Protocol for the Examination of Tumors of the Brain and Spinal Cord

Version: 1.0.0.0
Protocol Posting Date: September 2022
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

The following tumor types should NOT be reported using this protocol:

<table>
<thead>
<tr>
<th>Tumor type</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)</td>
</tr>
<tr>
<td>Primary bone tumors (consider the Primary Bone Tumor protocol)</td>
</tr>
<tr>
<td>Metastatic tumors</td>
</tr>
<tr>
<td>Malignant peripheral nerve sheath tumor (consider the Soft Tissue Tumor protocol)</td>
</tr>
</tbody>
</table>

Authors

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*Denotes primary review authors. All other authors are current members of the CAP Neuropathology Committee and are presented in alphabetical order. This protocol was prepared with guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.

Accreditation Requirements

The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Summary of Changes

v 1.0.0.0

- New protocol
Reporting Template
Protocol Posting Date: September 2022
Select a single response unless otherwise indicated.

CASE SUMMARY: (CENTRAL NERVOUS SYSTEM)

CLINICAL

+History of Prior Therapy for this Neoplasm (Note A)
___ Not administered
___ Not known: ____________________
___ Administered
+___ Chemotherapy
+___ Radiation therapy
+___ Corticosteroids
+___ Embolization
+___ Therapy performed, type not specified
+___ Other (specify): _________________

+History of Previous Tumor and / or Familial Syndrome (not the current neoplasm) (Note A)
___ Not known: ____________________
___ Known (specify): ____________________
___ Not specified

+Neuroimaging Findings (Note B)
___ Specify: ____________________
___ Not available

SPECIMEN

Procedure (Note C) (select all that apply)
___ Open biopsy
___ Biopsy with intraoperative consultation
___ Stereotactic biopsy
___ Resection
___ Other (specify): ____________________
___ Not specified

Specimen Size, Gross Description (Note D)
For fragmented tissue, an aggregate size may be given
___ Greatest dimension in Centimeters (cm): _________________ cm
+Additional Dimension in Centimeters (cm): ____ x ____ cm
___ Cannot be determined (explain): ____________________
TUMOR

Tumor Site (Note E) (select all that apply)
___ Skull / Bone
   +Specify Precise Location, if known (select all that apply)
      ___ Frontal: _________________
      ___ Parietal: _________________
      ___ Temporal: _________________
      ___ Occipital: _________________
      ___ Other (specify): _________________
___ Dura
   +Specify Precise Location, if known (select all that apply)
      ___ Convexity / lobe (specify): _________________
      ___ Falx
      ___ Tentorium
      ___ Posterior fossa
      ___ Sphenoid wing
      ___ Skull base
      ___ Spinal
      ___ Other (specify): _________________
___ Leptomeninges
   +Specify Precise Location, if known (select all that apply)
      ___ Cerebral convexity / lobe (specify): _________________
      ___ Posterior fossa
      ___ Spinal
      ___ Other (specify): _________________
___ Brain
   +Specify Precise Location, if known (select all that apply)
      ___ Cerebral lobes
         ___ Frontal: _________________
         ___ Temporal: _________________
         ___ Parietal: _________________
         ___ Occipital: _________________
         ___ Other (specify): _________________
      ___ Deep grey matter
   +Specify Precise Location, if known (select all that apply)
      ___ Basal ganglia
      ___ Thalamus
      ___ Hypothalamus
      ___ Ventricle
   +Specify Precise Location, if known (select all that apply)
      ___ Lateral: _________________
      ___ Third: _________________
      ___ Fourth: _________________
      ___ Cerebral Aqueduct: _________________
      ___ Other (specify): _________________
___ Cerebellum
Brain stem
  +Specify Precise Location, if known (select all that apply)
    ___ Midbrain: _________________
    ___ Pons: _________________
    ___ Medulla: _________________
    ___ Other (specify): _________________
    ___ Other (specify): _________________

Cerebellopontine angle

Sellar / Suprasellar / Pituitary

Pineal

Cranial nerve
  +Specify I-XII, if known (select all that apply)
    ___ I
    ___ II
    ___ III
    ___ IV
    ___ V
    ___ VI
    ___ VII
    ___ VIII
    ___ IX
    ___ X
    ___ XI
    ___ XII

