Abstract

Cerebral gliomas are a heterogeneous group of tumours of different histological subtypes, which differ in malignant potential, response to treatment and overall survival of patients. Their diffuse nature does not allow for complete surgical removal and therefore malignant relapse, or tumour recurrence occurs. Recent studies of recurrent gliomas have highlighted the accumulation of other genetic and epigenetic aberrations whose nature, frequency and role in tumour pathogenesis have not yet been sufficiently studied. In this study, molecular cytogenomic methods (aCGH/SNP, I-FISH and MLPA) were used to compare the genetic profiles of primary and recurrent gliomas in 26 patients with multiple resections during the course of the disease. Three groups were analysed according to tumour subtype at diagnosis: astrocytomas, oligodendrogliomas, and primary glioblastomas. The thesis presented a comparison of the genomic profiles of diagnostic and repeat samples for each of the three groups. Candidate aberrations with a potential relationship to disease progression were characterized for the largest group - patients with astrocytomas. These included gains and losses on chromosomes 5, 9, 11, 13, 15, 16 and 22. With the data obtained, a clonal evolution analysis was performed. Linear type of evolution was the primary type of evolution in oligodendrogliomas. Astrocytomas and primary glioblastomas were dominated by divergent evolution of tumour subclones. Monitoring the clonal development of diffuse gliomas as they progress is important for a better understanding of the pathogenesis and malignant development of these tumours. Identification of aberrations associated with tumour progression could contribute to the development of targeted therapies.

Keywords: diffuse glioma, astrocytoma, oligodendroglioma, primary glioblastoma, genetic aberrations, epigenetic aberrations, tumour progression