Brain and spinal tumors

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Lecture Outline

- Classification of CNS tumor
- Clinical presentation and management of glioma
- Metastatic brain tumor
- Meningioma
- Metastases of spine
- Primary spinal tumor

Learning Purpose

- Understanding of CNS tumor
- How to evaluate CNS tumor
- Learn to manage brain and spinal tumor

Classification of CNS tumor (WHO)

- Astrocytic tumors
- Oligodendroglial tumors
- Ependymal tumors
- Other neuroepithelial tumors
- Neuronal and mixed neuronal-glial tumors
- Tumors of pineal region
- Embryonal tumors
- Tumors of cranial and paraspinal nerves
- Tumors of meninges
- Mesenchymal tumors
- Primary melanocytic lesions
- Tumors of haematopoietic system
- Germ cell tumors
- Tumor of sellar region

Grading of Gliomas

TABLE 1. Comparison of the St. Anne–Mayo Grading Scheme With the Adaptation of the WHO

		St. Anne–Mayo	
WHO Grade	**WHO Designation**	**Designation**	**Discriminating Histological Criteria**
I	Pilocytic astrocytoma		
II	Diffuse astrocytoma	Astrocytoma grade 2	1 criterion: usually nuclear atypia
III	Anaplastic astrocytoma	Astrocytoma grade 3	2 criteria: usually nuclear atypia and mitoses
IV	Glioblastoma	Astrocytoma grade 4	3 criteria: nuclear atypia, mitoses, MVP and/or necrosis

WHO, World Health Organization; MVP, microvascular proliferation.

TABLE 2. Parameters Used for the Diagnosis of Anaplastic Astrocytoma Over Time

	WHO 1979	WHO 1993	WHO 2000/2007
Cellularity	+	+	(+)
Cellular pleomorphism	+	+	
Nuclear pleomorphism			+
Loss of cellular differentiation	+		
Presence of giant cells	+		
Mitoses	+	+	+
Microvascular proliferation	+	−	−
Necrosis	+	−	−

+, present or high; −, absent or low.
WHO, World Health Organization Classification System.

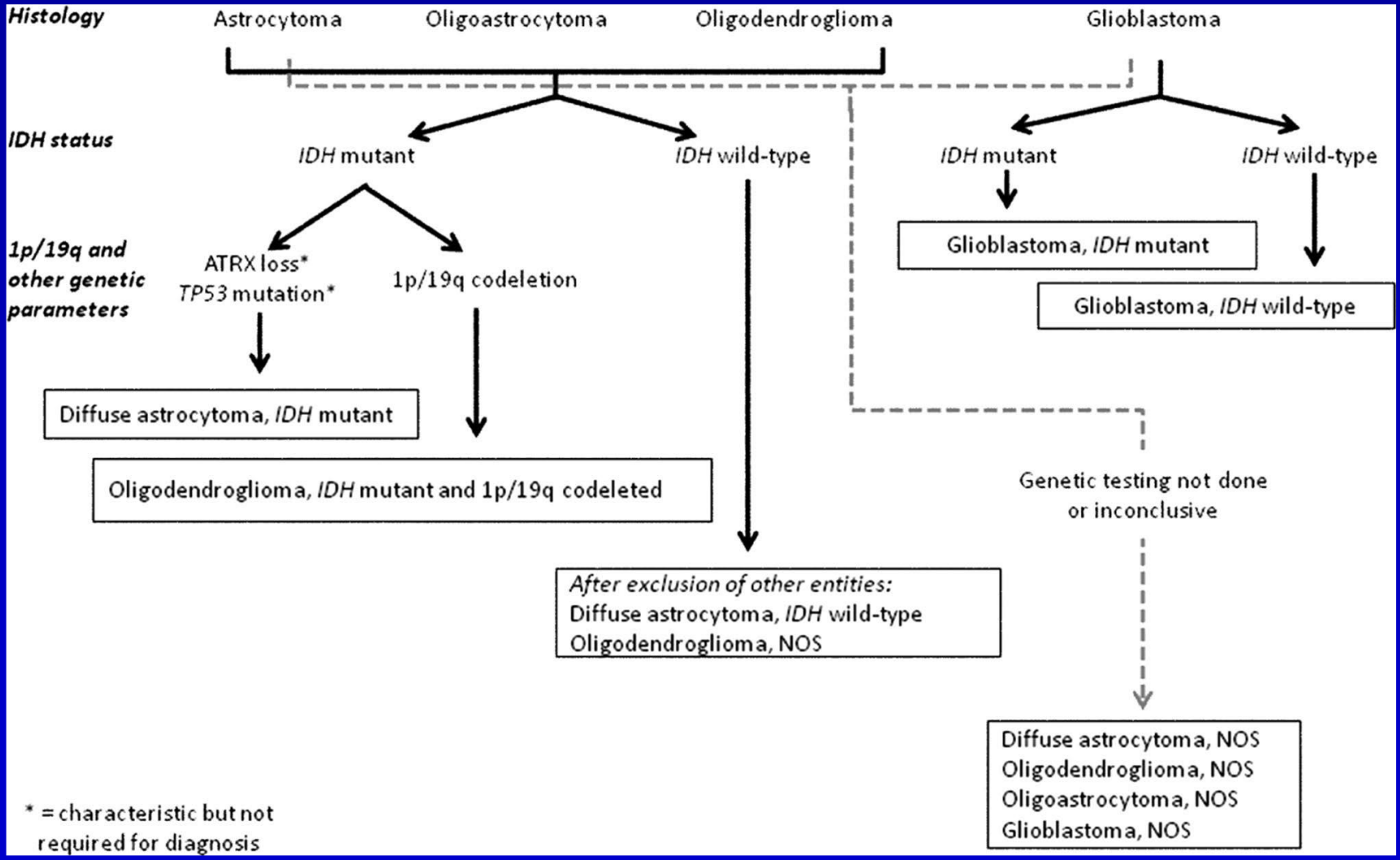
The 2007 WHO Classification of Tumours of the Central Nervous System

TUMOURS OF NEUROEPITHELIAL TISSUE	
Astrocytic tumours	
Pilocytic astrocytoma	9421/1[1]
Pilomyxoid astrocytoma	*9425/3**
Subependymal giant cell astrocytoma	9384/1
Pleomorphic xanthoastrocytoma	9424/3
Diffuse astrocytoma	9400/3
Fibrillary astrocytoma	9420/3
Gemistocytic astrocytoma	9411/3
Protoplasmic astrocytoma	9410/3
Anaplastic astrocytoma	9401/3
Glioblastoma	9440/3
Giant cell glioblastoma	9441/3
Gliosarcoma	9442/3
Gliomatosis cerebri	9381/3
Neuronal and mixed neuronal-glial tumours	
Dysplastic gangliocytoma of cerebellum (Lhermitte-Duclos)	9493/0
Desmoplastic infantile astrocytoma/ ganglioglioma	9412/1
Dysembryoplastic neuroepithelial tumour	9413/0
Gangliocytoma	9492/0
Ganglioglioma	9505/1
Anaplastic ganglioglioma	9505/3
Central neurocytoma	9506/1
Extraventricular neurocytoma	*9506/1**
Cerebellar liponeurocytoma	*9506/1**
Papillary glioneuronal tumour	*9509/1**
Rosette-forming glioneuronal tumour of the fourth ventricle	*9509/1**
Paraganglioma	8680/1