Spine / Bone (vertebral column)
  +Specify Precise Location, if known (select all that apply)
    ___ C1
    ___ C2
    ___ C3
    ___ C4
    ___ C5
    ___ C6
    ___ C7
    ___ T1
    ___ T2
    ___ T3
    ___ T4
    ___ T5
    ___ T6
    ___ T7
    ___ T8
    ___ T9
    ___ T10
    ___ T11
    ___ T12
    ___ L1
    ___ L2
___ L3
___ L4
___ L5
___ Sacrum
___ Coccyx
___ Other (specify): ________________
___ Spinal cord
  +Specify Precise Location, if known (select all that apply)
    ___ C1
    ___ C2
    ___ C3
    ___ C4
    ___ C5
    ___ C6
    ___ C7
    ___ T1
    ___ T2
    ___ T3
    ___ T4
    ___ T5
    ___ T6
    ___ T7
    ___ T8
    ___ T9
    ___ T10
    ___ T11
    ___ T12
    ___ L1
    ___ L2
    ___ L3
    ___ L4
    ___ L5
    ___ Sacral
    ___ Coccygeal
    ___ Other (specify): ________________
___ Spinal nerve root(s)
  +Specify Precise Location, if known (select all that apply)
    ___ C1
    ___ C2
    ___ C3
    ___ C4
    ___ C5
    ___ C6
    ___ C7
    ___ T1
    ___ T2
    ___ T3
Tumor Laterality (Note E)

- Right
- Left
- Midline
- Bilateral
- Other (specify): ________________________
- Not specified

Tumor Focality (Note E)

- Unifocal
- Multifocal (specify number of lesions): ________________________
- Cannot be determined: ________________________

Integrated Diagnosis (CNS WHO 2021) (Notes F,G)

- Gliomas, glioneuronal tumors, and neuronal tumors
  - Adult-type diffuse gliomas
    - Astrocytoma, IDH-mutant
    - Oligodendroglioma, IDH-mutant and 1p/19q-codeleted
    - Glioblastoma, IDH-wildtype
  - Pediatric-type diffuse low-grade gliomas
    - Diffuse astrocytoma, MYB- or MYBL1-altered
    - Angiocentric glioma
    - Polymorphous low-grade neuroepithelial tumor of the young
    - Diffuse low-grade glioma, MAPK pathway-altered
  - Pediatric-type diffuse high-grade gliomas
    - Diffuse midline glioma, H3 K27-altered
    - Diffuse hemispheric glioma, H3 G34-mutant
    - Diffuse pediatric-type high-grade glioma, H3-wildtype and IDH-wildtype
___ Infant-type hemispheric glioma

_Circumscribed astrocytic gliomas_
___ Pilocytic astrocytoma
___ High-grade astrocytoma with piloid features
___ Pleomorphic xanthoastrocytoma
___ Subependymal giant cell astrocytoma
___ Chordoid glioma
___ Astroblastoma, MN1-altered

_Glioneuronal and neuronal tumors_
___ Ganglioglioma
___ Gangliocytoma
___ Desmoplastic infantile ganglioglioma
___ Desmoplastic infantile astrocytoma
___ Dysembryoplastic neuroepithelial tumor
___ Diffuse glioneuronal tumor with oligodendroglioma-like features and nuclear clusters
___ Papillary glioneuronal tumor
___ Rosette-forming glioneuronal tumor
___ Myxoid glioneuronal tumor
___ Diffuse leptomeningeal glioneuronal tumor
___ Multinodular and vacuolating neuronal tumor
___ Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)
___ Central neurocytoma
___ Extraventricular neurocytoma
___ Cerebellar liponeurocytoma

_Ependymal tumors_
___ Supratentorial ependymoma
___ Supratentorial ependymoma, ZFTA fusion-positive
___ Supratentorial ependymoma, YAP1 fusion-positive
___ Posterior fossa ependymoma
___ Posterior fossa group A (PFA) ependymoma
___ Posterior fossa group B (PFB) ependymoma
___ Spinal ependymoma
___ Spinal ependymoma, MYCN-amplified
___ Myxopapillary ependymoma
___ Subependymoma
___ Choroid plexus tumors
___ Choroid plexus papilloma
___ Atypical choroid plexus papilloma
___ Choroid plexus carcinoma
___ Medulloblastoma

