1455 POSTER

EGFR and KRAS Gene Mutations in Lung Adenocarcinomas and Their Associations With Smoking in Turkish Patients

A. Guven Mert[1], P.F. Yumuk[1], M.A. Ozturk[2], F. Dane[1], S. Evman[3], M. Yuksel[3], C. Celikel[4], Z. Kucukodaci[5], H. Baloglu[5], N.S. Turhal[1]. *[1]Marmara University, Medical Oncology, Istanbul, [2]Istanbul University Cerrahpasa Faculty of Medicine, Medical Oncology, Istanbul, [3]Marmara University, Thoracic Surgery, Istanbul, [4]Marmara University, Pathology, Istanbul, [5]GATA Haydarpasa Training Hospital, Pathology, Istanbul, Turkey*

Background: EGFR and KRAS are the most frequently mutated protooncogenes in adenocarcinomas of the lung. Their incidences varies widely between Western and East Asian countries. The aim of this study is to reveal EGFR and KRAS gene mutations and their assosiations with smoking in Turkish lung adenocarcinoma patients.
Materials and Methods: EGFR gene copy numbers, EGFR gene exon 19, 21 mutatitons, KRAS codon 12, 13, 61 mutations were assessed in 22 patients with adenocarcinoma of the lung. All patients were surgically resected, treated and followed-up at Marmara University Medical School and 5 patients with synchronous, solitary brain metastasis were treated with gamma knife stereotactic radiosurgery. EGFR gene copy numbers were assessed by fluorescence in situ hybridization and mutations were determined by DNA sequencing. The frequency and type of KRAS codon 12, 13 and 61 mutations were analyzed by pyrosequencing. The associations between EGFR and KRAS and patients' demographical characteristics, smoking history, histopathological features, TNM stage, overall and disease free survival were revealed.
Results: Median age was 60 (range 36–82) and 4 were female. Three of these females never smoked cigarettes while 41% were current smokers. Median follow-up was 25.6 months. Median overall survival was not reached. There were no significant association between the demographical features, smoking history of the patients and EGFR gene amplification, EGFR and KRAS gene mutations. EGFR gene amplification was found in a patient who was current smoker, but this was not accompanied with activating EGFR mutation in the tyrosine kinase domain. EGFR exon 19 deletion was found in a never smoker female who also had KRAS codon 13 mutation. Patients with KRAS mutations were significantly less likely to have vascular invasion in their primary tumours than patients without KRAS mutations ($p = 0.011$). KRAS mutations were identified in 27% of all patients. All the mutations were G > T transversions except for a never smoker who had a transition mutation (G > A). There were no significant difference between patients' overall and disease free survivals in regard of EGFR gene amplification, EGFR and KRAS gene mutations.
Conclusion: Although patients recruited in our study were generally heavy smokers, similar percentage of KRAS mutations were seen as the world's literature. Although it has been reported that EGFR and KRAS mutations are "mutually exclusive" in early studies by significant amount of researchers, they can be coincidently found.

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Molecular Diagnostic Strategy to Identify Families With Hereditary Non-polyposis Colorectal Cancer Syndrome

O. Kostina[1], E. Rebane[1], M. Kask[1], W. Anderson[1]. *[1]Competence Centre for Cancer Research, Diagnostics, Tallinn, Estonia*

Background: Hereditary non-polyposis colorectal cancer (HNPCC), also called Lynch syndrome, is an autosomal dominantly inherited syndrome predisposing to the early development of cancers of colon, rectum, endometrial, small bowel and urinary tract and accounts for ~3% of all colon cancer cases. The most HNPCC families are associated with constitutional mutations in a class of genes (called *MLH1, MSH2, MSH6, PMS2* and probably others) involved in DNA mismatch repair. The large genomic deletions explain a proportion and epimutations in *MLH1* promotor a smaller fraction of point mutation-negative cases with MMR protein loss in tumour tissue. The aim of the study is to improve the diagnostic strategy of Lynch syndrome and characterize the MMR gene mutations of Estonian HNPCC families.
Methods: A systematic analysis of patients from Estonian HNPCC-suspected families is performed using complex analysis by immunohisto-chemistry, microsatellite instability and by detection of gene mutation. Additionally analysis of mutational spectrum and changes in methylation profiles of tumours is used in differential diagnostics of hereditary colorectal cancer and in prognosis for cancer outcome.
Results: A comprehensive analysis of samples from 100 HNPCC-suspected patients is ongoing, we will present preliminary results.
Conclusion: Based on traditional molecular genetics and combined with epigenetics, multiple detection methods can accurately diagnose HNPCC. As the results of the study, the precise molecular diagnostic scheme for diagnosing of HNPCC will be worked out for clinical use in Estonia.