The 2007 WHO Classification of Tumours of the Central Nervous System

Oligodendroglial tumours	
Oligodendroglioma	9450/3
Anaplastic oligodendroglioma	9451/3
Oligoastrocytic tumours	
Oligoastrocytoma	9382/3
Anaplastic oligoastrocytoma	9382/3
Ependymal tumours	
Subependymoma	9383/1
Myxopapillary ependymoma	9394/1
Ependymoma	9391/3
Cellular	9391/3
Papillary	9393/3
Clear cell	9391/3
Tanycytic	9391/3
Anaplastic ependymoma	9392/3
Choroid plexus tumours	
Choroid plexus papilloma	9390/0
Atypical choroid plexus papilloma	*9390/1**
Choroid plexus carcinoma	9390/3
Tumours of the pineal region	
Pineocytoma	9361/1
Pineal parenchymal tumour of intermediate differentiation	9362/3
Pineoblastoma	9362/3
Papillary tumour of the pineal region	*9395/3**
Embryonal tumours	
Medulloblastoma	9470/3
Desmoplastic/nodular medulloblastoma	9471/3
Medulloblastoma with extensive nodularity	*9471/3**
Anaplastic medulloblastoma	*9474/3**
Large cell medulloblastoma	9474/3
CNS primitive neuroectodermal tumour	9473/3
CNS Neuroblastoma	9500/3
CNS Ganglioneuroblastoma	9490/3
Medulloepithelioma	9501/3
Ependymoblastoma	9392/3
Atypical teratoid / rhabdoid tumour	9508/3

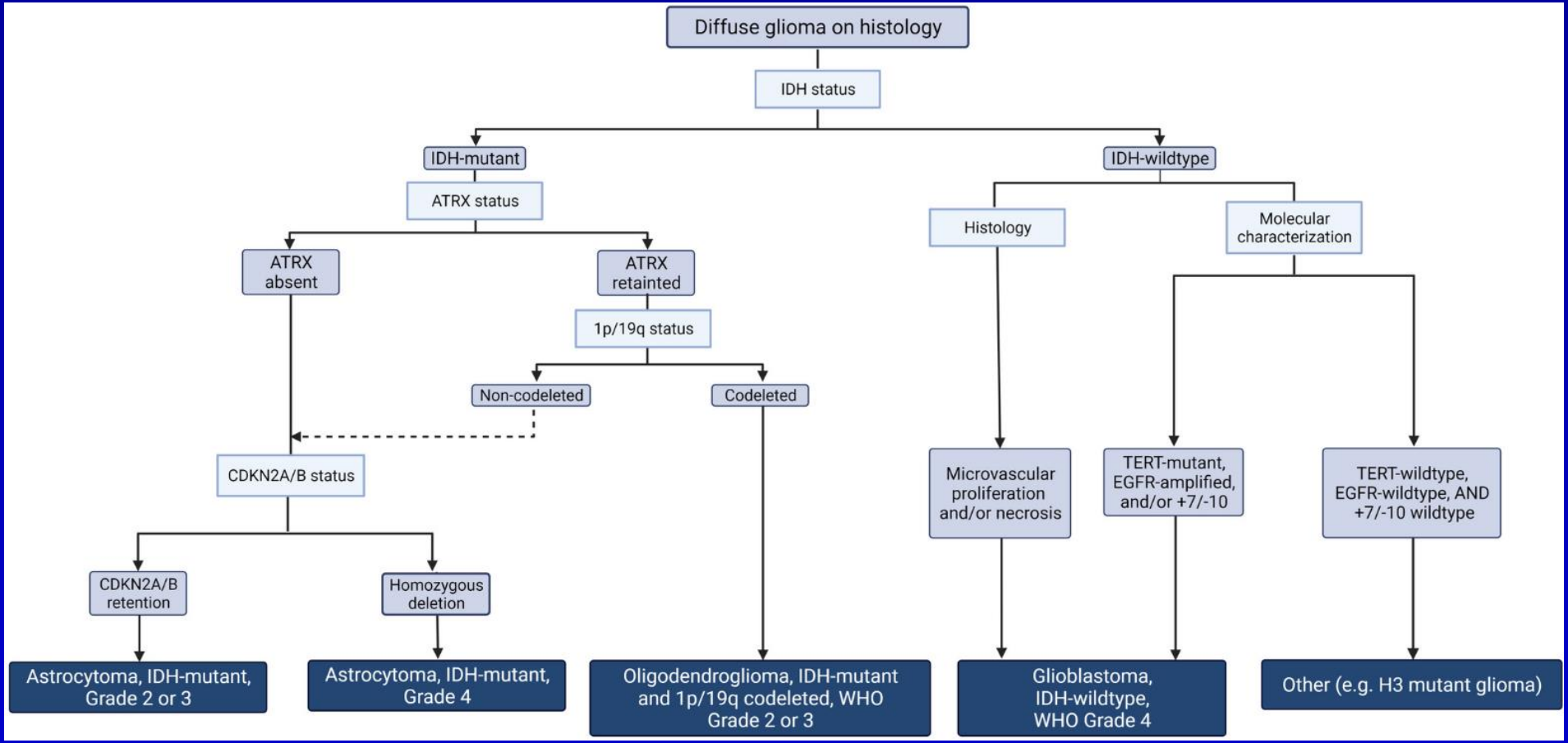
The 2016 World Health Organization Classification of Tumors of the Central Nervous System: a summary



The 2021 WHO Classification of Tumors of the Central Nervous System

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

The 2021 WHO Classification of Tumors of the Central Nervous System



NOS (not otherwise specified): used when genetic testing is not done or is inconclusive Oligodendroglioma is diagnosed based on histology of infiltrating glioma together with IDH-mutation AND 1p/19q co-deletion.