_Must select both molecularly defined and histologically defined subtypes_

_Molecularly Defined Medulloblastomas_
___ Medulloblastoma, WNT-activated
___ Medulloblastoma, SHH-activated and TP53-wildtype
___ Medulloblastoma, SHH-activated and TP53-mutant
___ Medulloblastoma, non-WNT / non-SHH

_Histologically Defined Medulloblastomas_
___ Classic medulloblastoma
___ Desmoplastic / nodular medulloblastoma
___ Medulloblastoma with extensive nodularity
___ Large cell / anaplastic medulloblastoma
___ Other CNS embryonal tumors
   ___ Atypical teratoid / rhabdoid tumor
   ___ Cribriform neuroepithelial tumor
   ___ Embryonal tumor with multilayered rosettes
   ___ CNS neuroblastoma, FOXR2-activated
   ___ CNS tumor with BCOR internal tandem duplication
   ___ CNS embryonal tumor, NEC / NOS
___ Pineal tumors
   ___ Pineocytoma
   ___ Pineal parenchymal tumor of intermediate differentiation
   ___ Pineoblastoma
   ___ Papillary tumor of the pineal region
   ___ Desmoplastic myxoid tumor of the pineal region, SMARCB1-mutant
___ Cranial and paraspinal nerve tumors
   ___ Schwannoma
   ___ Neurofibroma
   ___ Plexiform neurofibroma
   ___ Perineurioma
   ___ Hybrid nerve sheath tumor (specify subtype(s), if known): _________________
   ___ Malignant melanotic nerve sheath tumor
   ___ Malignant peripheral nerve sheath tumor
   ___ Cauda equina neuroendocrine tumor (previously paraganglioma)
___ Meningioma (specify subtype(s), if known): _________________
___ Mesenchymal, non-meningothelial tumors involving the CNS
   ___ Solitary fibrous tumor
___ Vascular tumors
   ___ Hemangioma
   ___ Cavernous malformation
   ___ Arteriovenous malformation
   ___ Capillary telangiectasia
   ___ Hemangioblastoma
___ Skeletal muscle tumors
   ___ Embryonal rhabdomyosarcoma
   ___ Alveolar rhabdomyosarcoma
   ___ Rhabdomyosarcoma, pleomorphic type
   ___ Spindle cell rhabdomyosarcoma
___ Tumors of uncertain differentiation
   ___ Intracranial mesenchymal tumor, FET::CREB fusion-positive
   ___ CIC-rearranged sarcoma
   ___ Primary intracranial sarcoma, DICER1-mutant
   ___ Ewing sarcoma
___ Chondrogenic tumors
   ___ Mesenchymal chondrosarcoma
   ___ Chondrosarcoma
___ Dedifferentiated chondrosarcoma

Notochordal tumors
___ Chordoma

Melanocytic tumors
___ Diffuse meningeal melanocytic neoplasms
   ____ Meningeal melanocytosis
   ____ Meningeal melanomatosis

Circumscribed meningeal melanocytic neoplasms
___ Meningeal melanocytoma
___ Meningeal melanoma

Hematolymphoid tumors involving the CNS
___ Primary diffuse large B-cell lymphoma of the CNS
___ Immunodeficiency-associated CNS lymphoma
___ Lymphomatoid granulomatosis
___ Intravascular large B-cell lymphoma

Miscellaneous rare lymphomas in the CNS
___ MALT lymphoma of the dura
___ Other low-grade B-cell lymphomas of the CNS (specify subtype(s), if known): ________________
___ Anaplastic large cell lymphoma (ALK+ / ALK-)
___ T-cell lymphoma
___ NK / T-cell lymphoma

Histiocytic tumors
___ Erdheim-Chester disease
___ Rosai-Dorfman disease
___ Juvenile xanthogranuloma
___ Langerhans cell histiocytosis
___ Histiocytic sarcoma

Germ cell tumors
___ Mature teratoma
___ Immature teratoma
___ Teratoma with somatic-type malignancy
___ Germinoma
___ Embryonal carcinoma
___ Yolk sac tumor
___ Choriocarcinoma
___ Mixed germ cell tumor (specify subtype(s), if known): ________________

