Introduction to Brain Tumors

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16.1 Epidemiology

Brain and other CNS tumors are the most common types of cancer in children aged 0–14 years, with an annual age-adjusted incidence rate of 5.47 per 100,000, and also the leading cause of cancer-related death in this age group, having recently surpassed leukemia in the US cancer registry. Brain cancer among the adult population accounts for 1.4% of all new cancers and 2.8% of all cancer deaths, with an annual incidence of 6.4 cases per 100,000 adults. Taking into consideration all primary brain and nervous system tumors in adults, the US incidence rate is estimated to be 29.18 per 100,000 population with approximately one-third of tumors being malignant and the remainder being benign or borderline malignant [1, 2]. The most common intracranial tumor is brain metastasis. They are ten times more frequent than primary brain tumors, and their incidence is increasing during the past decades, most probably due to the increased availability of brain imaging. More than 75% of the primary brain tumors are gliomas and meningiomas.

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16.2 Classification of Primary Brain Tumors

The classification is based on the World Health Organization (WHO) classification of CNS tumors as published in 1979 (Zuelch), followed by revisions in 1993, 2000, 2007, and 2016 [3]. Based on morphologic and immunohistochemical features, each tumor entity is basically classified according to its presumed cell of origin. However, the current WHO classification additionally incorporates molecular genetics and immunologic markers in an attempt to construct a cellular classification that is universally applicable and as prognostically valid as possible. Based on histological features, a classification scheme ranging from WHO grade I (benign) to WHO grade IV (malignant) is established. WHO grade I includes lesions with minimal proliferative potential and a high possibility of cure following surgical resection alone. Pilocytic astrocytomas, subependymomas, schwannomas, and most meningiomas are typical examples of WHO grade I tumors. WHO grade II tumors still demonstrate low mitotic activity but also a higher tendency for recurrence, diffuse astrocytomas, oligoastrocytomas, and ependymomas being the most classic examples. WHO grade III classified tumors include lesions with histologic evidence of malignancy, including nuclear atypia, cellular anaplasia, and increased mitotic activity. These lesions have anaplastic histology and infiltrative

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capacity. Anaplastic astrocytomas and anaplastic ependymomas are typical examples of WHO grade III tumors. The WHO grade IV classification is reserved for mitotically active, necrosis-prone, and rapid preoperative and postoperative progression tumors. These include glioblastoma and the various forms of embryonal tumors.

16.3 Metastatic Neoplasms

These tumors originate from tissues outside the central nervous system (CNS) and spread secondarily to the brain. They occur in up to 30% of cancer patients. The incidence of brain metastases is increasing over time. Several reasons may contribute, like the prolonged survival of patients due to improved adjuvant therapies, the improvement of neuroradiological techniques with the ability to detect minute lesions, and the use of standardized staging protocols to monitor the effect of treatment. The risk of developing a brain metastasis is highly dependent on the primary tumor site and its histological type. The most common cancer metastasizing the brain is lung cancer, accounting for up to 50% of all brain metastases, with breast cancer being the second most common cancer, accounting for up to 15–20% of all brain metastasis followed by melanoma (10%) [4]. Most tumors spread by hematogenous dissemination within the gray and white matter junction at the watershed areas of the arterial circulation, where the cells are usually trapped. Therefore, 80% of brain metastases are located in the cerebral hemispheres, 15% in the cerebellum, and 5% in the brain stem. A solitary brain metastasis, the absence of other distant metastases, a locally controlled primary tumor, a high Karnofsky Performance Scale, and age < 65 years are factors associated with a better prognosis [5, 6].

16.4 Gliomas

Glial tumors (astrocytomas, oligodendrogliomas, mixed gliomas, ependymomas, and choroid plexus tumors) represent approximately 25% of all primary CNS tumors diagnosed. The WHO grading can be used to provide information regarding tumor behavior. Immunohistochemical examination for specific proliferation-associated antigens and differentiation markers as well as molecular markers can be used to assess diagnosis, proliferation activity, response to adjuvant therapy, and prognosis. Immunohistochemistry examinations for antigens like GFAP and Ki-67 are well established in gliomas. Molecular biomarkers most commonly used to evaluate gliomas include 1p/19q co-deletion, methylation of the O6-methylguanine-DNA methyltransferase gene promoter, alterations of the epidermal growth factor (EGF) receptor pathway, isocitrate dehydrogenase (IDH) 1 and 2 gene mutations, and epidermal growth factor, lactophilin, and seven transmembrane domain-containing protein 1 on chromosome 1 (ELTD1) [7–9].

The prognosis in individual cases depends on the grade of tumor, its location, the age of the patient, the percentage of tumor that can be removed surgically, and the response to radio- and chemotherapy. WHO grade I is reserved for focal lesions. The pilocytic astrocytoma is the typical WHO grade I lesion. Complete removal of this lesion often means a definitive cure for the patient. WHO grade II lesions are diffuse but demonstrate only low-proliferation histological characteristics and may recur or change into higher-grade tumors. At 5 years after diagnosis, 65% of patients with WHO grade II astrocytomas are alive. The prognosis is significantly worse for grade III anaplastic astrocytomas (30%), oligodendrogliomas (40%), and grade IV glioblastomas (6%). The age-standardized 10-year relative survival for low-grade gliomas is estimated at 47%. The average survival of patients with glioblastoma is less than 12 months but can be extended to 14 months with more recent treatment protocols [10, 11].

In children more than 30% of CNS tumors are gliomas, with low-grade tumors being more common. Most gliomas are pilocytic WHO grade I lesions located in the cerebellum. At 5 years after diagnosis, 98% of patients are alive. The prognosis of diffuse WHO grade II lesions is worse (48%). Grade III and IV tumors have the same prognosis as in adults.

