Histological appearance (Non-core)

Reason/Evidentiary Support

In nearly all pathology reports of CNS neoplasms, the diagnosis should ideally include one of the >150 entities and variants listed in the 2016 CNS WHO[1,2] (see Table 1 below) and when additionally possible, the histological appearance should further be combined with signature molecular alterations to establish a more specific "integrated diagnosis" (e.g., diffuse astrocytoma, IDH-mutant; see section on **Integrated Diagnosis**). When using such an approach, histological impressions such as "oligoastrocytoma" and "anaplastic oligoastrocytoma" will virtually always be altered to either astrocytoma or oligodendroglioma categories based on specific molecular patterns identified. Similar modifications also apply to the RELA-fusion positive supratentorial ependymomas, diffuse midline gliomas, the solitary fibrous tumours/haemangiopericytomas, and the overarching group of embryonal neoplasms, such as medulloblastoma variants, atypical teratoid/rhabdoid tumour, and embryonal tumour with multilayered rosettes, each of which require additional molecular (or surrogate immunohistochemical biomarker) testing before a definitive diagnosis can be made. However, in the majority of entities still lacking disease-defining molecular signatures, the final diagnosis will be based on classical histopathology alone. In either approach (histological or integrated), obtaining as precise a final diagnosis as possible is critically important, as this forms the basis for all subsequent patient management decisions, accruing patients to the appropriate clinical trials, epidemiologically assessing disease trends over time, and establishing valid research conclusions.[3-6] As such, the strict application of WHO 2016 diagnostic guidelines is required to enhance both accuracy and interobserver reproducibility across the globe and it is noteworthy that for many entities, criteria have changed dramatically from the earlier 2007 WHO classification. In the remaining cases that do not neatly conform to a well-recognised entity or variant (see last category listed as "Other (specify)"), a descriptive diagnosis should be rendered instead, providing as much information as possible including relevant molecular information (e.g., small round cell sarcoma of indeterminate type; low-grade neuroepithelial tumour with oligodendroglial-like histological features suggestive of dysembryoplastic neuroepithelial tumour or paediatric oligodendroglioma; high-grade glioneuronal neoplasm; poorly differentiated malignancy; etc.). Such cases can be considered Not Elsewhere Classified (NEC).[7]

It should be noted that in some cases the results are not clear cut and the addition of a secondary diagnosis may be of benefit to record in the report.

This element should be considered CORE if it constitutes the final diagnosis.

Table 1 Histologically Defined Diagnostic Category (based on histological appearance <u>only, i.e., not full 2016 CNS WHO diagnoses)</u>

Diffuse glioma
Diffuse astrocytoma
Gemistocytic astrocytoma
Anaplastic astrocytoma
Glioblastoma
Giant cell glioblastoma
Gliosarcoma
Epithelioid glioblastoma

Oligodendroglioma
Anaplastic oligodendroglioma
Oligoastrocytoma
Anaplastic oligoastrocytoma
Pilocytic astrocytoma
Pilomyxoid astrocytoma
Subependymal giant cell astrocytoma
Pleomorphic xanthoastrocytoma
Anaplastic pleomorphic xanthoastrocytoma
Chordoid glioma of third ventricle
Angiocentric glioma
Astroblastoma
Subependymoma
Myxopapillary ependymoma
Ependymoma
Papillary ependymoma
Clear cell ependymoma
Tanycytic ependymoma
Anaplastic ependymoma
Choroid plexus papilloma
Atypical choroid plexus papilloma
Choroid plexus carcinoma
Dysembryoplastic neuroepithelial tumour
Gangliocytoma
Ganglioglioma
Anaplastic ganglioglioma
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos disease)
Desmoplastic infantile astrocytoma or ganglioglioma (DIA or DIG)
Papillary glioneuronal tumour
Rosette-forming glioneuronal tumour
Diffuse leptomeningeal glioneuronal tumour
Central neurocytoma
Extraventricular neurocytoma