Tumors of the sellar region
___ Adamantinomatous craniopharyngioma
___ Papillary craniopharyngioma
___ Pituicytoma
___ Granular cell tumor of the sellar region
___ Spindle cell oncocytoma
___ Pituitary adenoma / pituitary neuroendocrine tumor (PitNET)
___ Pituitary blastoma
___ Other (e.g., NEC, NOS) (specify): ________________
___ Cannot be determined: ________________
___ Pending
Specify Histologic Type: _________________
+Histologic Type Comments: _________________

Integrated Histologic Molecular Grade (CNS WHO 2021) (Note H)
___ CNS WHO grade 1
___ CNS WHO grade 2
___ CNS WHO grade 3
___ CNS WHO grade 4
___ Pending
___ Other (specify): _________________
___ Not applicable: _________________
___ Cannot be assessed: _________________

+Treatment Effect (Histological Evidence of Prior Therapy) (Note I)
___ Not identified
___ Present: _________________
+Specify Percentage of Tumor that is Necrotic: _________________ %
___ Cannot be determined: _________________

ADDITIONAL FINDINGS

+Additional Pathologic Findings (specify): _________________

SPECIAL STUDIES

+Molecular Information (Note J) (select all that apply)
___ Specify test(s) and results: _________________
___ Pending (specify test(s)): _________________
___ Not performed: _________________
___ Not applicable: _________________

+Designate Block(s) for Future Studies: _________________

COMMENTS

Comment(s): _________________
Explanatory Notes

A. Relevant History

Previous Therapy for CNS Tumors

Surgery, radiation, and chemotherapy are standard therapeutic options for brain tumors. However, these therapies pose neurotoxicity risks with long-term complications including radiation necrosis, chemotherapy-associated leukoencephalopathy, and secondary neoplasms. A tissue diagnosis remains the gold standard to assess for treatment response and treatment-related changes. Treatment-associated changes such as cytologic atypia, inflammation, vasculopathy, and tumor necrosis can create diagnostic challenges, so providing a detailed therapy history is essential for adequate specimen interpretation.1

Previous Diagnoses or CNS Biopsies

Knowledge of the presence or absence of previous intracranial or extracranial disease (e.g., immunosuppression or previous CNS or other primary neoplasm) is essential for specimen interpretation. If a previous tumor is included in the differential diagnosis, it is useful to have microscopic slides of the lesion available for review and comparison.2

Family History of Cancer or Primary CNS Tumors

Several genetic conditions/syndromes are associated with an increased predisposition to the development of specific forms of CNS neoplasms (e.g., neurofibromatosis types 1 and 2, constitutional mismatch repair syndrome, Lynch syndrome, tuberous sclerosis, von Hippel-Lindau, Cowden, Li-Fraumeni, and Gorlin syndromes).3

References


B. Neuroimaging Findings

Knowledge of neuroimaging features is extremely helpful in specimen interpretation.1,2,3 A differential diagnosis may be generated based on patient age, tumor location, and neuroimaging features. Neuroimaging also can be helpful in providing correlation with or highlighting discrepancies with pathologic diagnosis (e.g., contrast enhancement with hypocellularity). A close collaboration with the neuroradiologist and neurosurgeon is essential.

References

C. Procedure
It is useful to know if the specimen was procured by open craniotomy or stereotactic biopsy. Since tumors may be heterogeneous, adequate sampling is an issue. The reliability of the prognostic information derived from such specimens may vary depending on how the specimen was obtained.

D. Specimen Size
For most CNS tumors, specimen size is not used for grading. However, in heterogeneous lesions, tissue sampling may become important, and the size of the biopsy relative to the overall size of the lesion provides useful information concerning whether the sample is representative of the overall lesion. The total specimen size may not correspond to the tumor size within the specimen, and this discrepancy should be noted. The protocol may not be applicable to a biopsy specimen if the tissue sample is limited.

E. Primary Tumor Site, Laterality, and Focality
Since the anatomic site of a neoplasm may correlate with tumor type and prognosis, it should be recorded, if known.

