markers levels was: 6.2% for CYFRA 21-1, 25% for CEA and 19% for SCC-Ag. The increase of the markers in relation to recurrence disease (RD) is demonstrated in the table.

Increase of markers	CYFRA 21-1	CEA	SCC-Ag
Increased at RD	3/15(20%)	6/12(50%)	6/13(46%)
Increased before RD	12/15(80%)	6/12(50%)	7/13(54%)
Lead-time (months)			
median	3.1	2.5	2.6
range	2-6	2-4	2-4

Increase of CYFRA 21-1 before RD was observed in 80% (CEA in 50%, SCC-Ag in 54%) with a median lead-time of 3.1 months. In conclusion, CYFRA 21-1 proved to be the most useful marker for NSCLC.