Abstract

The glial tumors, so called gliomas, represent the largest group of the primary central nervous system malignancies. Gliomas remain generally an incurable disease progressing from the lower grades of malignancy to the more aggressive tumors in the course of time. This finally leads to the rapid patient's clinical deterioration and eventually the death. Recently there has been a significant expansion of knowledge in the neuro-oncology domain regarding the onset and development of neoplastic disease at the genetic as well as epigenetic level. Novel prognostic and predictive molecular genetic biomarkers are emerging that can be used for more precise diagnosis, for more accurate assessment of a patients´ prognosis, or for better selection of therapy and prediction of therapeutic response. The fundamental view of the histological-based classification of central nervous system tumors is gradually changing and the molecular biomarkers are incorporating in addition to histopathology to refine the diagnoses of many tumor entities at the moment. The recent findings from molecular genetics of gliomas together with the results from clinical trials incorporating the various biomarkers are discussed in this thesis.

In the first study the biomarker isocitrate dehydrogenases 1 (IDH1) R132H mutation was examined in the tumor tissue from patients with glioblastoma multiforme and the results were correlated with the clinical characteristics of patients. The prognostic value of this biomarker was proved. Patients with IDH1 R132H mutation in the tumor tissue had significantly longer survival than patients with IDH1 wild-type tumors. The presented results were included into the large recently published meta-analysis that confirmed positive prognostic effect of the IDH mutations on both overall survival and progression-free survival in patients with gliomas.

The second study examined the chromosomal aberration 1p/19q co-deletion in patients with anaplastic oligodendroglioma who were treated with the combined radiotherapy and chemotherapy (procarbazine, lomustine and vincristine regime - PCV). The results were correlated with the clinical characteristics of patients. The prognostic value of 1p/19q co-deletion was proved. The strong positive predictive value of this biomarker for overall survival was also shown for patients with co-deletion treated with neurosurgery and radiotherapy plus PCV chemotherapy by comparison with neurosurgery and radiotherapy alone.

The enormous advances in the molecular genetics of central nervous system tumors especially gliomas bring completely new opportunities for the optimization of the treatment strategies for an individual patient with these diagnoses. The analysis of molecular genetics in central nervous system tumors is now recommended in order to implement the principles of personalized medicine into the clinical management of these malignancies.