- For skull location, specify bone involved, such as frontal, parietal, temporal, occipital, etc., if known. The College of American Pathologists (CAP) cancer protocol for bone should be used for primary tumors of bone.¹
- For dural location, indicate cerebral convexity/lobe, falx, tentorium, posterior fossa, sphenoid wing, skull base, spinal, or other, if known.
- For leptomeningeal location, indicate cerebral convexity/lobe, posterior fossa, spinal, or other, if known.
- For cerebral lobe location, indicate frontal, temporal, parietal, or occipital lobe, if known.
- For a deep gray matter location, indicate basal ganglia, thalamus, or hypothalamus.
- For an intraventricular location, indicate lateral, third, fourth, or cerebral aqueduct, if known.
- For a brain stem location, indicate midbrain, pons, or medulla, if known.
- For spine (vertebral bone), spinal cord, spinal root or spinal ganglion, indicate level (e.g., C5, T2, L3), if known. The CAP cancer protocol for bone should be used for primary tumors of bone.¹

The laterality of a neoplasm should be indicated as involving the left or right side of the CNS structure. In some instances, such as tumors arising in the pineal, pituitary, third ventricle, or other locations, the tumor will be situated in the midline. A tumor would be considered bilateral if it involved both sides of the brain, such as glioblastoma extending across the corpus callosum to involve the left and right hemispheres. The focality of a lesion should be indicated, if possible. Multifocality implies that multiple, noncontiguous lesions are noted on neuroimaging, such as might be seen in primary CNS lymphoma. A solitary lesion would be considered unifocal.

Margins
Resection margins provide no prognostic information and generally are not required for most CNS neoplasms.²

References
F. Integrated Diagnosis
Historically, the diagnosis and classification of CNS tumors have been based exclusively on the histologic appearance of the tumor. In recent decades, however, our knowledge of the molecular basis of many of these tumors has increased significantly. In the 5th edition of the WHO Classification of Tumours of the Central Nervous System\(^1\), molecular information is now integrated into many of the tumor diagnostic entities. In such cases, including the diffuse gliomas and embryonal tumors, the final diagnosis should reflect the integration of both histologic and molecular information.

One optional method of reporting the histologic and molecular information is through a “layered” report format with the tumor site as follows:\(^2\):

Layer 1: Integrated diagnosis (combined tissue-based histological and molecular diagnosis)
Layer 2: Histopathological classification
Layer 3: CNS WHO grade
Layer 4: Molecular Information

At centers where molecular testing is not available, an NOS (not otherwise specified) designation is available for tumor entities that include molecular alterations as part of the definitions. The NOS designation implies that insufficient information is available to provide a more specific integrated diagnosis and may occasionally be used for tumors that do not precisely fit into one of the defined tumor categories. A designation of NEC (not elsewhere classified) can be added when necessary diagnostic testing was successfully performed but the results do not readily permit a WHO diagnosis. Both NOS and NEC can be used for all tumor types.

References

G. Histologic Type
Classification should be made according to the WHO classification of tumors of the nervous system and the WHO classification of tumors of the endocrine organs whenever possible.\(^1,2\) Table 1 listed in Note H (Histologic Grade) contains WHO 2021 diagnostic entities for which the Central Nervous System (CNS) Cancer Protocol is recommended.

References

H. Histologic Grade
Below is a list of possible WHO grades for CNS tumors. The WHO grading of some of the more common CNS tumors is shown in Table 1. There is no formal TNM-based classification and staging system for CNS tumors.
CNS WHO Grades for CNS Tumors

CNS WHO grade 1
CNS WHO grade 2
CNS WHO grade 3
CNS WHO grade 4
CNS WHO grade not assigned

