INCIDENCE OF CYTOMEGALOVIRUS INFECTION IN NSCLC CYTOLOGY

HARABAJSA S., Šefčić H., Vrabec Branica B., Šimić V., Milavić M., Židovec Lepej S., Badovinac S., Jakopović M., Smojver-Ježek S., Korač P.

1 University Hospital Centre Zagreb, Zagreb, Croatia
   Department of Pathology and Cytology, Division of Pulmonary Cytology Jordanovac

2 Faculty of Science, University of Zagreb, Zagreb, Croatia
   Department for Biology, Division of Molecular Biology

3 School of Medicine, University of Zagreb, Zagreb, Croatia
   Institute of Pathology

4 University Hospital for Infectious Diseases Zagreb, Zagreb, Croatia
   Division of Immunology and Molecular Diagnostics

5 University Hospital Centre Zagreb, Zagreb, Croatia
   Department of Respiratory Diseases Jordanovac

6 School of Medicine, Zagreb, Croatia
   University of Zagreb

Aim: Presence of human cytomegalovirus DNA (HCMV) in lung cancer cells may alter the activity of cellular proto-oncogenes or tumor suppressor genes which further can result in cancer development
as well as modulation of response to the cancer treatment. Aim of this study was to determine the incidence of HCMV infection in non-small cell lung cancer (NSCLC) cytology.

**Methods:** This study included 67 NSCLC cytological smears and their DNA isolates from newly diagnosed lung cancer patients hospitalized at the Department of Respiratory Diseases Jordanovac, University Hospital Centre Zagreb. The cytological smears were from samples obtained during bronchoscopy, fine needle aspirations and pleural effusions. The DNA was extracted from NSCLC cytological smears stained by May Grünwald Giemsa staining. The two years retrospective analysis included 34 NSCLC with *EGFR* gene mutations and 33 NSCLC without *EGFR* gene mutations. Specific fragments for glycoprotein B (*gB*) and immediate-early (*MIE*) gene of HCMV were amplified by polymerase chain reaction method.

**Results:** Among 34 NSCLC with *EGFR* mutations were 14 males (41,2%) and 20 females (58,8%). Among 33 NSCLC without *EGFR* mutations were 13 males (39,4%) and 20 females (60,6%). The median age of both groups was 69 years. Among NSCLC with *EGFR* mutations were 24 non-smokers, 8 smokers (including ex-smokers), and two with no smoking status. Among NSCLC without *EGFR* mutations were 23 smokers (including ex-smokers) and 10 non-smokers. The HCMV *MIE* gene was detected in: 13 (38,2%) samples of NSCLC with *EGFR* gene mutations, in one (12,5%) smoker and 11 (45,8%) non-smokers, four (28,6%) males and nine (45,0%) females. The HCMV *MIE* gene was not detected in samples without *EGFR* mutations. The HCMV *gB* gene was detected in: four (13.3%) samples of NSCLC with *EGFR* gene mutations and in one (3,1%) sample without *EGFR* gene mutations, in three (37,5%) smokers and one (4,2%) non-smoker, two (14,3%) males and two (10,0%) females. More frequent HCMV infection was determined on the basis of *MIE* gene detection in NSCLC with *EGFR* gene mutations (p <0.001). There was no statistically significant association of HCMV (*MIE* and *gB*) infection with age, gender, and smoking status in NSCLC with *EGFR* gene mutations.
**Conclusion:** Our results indicate more frequent HCMV (*MIE*) infection in NSCLC with *EGFR* gene mutations. More extensive research is needed to determine the incidence of HCMV infection in NSCLC cytology and its possible role in NSCLC pathogenesis.