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The Clinical Significance of CRP and Serum Albumin in Primary Lung Cancers

N. Tsoukalas[1], T. Oikonomaki[2], M. Tolia[2], A. Tzovaras[3], A. Papakostidi[2], N. Pistamaltzian[3], A. Ardavanis[3], V. Barbounis[3], S. Theocharis[2], K. Liaskonis[4]. *[1]401 General Army Hospital, Medical Oncology, Athens, [2]National and Kapodistrian University of Athens, Medical School, Athens, [3]Aghios Savvas Anticancer Hospital, Medical Oncology, Athens, [4]401 General Army Hospital, Biochemistry Laboratory, Athens, Greece*

Background: CRP and serum albumin are indicators of systemic inflammatory reaction and the status of patient's nutritional condition respectively. It has been found that CRP has a prognostic value in advanced neoplasms of various types while its combination with serum albumin has additional prognostic value in certain tumours.
Material and Methods: Patients with primary lung cancer and no active infection were included in the study. The diagnosis of the neoplasm was made by means of histology or cytology. A blood sample was taken prior to any therapeutic intervention. The samples were centrifuged and the serum was stored in deep freezer until the measurement. CRP and albumin were assessed using nephelometry and photometry respectively. Finally, a database was created with all the clinical and histological data of the patients.
Results: Overall, 129 patients (114 men and 15 women) with a mean age of 64 years were assessed. The histology types were: 79% non small cell and 21% small cell neoplasms. Associations between variables were analyzed by the application of Univariate Analysis Of Variance with SPSS v15.0 software (SPSS Inc., Chicago, IL, v.15.0). Two tailed p values $\leqslant 0.05$ were considered to be statistically significant. Statistical significance was identified correlating lower albumin's values to stage IV of the tumours (p-value 0.027) and to the age of patients (p-value 0.021). Moreover, statistical significance was identified correlating higher CRP's values to stages IIIB (p-value 0.010) and IV (p-value 0.016) and to grade III (p-value 0.024). Also, there is a trend of CRP increase in correlation with some TNM characteristics (T4, N2, N3, M1β) and performance status 2.
Conclusions: The most important conclusions of this study are that there is a correlation between lower albumin and metastatic disease or elderly patients and that higher CRP correlates with advanced or metastatic disease and grade III tumours.

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Dynamic Follow-up of Plaque Type Mycosis Fungoides With Reflectance Confocal Microscopy Of: a Preliminary Study in Chinese Cases

M. Gao[1], H.X. Liu[2]. *[1]Shandong Cancer Hospital & Institute, Radiation Physics, Jinan Shandong, [2]Shandong Provincial Institute of Dermatology and Venereology, Skin Imaging, Jinan Shandong, China*

Objective: Our aim was to dynamically investigate Mycosis fungoides(MF) lesions using in vivo reflectance confocal microscopy (RCM) and to evaluate whether RCM could be used in the follow-up of MF.
Methods: After written informed consent obtained, a total of 7 lesions from 7 patients with a history of biopsy-proven MF were enrolled in the study. The lesions were imaged with RCM monthly for 6 times followed each time by a skin biopsy. Then the images of RCM were correlated with the HE images. The dynamic changes of cell infiltration in epidermis and superficial dermis is highly concentrated.
Results: In plaque-type MF lesions, at the level of the epidermis, the weakly refracted oval to round structures on RCM images corresponded to epidermotropic lymphocytes on histopathology, and vesicle-like dark spaces filled with collections of monomorphous weakly refracted oval to round cells corresponded to Pautrier's microabscesses on histopathology. During the treatment, 5 of the 7 cases showed dynamic reduction of monomorphous cells in epidermis and superficial dermis, while the other 2 cases showed no significant changes about the monomorphous cells in epidermis, which correlated well with the histopathology results.
Conclusion: Features correlating well to histopathology are observed on dynamic RCM of MF lesions, and the RCM could be used in the dynamic evaluation of MF lesions during the treatment, which may provide a new, non-invasive method for MF follow-up. However, because of the limited imaging depth, the RCM could not be used in the follow-up of the dynamic changes of the deep dermis.