Key Diagnostic Genes, Molecules, Pathways, and/or Combinations in Major Primary CNS Tumors

Tumor Type	Genes/Molecular Profiles Characteristically Altered[a]
Astrocytoma, IDH-mutant	*IDH1*, *IDH2*, *ATRX*, *TP53*, *CDKN2A/B*
Oligodendroglioma, IDH-mutant, and 1p/19q-codeleted	*IDH1*, *IDH2*, 1p/19q, *TERT* promoter, *CIC*, *FUBP1*, *NOTCH1*
Glioblastoma, IDH-wildtype	IDH-wildtype, *TERT* promoter, chromosomes 7/10, *EGFR*
Diffuse astrocytoma, *MYB*- or *MYBL1*-altered	*MYB*, *MYBL1*
Angiocentric glioma	*MYB*
Polymorphous low-grade neuroepithelial tumor of the young	*BRAF*, FGFR family
Diffuse low-grade glioma, MAPK pathway-altered	*FGFR1*, *BRAF*
Diffuse midline glioma, H3 K27-altered	H3 K27, *TP53*, *ACVR1*, *PDGFRA*, *EGFR*, *EZHIP*
Diffuse hemispheric glioma, H3 G34-mutant	H3 G34, *TP53*, *ATRX*

Low grade glioma

- Gliomas - astrocytes, oligodendrocytes, and ependymal cells
- Headache, seizure, neurological deficits
- Grading characteristics: atypia, mitoses, endothelial proliferation, and necrosis
- Adult gliomas approximately 5.4 cases/100,000 population (low grade 10-20 %; 0.8/100,000)
- Children glioma, 2.4 cases/100,000 population (0.6 case/100,000)

Low grade gliomas

* Surgical resection
* Observation
* Radiotherapy
* Medical Care

  Seizures - phenytoin (Dilantin) or carbamazepine (Tegretol)

  Increasing intracranial pressure, peritumor edema - dexamethasone (Decadron, 2-4 mg every 6 hours)

  H2 blocker

Low grade glioma

- 5-year survival rate - 65-80%;
  10-year survival rate - 20-45%
- Male predominance (55%-65%)
- median age - 35 years
- Seizure, headache, focal neurological deficits

Malignant Gliomas in Adults

* Grade III: anaplastic astrocytoma, anaplastic oligodendroglioma, anaplastic oligoastrocytoma

  Grade IV: glioblastoma

- Primary glioblastoma: > 50 y/o

  Secondary glioblastoma: < 45 y/o

* Median survival:

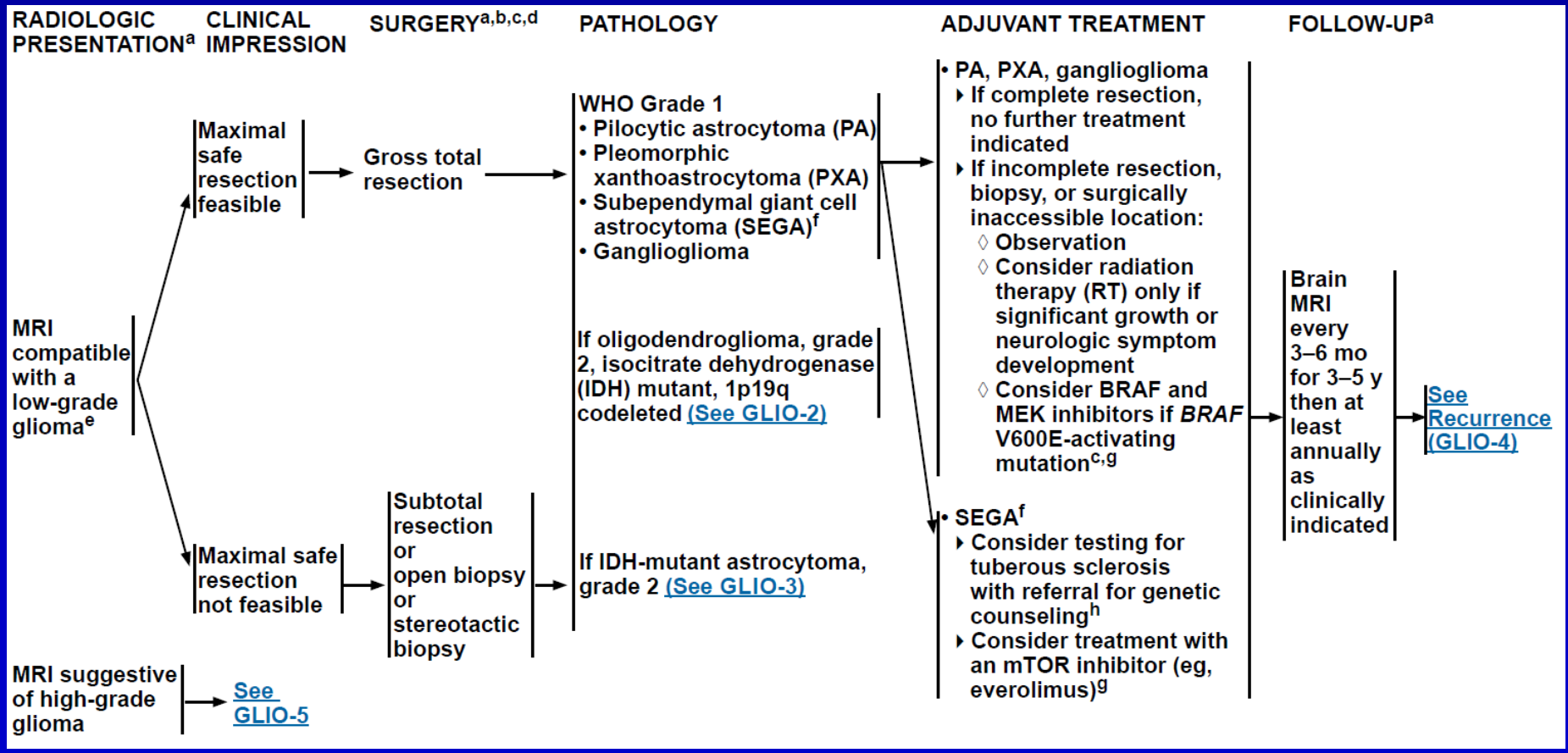
  12 to 15 months - glioblastomas

  2 to 5 years - anaplastic gliomas

Clinical presentations of Malignant gliomas

- Headaches (30-50%) -
  increased intracranial pressure
- Seizures (30-60%) -
  simple partial, complex partial, or generalized
- Focal neurologic deficits (40-60%) -
  cognitive problems
  neurological deficits resulting from radiation necrosis
  hydrocephalus
  cranial neuropathies and polyradiculopathies from leptomeningeal spread
- Mental status changes (20-40%) -
  earlier stage with subtle personality changes

