The Classification of Tumours of the Central Nervous System in the Molecular Era

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The traditional classification of brain tumours has been mainly centred on the histological similarities, depending on light microscopic features in hematoxylin and eosin stained specimens, immunohistochemical expression of proteins and on their ultrastructural features as these can be identified under the electron microscope. In the WHO classifications of brain tumours of 2000 and 2007, the rapidly increasing knowledge of the genetic changes that underlie tumorigenesis of central nervous system tumours had been considered along with the histological features, but at that time genetic tests could not yet be used to define neoplasms, providing though supplementary information. The classification of 2016 modifies this traditional classification and integrates standard molecular genetic tests, the majority of which can be assessed using immunohistochemistry or FISH, into classification of the tumours of the central nervous system.

Histological grading of the neoplasms of the central nervous system is a systematic approach to predict their biological behaviour. Grade I tumours are generally characterised by low proliferative potential, and mostly possible to cure after surgical resection alone. Grade II tumours are usually infiltrative in nature, often recurrent with a survival rate more than 5 years. Grade III lesions have clear histological evidence of malignancy, including nuclear atypia and brisk mitotic activity. Although patients receive radiation and/or chemotherapy, the survival rate is usually between 2 - 3 years. Finally grade IV tumours are cytologically malignant, mitotically active and necrosis-prone neoplasms, often associated with rapid pre- and postoperative disease evolution and fatal outcome. Most glioblastoma patients and especially the elderly do not survive more than a year, nevertheless grade IV cerebellar medulloblastoma and germ cell tumours, are characterised by 60 - 80% 5-year survival rates after radiation and chemotherapy. Certain molecular parameters are strongly related to the biological behaviour and therefore to the survival rates of the CNS neoplasms. The main parameters that are considered are: whole arm 1p-19q co-deletion, TP53 mutation, ATRX mutation, or mutation on the IDH-1 and IDH-2 genes. It is noteworthy that according to the 2016 classification the genetic profile of the tumour exceeds the histological features, for example a tumour with histological features of astrocytoma, but IDH mutant and characterised by 1p-19q co-deletion is currently classified as an oligodendroglioma.

The core changes in 2016 classification are: the major restructuring of diffuse gliomas, medulloblastomas and embryonal tumours with incorporation of genetically defined entities, the incorporation of a genetically defined ependymoma variant, the addition of newly recognized entities, variants and patterns, namely the IDH-wildtype and IDH-mutant glioblastoma entities, the entity of embryonal tumour with multilayered rosettes, the entities of ependymoma RELA fusion-positive, diffuse leptomeningeal glioneuronal tumour, anaplastic PXA, the variant of the epithelioid glioblastoma, the patterns of glioblastoma with primitive neuronal component and the multinodular and vacuolated ganglion cell tumour. Furthermore the gliomatosis cerebri, the protoplasmic and fibrillary astrocytoma variants, the cellular ependymoma variant, and the term primitive neuroectodermal tumour have been deleted. Brain invasion added as a criterion for atypical meningioma, solitary fibrous tumor and hemangiopericytoma restructured as one entity, melanotic Schwannoma has been separated from other Schwannomas and hematopoietic and lymphoid tumours of the central nervous system are now included.

The classification of central nervous system tumours in the molecular era represents a crucial step towards an amended adapting patient therapy, and offers a better classification for trials and experimental studies.

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