Table 1. CNS WHO Grading System for Some of the More Common Tumors of the CNS

<table>
<thead>
<tr>
<th>Group</th>
<th>Type</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Grade 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult-type diffuse gliomas</td>
<td>Astrocytoma, IDH-mutant</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td></td>
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<tr>
<td></td>
<td>Oligodendroglioma, IDH-mutant and, 1p/19q co-deleted</td>
<td>X</td>
<td>X</td>
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<td></td>
<td>Glioblastoma, IDH-wildtype</td>
<td></td>
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<td>X</td>
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<tr>
<td>Pediatric-type diffuse low-grade gliomas</td>
<td>Diffuse glioma, MYB- or MYBL1- altered</td>
<td>X</td>
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<td></td>
<td>Angiocentric glioma</td>
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<td>X</td>
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<td></td>
<td>Polymorphous low-grade neuroepithelial tumor of the young</td>
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<td>X</td>
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<td></td>
<td>Diffuse low-grade glioma, MAPK pathway-altered*</td>
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<tr>
<td>Pediatric-type diffuse high-grade gliomas</td>
<td>Diffuse midline glioma, H3 K27-altered</td>
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<td>X</td>
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<td></td>
<td>Diffuse hemispheric glioma, H3 G34-mutant</td>
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<td>Diffuse pediatric-type high-grade glioma, H3/IDH-wildtype</td>
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<td>Infant-type hemispheric glioma*</td>
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<td>Circumscribed astrocytic gliomas</td>
<td>Pilocytic astrocytoma</td>
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<td></td>
<td>High-grade astrocytoma with piloid features*</td>
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<td></td>
<td>Pleomorphic xanthoastrocytoma</td>
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<td>X</td>
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<td>Subependymal giant cell astrocytoma</td>
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<td>Chordoid glioma</td>
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<td></td>
<td>Astroblastoma, MN1-altered*</td>
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<tr>
<td>Glioneuronal and neuronal tumors</td>
<td>Ganglioglioma</td>
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<td></td>
<td>Gangliocytoma</td>
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<td>Desmoplastic infantile ganglioglioma/astrocytoma</td>
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<td>Dysembryoplastic neuroepithelial tumor</td>
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<td>Rosette-forming glioneuronal tumor</td>
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<td>Myxoid glioneuronal tumor</td>
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<tr>
<td>Group</td>
<td>Type</td>
<td>Grade 1</td>
<td>Grade 2</td>
<td>Grade 3</td>
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<tr>
<td>Diffuse glioneuronal tumor with oligodendroglioma features and nuclear clusters*</td>
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<tr>
<td>Multinodular and vacuolating neuronal tumor</td>
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<tr>
<td>Dysplastic cerebellar gangliocytoma (Lhermitte-Duclos disease)</td>
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<td>Central neurocytoma</td>
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<td>Extra-ventricular neurocytoma</td>
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<td>Cerebellar liponeurocytoma</td>
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<tr>
<td>Ependymal tumors</td>
<td>Supratentorial ependymoma</td>
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<td>Supratentorial ependymoma, ZFTA fusion-positive</td>
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<td></td>
<td>Supratentorial ependymoma, YAP1 fusion-positive</td>
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<td>Posterior fossa ependymoma</td>
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*WHO does not currently grade these tumor types
References


I. Preoperative Treatment and Treatment Effect

Knowledge of preoperative treatment, including radiation therapy, chemotherapy, corticosteroid therapy, embolization, and other therapy, is helpful for specimen interpretation. In particular, prior radiation therapy or radiosurgery may alter the interpretation of specimens in which there is increased cellular atypia, decreased proliferative activity, or large areas of radiation-induced change (e.g., coagulative [nonpalisading] necrosis, vascular hyalinization, and gliosis). The addition of chemotherapy to radiation may further alter histomorphological appearance. For patients with malignant gliomas, the presence and degree of radiation necrosis appear to be of prognostic significance. Tumors that show evidence of radiation necrosis are associated with a longer survival, and the degree of necrosis appears to be prognostically significant. Corticosteroid treatment can alter the pathologic features of some CNS diseases. In particular, the treatment of primary CNS lymphoma with corticosteroids can be associated with widespread tumor cell dropout and infiltration by macrophages, which may limit or misguide interpretation. Embolization of certain tumor types, especially meningiomas, may introduce histologic changes in the neoplasm.

References


J. Biomarker Studies

Immunohistochemical and molecular genetic studies are often performed to assist with diagnosis, prognosis, or to predict therapeutic response. The most recent update of the World Health Organization’s Classification of Tumours of the Central Nervous System has incorporated many of these biomarkers into this formal diagnostic classification system, thereby formally encouraging their use in the evaluation of these neoplasms. Currently, the 2021 WHO Classification of Tumours of the Central Nervous System and the 2022 (WHO) Endocrine and Neuroendocrine Tumours incorporate molecular genetic studies into many entities while the diagnoses of some CNS tumors remain largely morphologic. As our understanding of the pathobiology of CNS tumors is ever expanding, the list of entities requiring molecular genetic studies will continue to grow. New methodologies of biomarker tests must be accompanied with careful validation studies to support their use.

References