NCCN Guidelines Version 2.2022
Adult Glioma: WHO Grade 1



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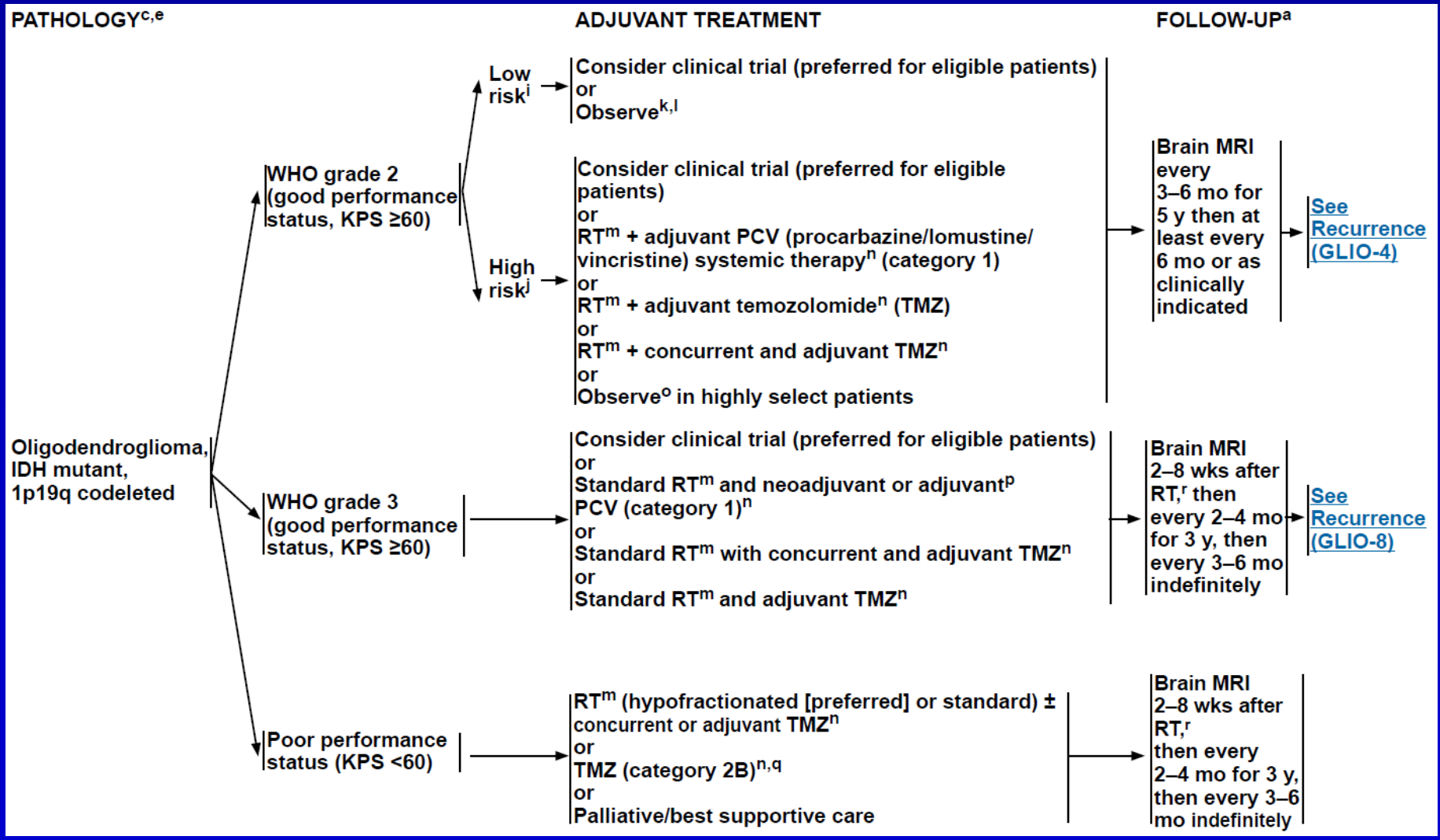
Adult Glioma: Oligodendroglioma (IDH mutant, 1p19q codeleted)



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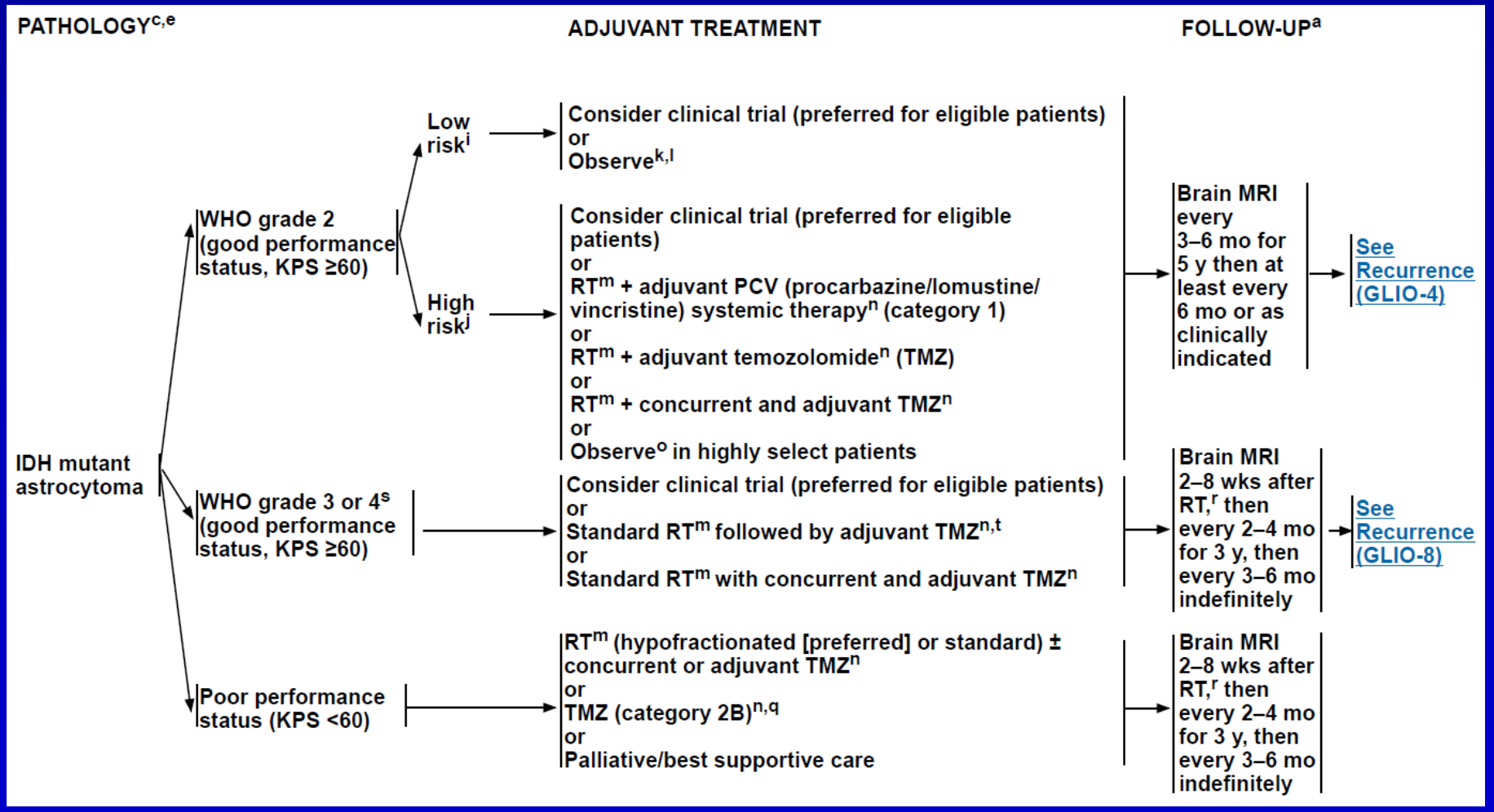
Adult Glioma: IDH-mutant Astrocytoma



