

The 2007 WHO Classification of Tumours of the Central Nervous System, 4th Edition: Recent advances in Diagnosis and Classification

Classification has always been the language of medicine; diseases must be described, defined and named before they can be diagnosed, treated and studied. A consensus on definitions and terminology is essential for both clinical practice and investigation. Classification of brain tumours is an evolving process, with obsolete entities discarded and newly recognized tumours added with each successive revision. In the past, classification has relied heavily on morphologic pattern recognition and immunohistochemical identification of differentiation antigens. A new entity had to be characterized by distinctive morphology, location, age distribution, clinical features or biologic behaviour, genetic profile or prognostic significance and not simply by an unusual histopathological pattern. The current World Health Organization Classification of tumours of the Central Nervous System (WHO 2000) lists more than 120 types of brain tumours. In recognition of the emerging role of molecular diagnostic approaches to tumour classification, genetic profiles have been emphasized, as in the distinct subtypes of glioblastoma, the already clinically useful 1p and 19q markers and the chemosensitivity of anaplastic oligodendrogliomas and 22q/IN1 for atypical teratoid/rhabdoid tumours. It is a virtual certainty that current advances in molecular methodologies, particularly in the fields of genomics, transcriptomics, and proteomics, will revolutionize brain tumour classification in the very near future.

The new classification essentially dealt mainly with three main issues:

1. New clinicopathological entities, variants and patterns entries,
2. Tumour subclassification changes,
3. Tumours grading changes.

In this report only two neoplasms which are frequently observed in neurosurgical practice receive brief analysis; the other five rare entities will be discussed in future reports. These include:

- Brain invasion by a meningioma
- Anaplastic oligoastrocytomas with necrosis

Meningioma with brain invasion, WHO Grade II

Traditionally, the WHO grading schemes for meningiomas have assigned tumours as “meningioma, WHO grade I,” “atypical meningioma, WHO grade II,” or “anaplastic (malignant) meningioma, WHO grade III,” depending upon the presence of histopathologic features that indicate increasingly aggressive behaviour. In the 3rd edition, the criteria for atypical meningioma, WHO grade II included a mitotic index of 4 or more per 10 high-power fields (HPFs) or more than 3 of the following features: increased cell density, small cells with a high nuclear-cytoplasmic ratio, prominent nucleoli, sheet-like growth pattern, and geographic necrosis. Similarly, the presence of brain invasion was listed as a feature that indicated an increased likelihood of recurrence and/or aggressive behaviour, but was not formally included as a criterion for grade II or grade III. Prior to 1997, most grading systems for meningioma considered brain invasion the best evidence of “malignancy.”

The prognostic significance of brain invasion in a large series of patients who had been diagnosed previously with “malignant meningioma” due to the presence of brain invasion, histologic anaplasia, or metastasis was studied. Based on a multivariate analysis of histopathologic features and their relationship to tumour recurrence and patient survival, brain invasion revealed to be an indicator of greater likelihood of recurrence rather than a frankly anaplastic meningioma (grade III), and is therefore regarded as one of the diagnostic features of grade II meningioma. Brain invasiveness was not associated with the same increased mortality rate as grade III meningiomas with anaplastic features.

The relationship of GBM to anaplastic mixed oligoastrocytomas

Oligoastrocytomas are designated as tumours that contain distinct regions of oligodendroglial and astrocytic differentiation.

The debate is still on as to the minimal percentage of each component required for the diagnosis of a mixed glioma. In the previous WHO classification edition, anaplastic oligoastrocytoma was graded as WHO grade III; it included “features of anaplasia” which were listed as nuclear atypia, cellular pleomorphism, high cellular density, high mitotic activity, microvascular proliferation and necrosis. These features could be present in the astrocytic component, the oligodendroglial component, or both. The results of recent clinicopathologic investigations have suggested that this grading scheme could be improved by dividing anaplastic oligoastrocytomas into prognostically distinct groups based upon the presence or absence of necrosis. In the presence of necrosis, the median survival is significantly shorter in the group of patients whose anaplastic oligoastrocytomas had necrosis (22.8 months) than with anaplastic oligoastrocytomas that lacked necrosis (86.9 months); similarly, the presence of endothelial proliferation was not found to be prognostically important among anaplastic mixed tumours. Thus, these data indicated that patients with anaplastic oligoastrocytomas with necrosis had shorter survival and that these tumours should be regarded as grade IV tumours rather than grade III. It can be debated whether anaplastic oligoastrocytomas with necrosis should be considered “oligoastrocytoma, grade IV” or should be classified as “glioblastoma with an oligodendroglial component, grade IV.” In the 4th edition, the WHO classification indicates that oligoastrocytomas with necrosis should be classified as glioblastoma with oligodendrogloma component, WHO grade IV.

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