Abstract

Malignant transformation of cell is characterized by genomic instability that involves unbalanced changes besides other things. We analyzed genomic aberrations, promoter methylation and mutations of several clinically relevant genes using I-FISH, mFISH, mBAND, CGH array, SNP array, MLPA, MS-MLPA and MS-PCR methods. We focused on two groups of patients well known for frequent appearance of unbalanced changes – patients with malignant brain tumors (gliomas) and patients with myelodyspastic syndromes (MDS).

In patients with low grade glioma (WHO grade I – II), the codeletion of 1p/19q (82,6% oligodendrogliomas and oligoastrocytomas), mutation of *IDH1/IDH2* genes (87% WHO grade I-II gliomas), copy neutral loss of heterozygozyty of 17p (72,2% astrocytomas) and higher presence of unbalanced aberration in astrocytomas belongs to the most frequent findings. We described yet unpublished methylation of *MLH3* gene promoter in 60,9% oligodendrogliomas and in 27,3% astrocytomas. We also observed clonal evolution in patients with recurrent tumors.

We studied secondary rearrangements of deleted chromosome 5 in patients with MDS and complex karyotype and we described its most recurrent translocation partners and breakpoints. We observed chromothripsis in 49% of these patients and it was frequently associated with high number of deletions/ amplifications, aberrations of short arm of chromosome 17, poor prognosis and higher risk of transformation to acute myeloid leukemia (AML). We also described a new fusion gene *ASXL1-TSHZ2* in patient with MDS and isoderivative chromosome 20 [ider(20q)] using CGH array, I-FISH and sequencing methods.

These findings contribute to early and specific classification of cancer subtype as well as to determination of patient's prognosis. They may also help better understanding of hematologic malignancies or solid tumor pathogenesis and therefore assist in the development of new therapeutic approaches targeted to the particular genetic profile of cancer cells.

Key words: molecular analysis, cytogenetic analysis, malignant brain tumor, myelodysplastic syndromes