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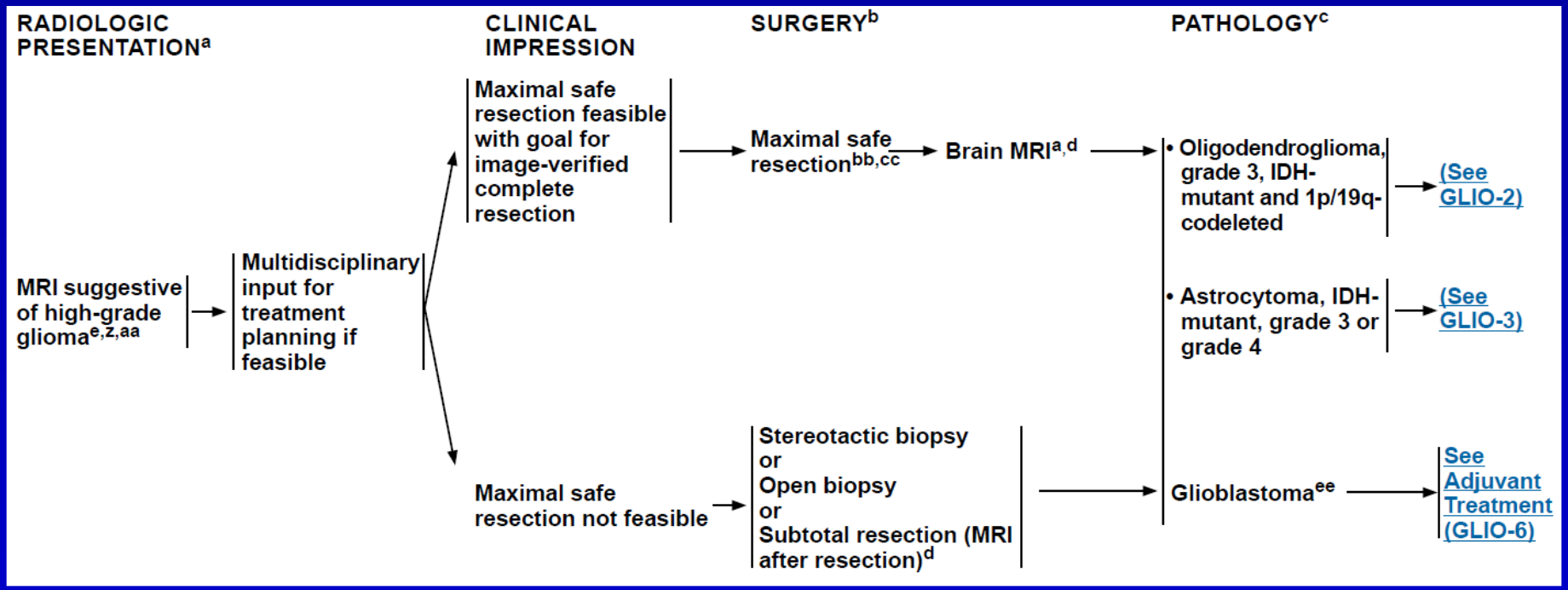
Adult Glioma: High-Grade



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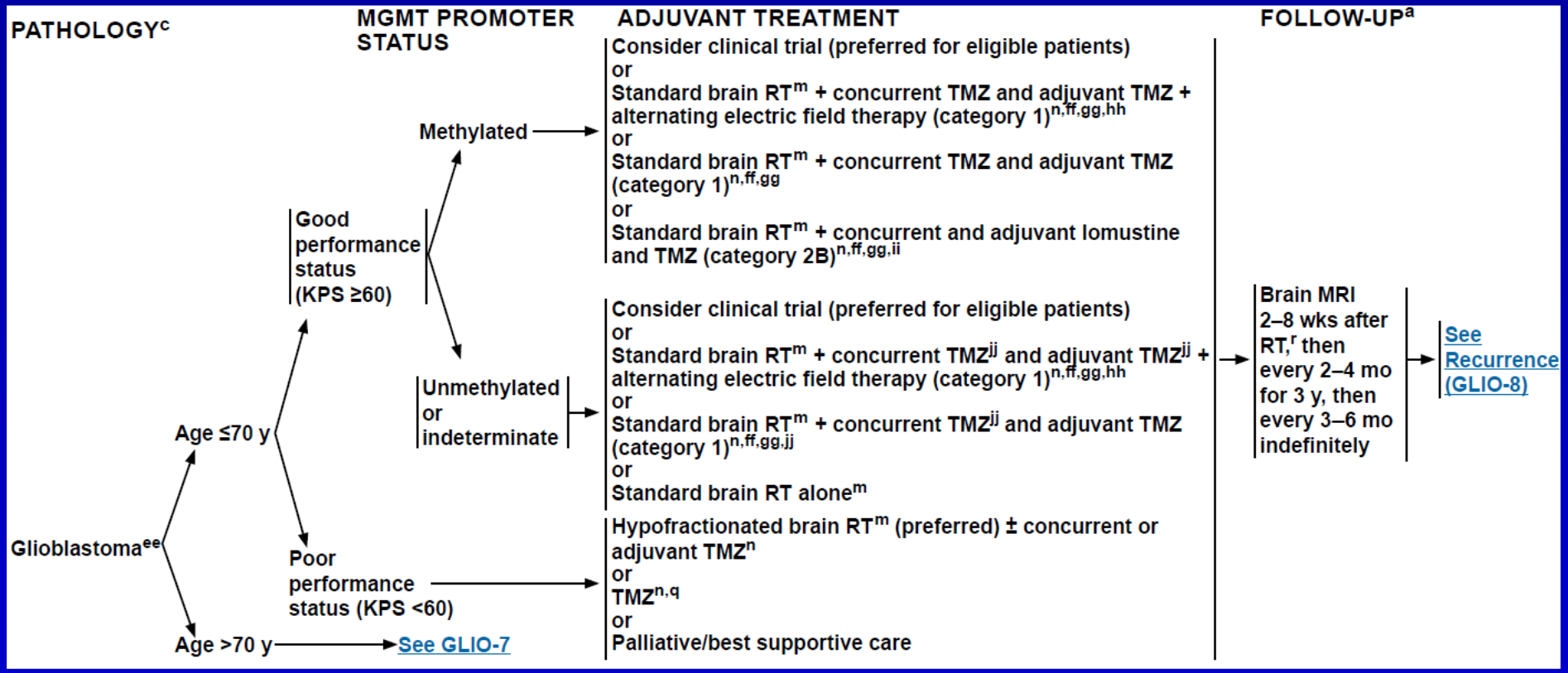
Adult Glioma: Glioblastoma