Cerebellar liponeurocytoma
Paraganglioma
Pineocytoma
Pineal parenchymal tumour of intermediate differentiation
Pineoblastoma
Papillary tumour of the pineal region
CNS Embryonal tumour
CNS Embryonal tumour with rhabdoid features
Medulloblastoma
Medulloblastoma, classic
Medulloblastoma, desmoplastic/nodular
Medulloblastoma with extensive nodularity
Medulloblastoma, large cell/anaplastic
Embryonal tumour with multilayered rosettes
Medulloepithelioma
CNS Neuroblastoma
CNS Ganglioneuroblastoma
Schwannoma
Cellular schwannoma
Plexiform schwannoma
Melanotic schwannoma
Neurofibroma
Plexiform neurofibroma
Perineurioma
Hybrid nerve sheath tumour
Malignant peripheral nerve sheath tumour (MPNST)
Epithelioid MPNST
Melanotic MPNST
MPNST with mesenchymal differentiation
MPNST with glandular differentiation
MPNST with perineurial differentiation
Meningioma
Meningothelial meningioma

Fibrous meningioma
Transitional meningioma
Psammomatous meningioma
Angiomatous meningioma
Microcystic meningioma
Secretory meningioma
Lymphoplasmacyte-rich meningioma
Metaplastic meningioma
Chordoid meningioma
Clear cell meningioma
Atypical meningioma
Papillary meningioma
Rhabdoid meningioma
Anaplastic (malignant) meningioma
Solitary fibrous tumour/haemangiopericytoma
Haemangioblastoma
Haemangioma
Epithelioid hemangioendothelioma
Angiosarcoma
Kaposi sarcoma
Ewing sarcoma-peripheral primitive neuroectodermal tumour
Lipoma
Angiolipoma
Liposarcoma
Desmoid-type fibromatosis
Myofibroblastoma
Inflammatory myofibroblastic tumour
Benign fibrous histiocytoma
Fibrosarcoma
Undifferentiated pleomorphic sarcoma (UPS)/malignant fibrous histiocytoma (MFH)
Leiomyoma
Leiomyosarcoma
Rhabdomyoma
Rhabdomyosarcoma
Chondroma
Chondrosarcoma
Osteoma

Osteochondroma
Osteosarcoma
Diffuse melanocytosis
Meningeal melanocytoma
Melanoma
Meningeal melanomatosis
Diffuse large B cell lymphoma (DLBCL) of the CNS
Immunodeficiency-associated lymphoproliferative disorders of the CNS
Low grade B cell lymphomas of the CNS
T-cell and NK/T-cell lymphomas of the CNS
Anaplastic large cell lymphoma
Lymphomatoid granulomatosis
Intravascular large B-cell lymphoma
MALT lymphoma of the dura
Langerhans cell histiocytosis
Erdheim-Chester disease
Rosai-Dorfman disease
Juvenile xanthogranuloma
Histiocytic sarcoma
Germinoma
Embryonal carcinoma
Yolk sac tumour
Choriocarcinoma
Teratoma
Mature teratoma
Immature teratoma
Teratoma with malignant transformation
Mixed germ cell tumour
Craniopharyngioma
Adamantinomatous craniopharyngioma
Papillary craniopharyngioma
Granular cell tumour
Pituicytoma

Spindle cell oncocytoma
Pituitary adenoma
Somatotroph adenoma
Lactotroph adenoma
Thyrotroph adenoma
Corticotroph adenoma
Gonadotroph adenoma
Null cell adenoma
Plurihormonal and double adenomas
Pituitary carcinoma
Pituitary blastoma
Gangliocytoma and mixed gangliocytoma-adenoma
Granular cell tumour
Pituicytoma
Spindle cell oncocytoma
Metastatic carcinoma
Metastatic melanoma
Metastatic sarcoma
Metastatic lymphoma/leukemia

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