602 Poster

Tumor markers in lung adenocarcinoma-associated cytologically negative pleural effusions

C.C. Su[1], W.W. Huang[2], S.M. Tsao[3], C.L. Lai[4], C.E. Tseng[4]
[1]Buddhist Dalin Tzu Chi General Hospital, Department of Clinical Pathology, Chiayi County, Taiwan; [2] Buddhist Dalin Tzu Chi General Hospital, Department of Family Medicine, Chiayi County, Taiwan; [3] Chung Shan Medical University Hospital, Division of Chest Medicine Department of Internal Medicine, Taichung, Taiwan; [4] Buddhist Dalin Tzu Chi General Hospital, Division of Chest Medicine Department of Internal Medicine, Chiayi County, Taiwan

Background: Cytology fails to detect neoplastic cells in approximately 40–50% of malignant pleural effusions, which commonly accompany lung adenocarcinomas. Diagnostic accuracy of various tumor markers in lung adenocarcinoma-associated cytologically negative pleural effusions has been poor. This study aimed to maximize diagnostic efforts in distinguishing lung adenocarcinoma-associated cytologically negative pleural effusions from benign pleural effusions.

Materials and methods: Pleural effusion samples were collected from 74 lung adenocarcinoma patients with associated cytologically positive (41) and negative (33) effusions, and from 99 patients with benign conditions including tuberculosis (26), pneumonia (28), congestive heart failure (25), and liver cirrhosis (20). We evaluated the diagnostic sensitivity, specificity and optimal cutoff points for tumor markers Her-2/neu, Cyfra 21-1, and carcinoembryonic antigen to distinguish lung adenocarcinoma-associated cytologically negative pleural effusions from benign pleural effusions.

Results: The cutoff points for Her-2/neu, Cyfra 21-1 and were optimally set at 3.6 ng/mL, 60 ng/mL, and 6.0 ng/mL; and their accuracy levels ranged from 73.48%, to 81.06%, to 90.91%, respectively. Carcinoembryonic antigen combined with Cyfra 21-1 increases diagnostic sensitivity to 66.7%. False-positive rates of these markers in benign effusions were 6.1%, 2.0% and 0%, respectively.

Conclusions: Ours is the largest known study, describing 33 cases. Combining carcinoembryonic antigen with Cyfra 21-1 will provide the best differentiation between lung adenocarcinoma-associated cytologically negative pleural effusions and benign pleural effusions with two tumor markers to date, and allows early diagnosis and early treatment for two-thirds of affected patients.

603 Poster

Biological prognostic factors for disease free survival in breast cancer patients treated with adjuvant anthracycline chemotherapy

B. Biesaga[1], J. Niemiec[1], Z. Ziobro[2], J. Wysocka[3], A. Kruczak[3]
[1]Maria Sklodowska Curie Institute, Department of Radiation Biology, Krakow, Poland; [2] Maria Sklodowska Curie Institute, Department of Medical Oncology, Krakow, Poland; [3] Maria Sklodowska Curie Institute, Department of Pathology, Krakow, Poland

Background: In about 60 % of breast cancer patients ((T1-T2, N1-N2, M0) after surgery and adjuvant treatment with anthacyclines local reccurance is observed. These differences in treatment outcome indicate the need to identify biological markers for probability of patients' disease free survival (DFS). The aim of this study was to assess the influence of tumour proliferation rate, microvessel density (MVD), apoptosis level, expression of HER-2, oestrogen (ER) and progesterone (PR) receptors, and expression of topoisomerase II (TOPOII) and P53 protein on 5-year DFS in the group of breast cancer patients treated radically with surgery and adjuvant chemotherapy with anthracyclines.

Material and methods: The study was performed in the group of 94 breast cancer patients (mean age: 50.5 years; range: 27 – 69). Proliferation rate (labelling index of Ki-67 - Ki-67LI), MVD (CD34 antibody) and expressions of HER-2, ER, PR and P53 protein were studied immunohistochemically before treatment. These data were correlated with DFS estimated by Kaplan-Meier method. Data concerning apoptosis level and expression of TOPO II will be presented during the conference.

Results: Among 94 tumours, 83.9% were positive for ER, 82.8% expressed PR and in 48.0% expression of HER-2 was detected. The mean values of Ki-67LI, P53LI and MVD were 23.0% ±1.3 (SE), 10.1%±3.4 and 156.0 vessels/mm2±6.6, respectively. All women (n=13) with tumours characterized by positive expression of ER and higher proliferation rate (optimal cut off point Ki-67 LI >16.5%) survived 5 years without any evidence of cancer, whereas in patients having slower proliferating tumours and lack of oestrogen expression, DFS was significantly lower (40.0%; p=0.003). No other significant relation was found between the assessed biological parameters and DFS.

Conclusion: On the basis of oestrogen status and tumour proliferation rate, we are able to identify breast cancer patients without risk of cancer progression during 5 years after completing of anthracycline treatment.

This study is supported by Polish Ministry of Education and Science; grant number N401 173 31/3808.