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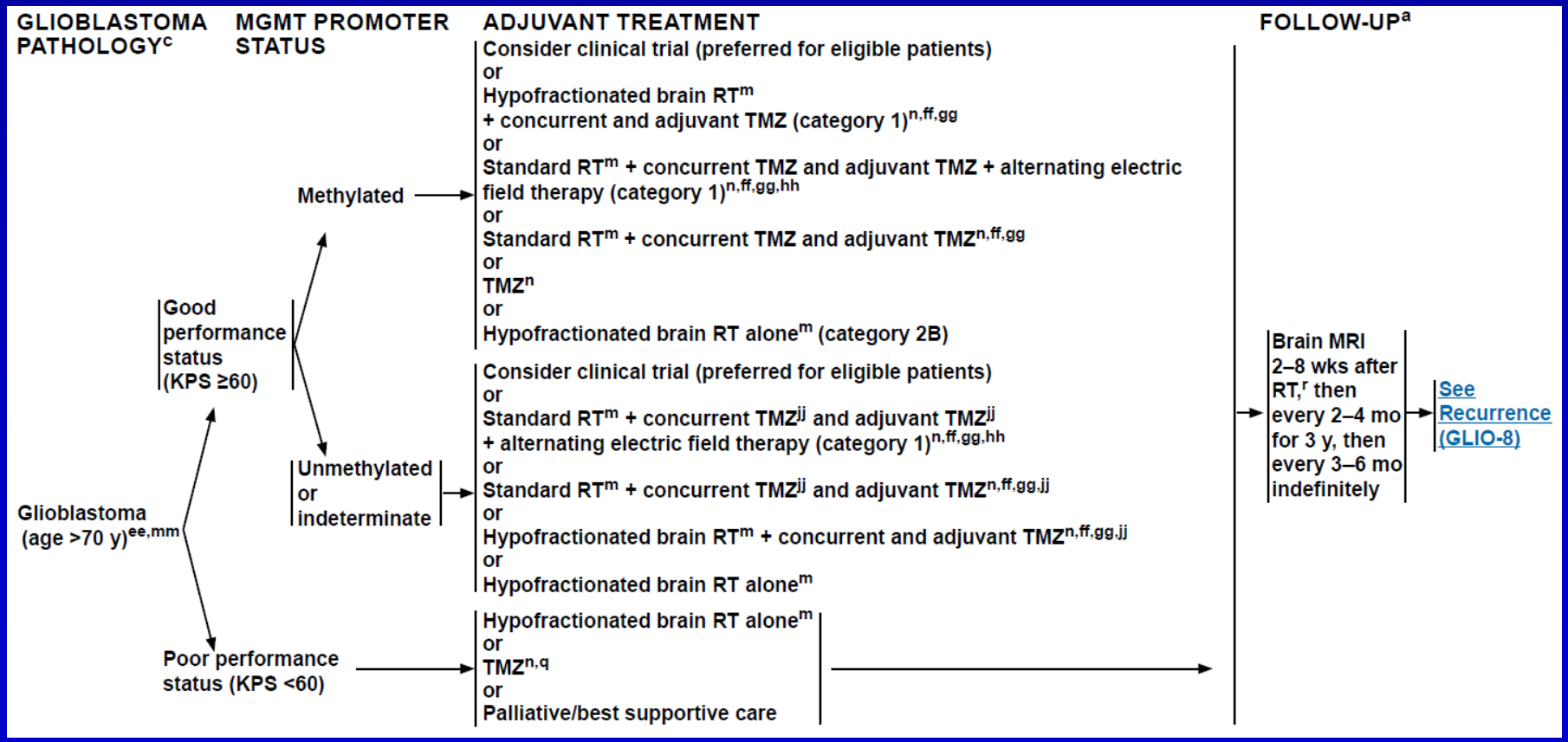
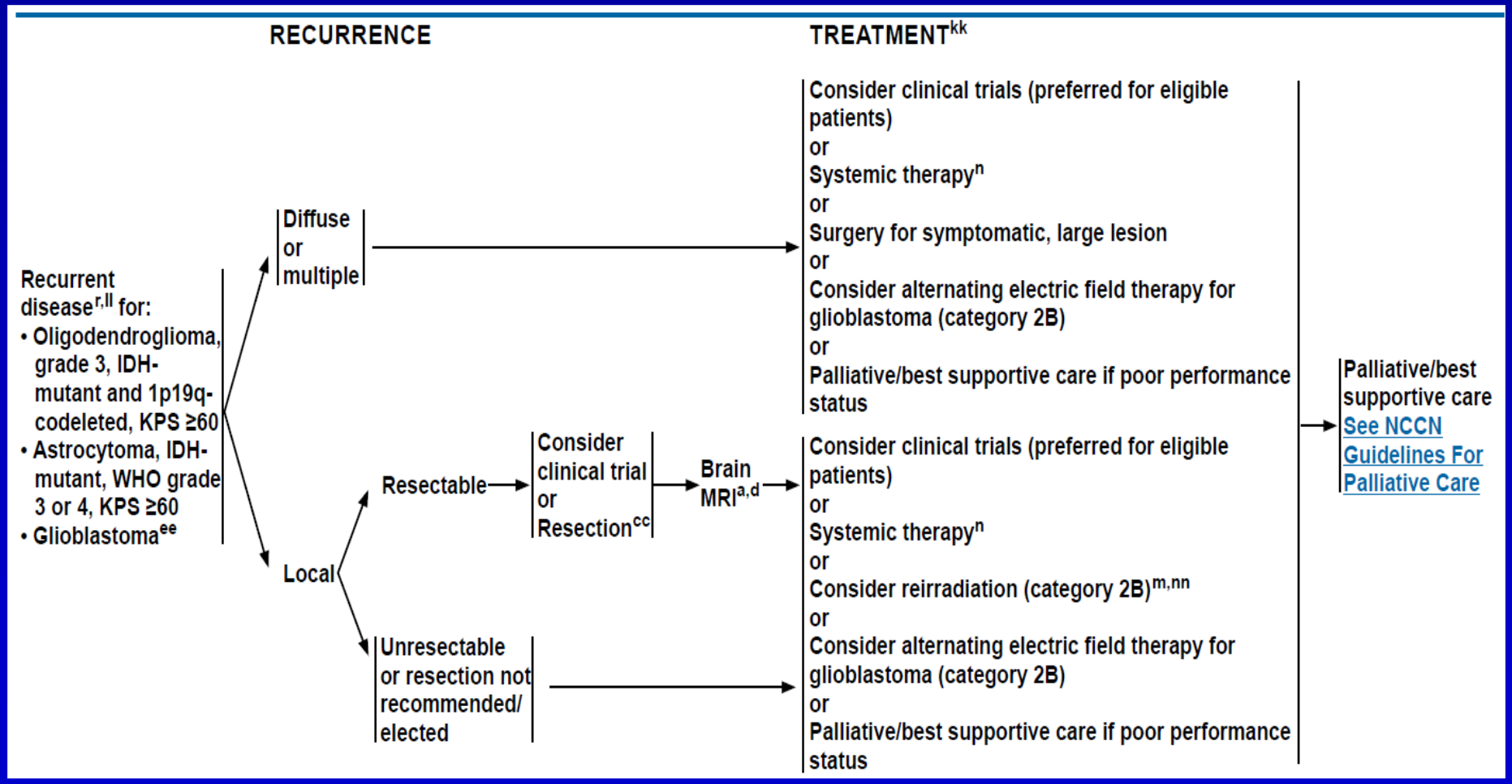
Adult Glioma: Glioblastoma