16.5 Meningiomas

36.6% of primary brain tumors are meningiomas, which are extra-axial lesions originating from the arachnoid mater and are composed by neoplastic meningothelial cells. Women are more commonly affected than men in a ratio almost 2:1. Meningiomas are usually sporadic tumors, but patients with neurofibromatosis have a significantly increased risk of developing such lesions. The vast majority of them (85%) are WHO grade I tumors. Atypical WHO grade II meningiomas are uncommon (12%), and malignant WHO grade III lesions are rare (2–3%). Since benign meningiomas are slow-growing lesions, the prognosis is favorable, even in those cases where the lesion cannot be completely removed by surgery. In some, most often elderly, patients, a substantial percentage of incidentally found meningiomas (up to 30%) do not grow at all in serial MRI controls over extended periods of time. Eighty percent of the patients harboring WHO grade I lesions are alive 5 years after diagnosis, but the same is true in only 50% of the patients with malignant meningiomas. Meningiomas were the first neoplasm shown to carry a characteristic cytogenetic alteration, monosomy 22. In several studies, loss of expression of protein molecules has been demonstrated, and a number of genomic alterations have been associated with progression and atypical histology, including losses of chromosome arms 1p, 6q, 9p, 10, 14q, and 18q, as well as gains/amplifications on 1q, 9q, 12q, 15q, 17q, and 20q [12, 13]. Deletion of the tumor suppressor gene CDKN2 A has also been associated with aggressive and/or anaplastic tumors [14].

16.6 Pituitary Tumors

Tumors of the pituitary are the second most common primary brain tumor histology type (17%) in the latest statistical reports of the Central Brain Tumor Registry of the United States. The pituitary and the craniopharyngeal duct range also very high in tumor site statistical distribution, second only to meningeal tumors.

The majority of pituitary tumors are benign adenomas originating from the adenohypophysis. This is a diverse group of tumors with various precursor cell histologies, traditionally classified as secreting or non-secreting, depending on the production (or lack of) of pituitary hormones, and micro- and macroadenomas depending on their size (smaller and larger than 10 mm in diameter, respectively). Patients with adenomas present often with symptoms related to either hormone imbalance or, as in the case of bigger macroadenomas, mass effects on adjacent cranial nerves or CSF circulation.

MR imaging and pituitary hormone screening are the most important parts in the evaluation of patients with tumors in the sellar region. Adenomas of the pituitary are best visualized with thin coronal slices with the field of view centered at the sella. Small microadenomas of the pituitary can be difficult to identify occasionally, even with high-field MRI, without dynamic contrast-enhanced sequences. Other tumors arising in the sellar and parasellar area are meningiomas, craniopharyngiomas, chordomas, chondrosarcomas, schwannomas, germ cell tumors, plasmacytomas, and metastases. Pituitary metastases are rare and occur most frequently in patients with lung or breast cancer. Rapid developing pituitary hormone insufficiency is very common in patients with metastatic tumors which can be difficult to distinguish from adenomas in MRI. Loss of the pituitary bright spot and high tumor contrast enhancement in contrast-enhanced T1-weighted images are findings that might suggest a metastatic histology [15].

References

1. Ostrom TQ, Gittleman H, Xu J et al (2016) CBTRUS statistical report: primary brain and other central nervous system tumors diagnosed in the United States in 2009–2013. Neuro Oncol 18(suppl_5):v1–v75
2. National Cancer Institute, SEER Cancer Statistics Review (CSR) 1975–2014. Released April 2017
3. Louis DN, Perry A, Reifenberger G et al (2016) The 2016 World Health Organization classification of tumors of the central nervous system: a summary. Acta Neuropathol 131(6):803–820

4. Norden AD, Wen YP, Kesari S (2005) Brain metastases. Curr Opin Neurol 18:654–661
5. Diener-West M, Dobbins TW, Phillips TL et al (1989) Identification of an optimal subgroup for treatment evaluation of patients with brain metastases using RTOG study 7916. Int J Radiat Oncol Biol Phys 16(3):669–673
6. Lagerwaard FJ, Levendag PC, Nowak PJ et al (1999) Identification of prognostic factors in patients with brain metastases: a review of 1292 patients. Int J Radiat Oncol Biol Phys 43(4):795–803
7. Louis DN (2006) Molecular pathology of malignant gliomas. Annu Rev Pathol 1:97–117
8. Riemenschneider MJ, Jeuken JW, Wesseling P et al (2010) Molecular diagnostics of gliomas: state of the art. Acta Neuropathol 120(5):567–584
9. Towner RA, Jensen RL, Colman H et al (2012) ELTD1, a potential new biomarker for gliomas. Neurosurgery 72:77
10. Stewart LA (2002) Chemotherapy in adult high-grade glioma: a systematic review and meta-analysis of individual patient data from 12 randomised trials. Lancet 359(9311):1011–1018
11. Ohgaki H, Kleihues P (2005) Population-based studies on incidence, survival rates, and genetic alterations in astrocytic and oligodendroglial gliomas. J Neuropathol Exp Neurol 64(6):479–489
12. Lamszus K (2004) Meningioma pathology, genetics, and biology. J Neuropathol Exp Neurol 63(4):275–286
13. Perry A, Gutmann DH, Reifenberger G (2004) Molecular pathogenesis of meningiomas. J Neuro-Oncol 70(2):183–202
14. Perry A, Banerjee R, Lohse CM et al (2002) A role for chromosome 9p21 deletions in the malignant progression of meningiomas and the prognosis of anaplastic meningiomas. Brain Pathol 12(2):183–190
15. Zamora C, Castillo M (2017) Sellar and parasellar imaging. Neurosurgery 80(1):17–38