604 Poster

Hormonal regulation of breast cancer associated chemokines

S. Potter[1], R.M. Dwyer[2], E. Hennessy[1], D.G. Griffin[3], M.J. Kerin[1]
[1]Department of Surgery Clinical Science Institute, National University of Ireland Galway, Co Galway, Ireland; [2] Department of Surgery and Regenerative Medicine Institute, National University of Ireland Galway, Co Galway, Ireland; [3] Department of Clinical Biochemistry, University Hospital Galway, Co Galway, Ireland

Introduction: Chemokines such as Stromal Cell-Derived Factor-1a(SDF-1a) and Monocyte Chemotactic Protein-1 (MCP-1), are chemotactic cytokines that have been implicated in breast cancer progression. This laboratory previously reported elevated systemic levels of SDF-1a and MCP-1 in breast cancer patients. In the case of SDF-1a, these elevated levels correlated with clinical prognostic indicators including tumour grade and epithelial subtype. The aim of this study was to investigate potential regulation of circulating chemokines by endogenous hormones, as knowledge of these regulatory mechanisms is essential for chemokines to be valid targets in breast cancer management.

Methods: Plasma and serum samples were collected from 36 premenopausal healthy females, on a weekly basis for four consecutive weeks, i.e. 144 samples in total. Measurement of Follicle Stimulating Hormone (FSH), Luteinizing Hormone (LH), Oestradiol and Progesterone were preformed using a Bayer ADVIA® Centaur Immunoassay system. Simultaneous measurements of plasma SDF-1a and serum MCP-1 were performed using ELISA. Demographic data including age, date of last menstrual period and current medications was also collected on each volunteer.

Results: Menstrual cycles of all subjects were found to be ovulatory, that is, each showed an LH surge followed by an appropriate mid-luteal peak of Progesterone. Nine patients were taking an oral contraceptive pill at the time of the study, and this was found to have no influence on SDF-1a and MCP-1 levels. Plasma SDF-1a was significantly lower in the mid-luteal phase (2157 ± 60 pg/ml, $p<0.05$) than other phases of the menstrual cycle, late luteal/early follicular (2387 ± 69 pg/ml), mid-follicular (2267 ± 65 pg/ml), and mid-cycle (2349 ± 71 pg/ml). SDF-1a displayed a significant positive correlation with Oestradiol ($r =0.213$, $p<0.05$) throughout the cycle. MCP-1 levels did not differ significantly across the menstrual cycle and did not show any significant correlation to menstrual hormones.

Conclusion: The results presented here are an important first step in elucidation of the relationship between menstrual hormones and chemokines, which play an important role in breast cancer progression. Further understanding of the mechanisms of control, and mode of action of these chemokines, will support development of novel therapeutic strategies and may influence timing of surgical intervention for premenopausal breast cancer patients.

605 Poster

Diagnosis value of EGFR gene expression for early diagnosis in oral leukoplakias

G. Aparicio Gallego[1], S.m. Díaz Prado[2], V. Medina Villaamil[1], L.m. Antón Aparicio[2], J.l. López Cedrún[3], X. Collado López[3], M. Valladares Ayerbes[4], R. García Campelo[4], I. Santamarina Caínzos[1], M. Haz Conde[1]
[1]Complejo Hospitalario Universitario Juan Canalejo, Unidad De InvestigaciÓn, Coruna, Spain; [2] Universidade Da Coruña, Dpto. Medicina, Coruna, Spain; [3] Complejo Hospitalario Universitario Juan Canalejo, Servicio Cirugía Maxilofacial, Coruna, Spain; [4] Complejo Hospitalario Universitario Juan Canalejo, Servicio De Oncologia Médica, Coruna, Spain

Background: Field cancerization theory has been proposed as an explanation for the increased risk of transformation in upper airway-digestive tract. Oral cancer development involves several steps previously to malignant progression through increasing levels of dysplasia as a result of the accumulation of diverse genetic alterations. Oral premalignant lesions include leukoplakias. Since there is evidence that EGFR participates in tumorigenesis, according to analysis of RNA and protein from squamous cell carcinoma (SCC) mucosa, routine molecular study of EGFR gene expression would contribute to an improved diagnosis and treatment of premalignant oral epithelial lesions. Objective: Study the utility of EGFR gene expression as diagnosis factor in oral leukoplakias by means of Quantitative Real Time PCR (qPCR). Materials and Methods: Expression levels of EGFR gene, in 20 unique freeze samples from 20 patients with leukoplakia, were measured. From each patient, 2 samples were obtained: opposed lateral oral mucosa and leukoplakia mucosa. As control, a pool of healthy human oral mucosa from healthy donors (n=4) was used. Quantitative Real Time PCR (qPCR) experiments were performed on a LightCycler 480 Instrument (Roche) using LightCycler 480 SYBR Green I Master (Roche). A constitutively expressed gene, HPRT, was used as internal control. Results: The expression levels of EGFR were higher in opposed lateral oral mucosa and leukoplakia both from patient,