NCCN Guidelines Version 2.2022
Adult Glioma: High-Grade



Increasing importance of chemotherapy

* Glioblastoma treated with temozolomide
  - *MGMT* promoter methylation (45% of the total)
    median survival of 21.7 months; 2-year survival rate of 46%
  - *MGMT* no methylation
    median survival of 12.7 months; 2-year survival rate of 13.8%
* Biodegradable polymers containing carmustine (Gliadel Wafers, MGI Pharma)
  - median survival from 11.6 months to 13.9 months (P = 0.03)

Increasing importance of chemotherapy

* Codeletion of chromosomes 1p and 19q
  - 61 to 89% of anaplastic oligodendrogliomas
    14 to 20% of anaplastic oligoastrocytomas
  - PCV — procarbazine, lomustine (CCNU), and vincristine
  - response rates of 100%; 3 to 31% among no deletion

Radiotherapy + PCV increased 10 to 12 months of tumor progression free, did not improve overall survival (median, 3.4 and 4.9 years)

Brain metastasis

- 120,000-140,000 per year in USA
- 20% of cancer deaths annually
- Over 50% of brain tumor
- 15% present with neurologic symptoms before diagnosis
- 43-60% have an abnormal chest radiograph
- In 9%, the CNS is the only site of spread
- 10% of patients with no identifiable primary source

Brain metastasis

- Lung 48%
- Breast 15%
- Melanoma 9%
- Lymphoma 1% (mainly non-Hodgkin)
- G-I system 3% (3% colon, 2% pancreatic, hepatoma)
- Genitourinary system 11% (21% kidney, 46% testes, 5% cervix, 5% ovary)
- Osteosarcoma 10%
- Neuroblastoma 5%
- Head and neck tumors 6%

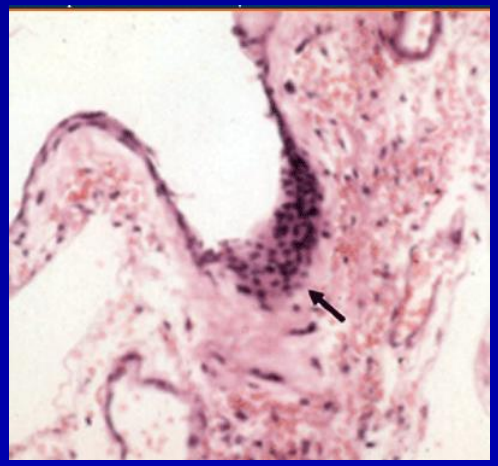
Lung-originated brain metastasis

- Lung cancer patients, survive for more than 2 years, 80% will have brain metastases
- Brain metastases within 4 months
- Small cell carcinomas, 20% of all lung cancers, but 50% of brain metastases

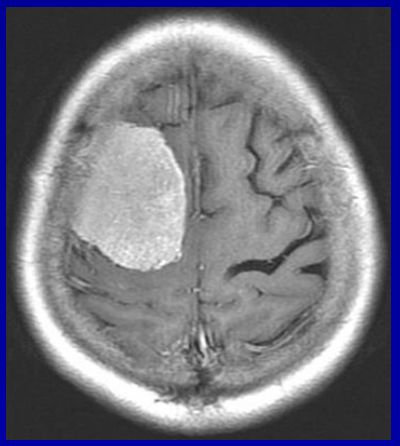
Treatment of brain metastasis

- Surgical treatments
- Medical treatments - symptomatic and systematic treatments
- Radiation therapy – WBRT; multiplanar fractionated radiation; and stereotactic radiosurgery
- Chemotherapy depends on original tumor
- Integration therapy - multidiscipline approach
  - behavioral modification
  - nutritional counseling
  - alternative medicine (herbal)
  - physical and occupational therapy

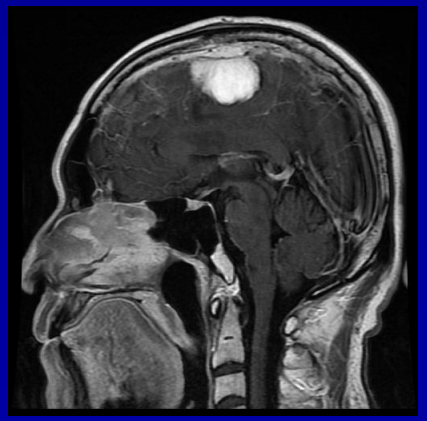
Meningioma



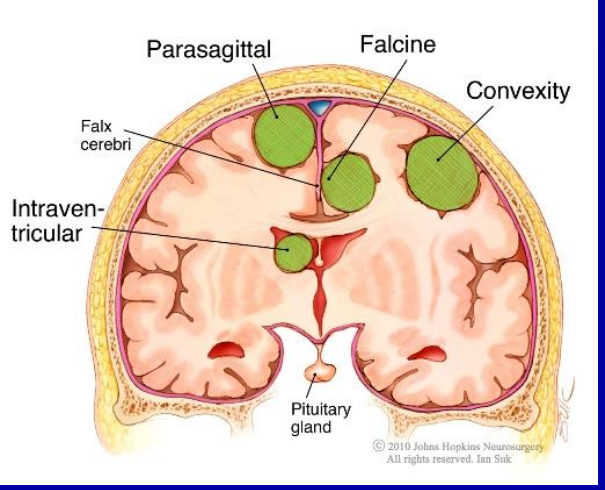
- Arise from arachnoidal cap cells
- 20% of all primary intracranial neoplasms
- 5-year survival: 73-94%
- Usually grow slowly, may produce severe morbidity before causing death.
- Male-to-female : 1:1.4 to 1:2.8



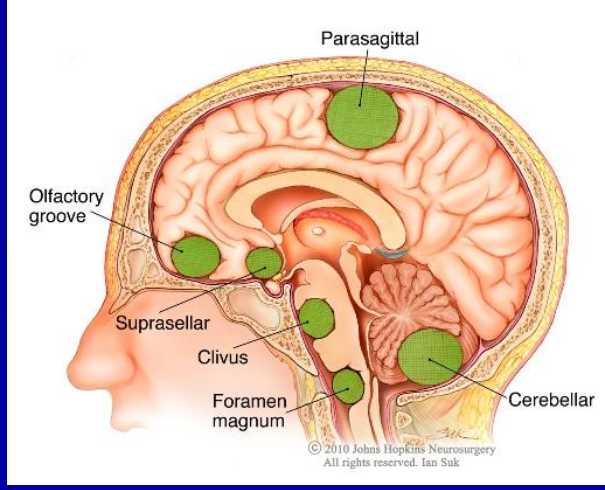
Classification of meningioma



Location	Symptoms
Parasagittal	Monoparesis of the contralateral leg
Subfrontal	Change in mentation, apathy or disinhibited behavior, urinary incontinence
Olfactory groove	Anosmia with possible ipsilateral optic atrophy and contralateral papilledema (this triad termed Kennedy-Foster syndrome)
Cavernous sinus	Multiple cranial nerve deficits (II, III, IV, V, VI), leading to decreased vision and diplopia with associated facial numbness
Occipital lobe	Contralateral hemianopsia
Cerebellopontine angle	Decreased hearing with possible facial weakness and facial numbness



Classification of meningioma



Location	Symptoms
Spinal cord	Localized spinal pain, Brown-Sequard (hemispinal cord) syndrome
Optic nerve	Exophthalmos, monocular loss of vision or blindness, ipsilateral dilated pupil that does not react to direct light stimulation but might contract on consensual light stimulation; often, monocular optic nerve swelling with optociliary shunt vessels
Sphenoid wing	Seizures; multiple cranial nerve palsies if the superior orbital fissure involved
Tentorial	May protrude within supratentorial and infratentorial compartments, producing symptoms by compressing specific structures within these 2 compartments
Foramen magnum	Paraparesis, sphincteric troubles, tongue atrophy associated with fasciculation

Grading of meningioma

WHO Grade	Histological Subtype	Histological Features
I	Meningothelial fibroblastic transitional angiomatous microcystic secretory lymphoplasmacytic metaplastic psammomatous	Does not fulfill criteria for grade II or III
II (Atypical)	Chordoid Clear cell	4 or more mitotic cells per 10 hpf and/or 3 or more of the following: increased cellularity, small cells, necrosis, prominent nucleoli, sheeting, and/or brain invasion in an otherwise Grade I tumor
III (Anaplastic)	Papillary Rhabdoid	20 or more mitoses per 10 hpf and/or obviously malignant cytological characteristics such that tumor cell resembles carcinoma, sarcoma, or melanoma

Treatment of meningioma

- Surgical principle
  - All involved or hyperostotic bone, free of dura rim
- Radiotherapy (adjuvant therapy)
  - incomplete resection
    high-grade
    recurrent
- Stereotactic radiosurgery
  - high risk of surgery
    small (<3 cm in diameter)
    residual
    recurrent lesions
  - small meningiomas
  - skull base
  - cavernous sinus

Spinal metastasis

- Common sites for cancer metastasis – lung, liver, spine
- Systemic cancer – 60-70% spinal metastasis
- Epidural and/or vertebral involvement - 94-98%
- Intradural extramedullary – 5-6%
- Intramedullary - 0.5-1%
- Thoracic - 70%, T4-T7
- Lumbar - 20%
- Cervical - 10%
- Multiple levels - 50%

Spinal metastasis

- Lung - 31%
- Breast - 24%
- GI tract - 9%
- Prostate - 8%
- Lymphoma - 6%
- Melanoma - 4%
- Unknown - 2%
- Kidney - 1%
- Others including multiple myeloma - 13%

Clinical presentations of spinal metastasis

* Median survival - 10 months
* Paralysis and/or bowel and bladder involvement
* Cord compression –
  preterminal event
  median survival 3 months
* Initial presentation
  - 90%, bone and/or back pain followed by radicular pain.
  - 50%, sensory and motor dysfunction
  - more than 50%, bowel and bladder dysfunctions
* 5-10% of patients initiated with cord compression

Management of spinal metastasis

- No treatment has been proven to increase the life expectancy.
- Therapeutic goals - pain control and functional preservation
- Bone pain - bony destruction or pathologic fractures
- Local pain - stretching of the periosteum, respond to irradiation

Management of spinal metastasis

- Axial pain - vertebral compression and/or collapse, mechanical instability
- Neuropathic pain - root irritation and/or meningeal irritation secondary to cancer infiltration
- Steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) for bone pain

Steroid for spinal metastasis

* Dexamethasone 10 mg then 4 mg every 6 hours
  - Least mineralocorticoid effects
  - Least likely to be associated with infection or cognitive dysfunction
  - Increase the risk of myopathy
* Adverse effects:
  - psychotic reaction (5%)
  - GI bleeding (<1%)
  - glucose intolerance (19%)
* More than 3 weeks - associated with complications
* Hypoalbuminemia increases the risks

Steroid for spinal metastasis

* 70-80%, symptoms improve within 48 hours of treatment
* ～64%, alleviation of pain within 24-48 hours
* 57% improvement in motor function
* Most patients continued until radiotherapy is completed.

Treatment of spinal metastasis

- Radiation therapy –

  67% pain control

  17% further deterioration of mobility or sphincter control
- Surgery –

  36% pain control

  surgery alone is the least effective

  20-26% further deterioration of mobility or sphincter control

Radiotherapy for spinal metastasis

* Radiosensitive tumors –
  lymphoma, neuroblastoma, seminoma, myeloma
* Relative insensitivity of radiotherapy –
  prostate carcinoma, lung and breast
* Resistant to radiotherapy –
  tumors of the GI system, kidney, melanomas
* The common regimen is 30 Gy in 10 fractions
* Stereotactic radiosurgery

Spinal cord tumors

- Epidural, intradural extramedullary, and intradural intramedullary
- Primary spinal tumors - intradural
- Metastatic spinal tumors - extradural
- Intramedullary neoplasms –
  astrocytomas
  ependymomas (60-70%)
  hemangioblastomas
- Astrocytomas and ependymomas –
  neurofibromatosis type 2, abnormal chromosome 22
- Hemangioblastomas –
  30% of patients with von Hippel-Lindau syndrome, abnormal chromosome 3

Treatment of spinal cord tumors

*Surgical therapy

*Standard fractionated radiation is used for astrocytomas of residual and recurrent neoplasm.

*Stereotactic spinal radiosurgery may be helpful for treating these lesions.

*Chemotherapeutic regimens have limited success.

Further study

- Pituitary adenoma
- Craniopharyngioma
- Germ cell tumor
- Medulloblastoma

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1. 轉移性脊椎腫瘤最常在何處發生?

a. 頸椎

b. 胸椎

c. 腰椎

d. 薦椎

2. 最容易轉移到腦的腫瘤為下列何者?

a. 肝癌

b. 大腸癌

c. 淋巴癌

d. 肺癌

3. Glioblastoma的治療應包括下列何者?

a. Radiotherapy

b. Surgical excision

c. Chemotherpy with temozolamide

d. 以上皆是

4. Meningiomam源自於何種細胞?

a. arachnoidal cap cell

b. endothelial cell of dura matter

c. epithelial cell of dura mater

d. fibroblast cell of leptomeninges