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Current approaches and clinical findings in brain tumor evaluation

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ABSTRACT

Brain tumors are a serious health issue with high mortality and morbidity rates. This review addresses current approaches in the diagnosis and treatment of brain tumors. Advanced techniques, such as magnetic resonance imaging and magnetic resonance spectroscopy, play a significant role in examining the biological and biochemical properties of tumors. In aggressive tumors like glioblastoma, genetic factors and molecular changes are crucial in determining treatment response and prognosis. Surgery, chemotherapy, and immuno-oncological approaches are the fundamental methods that shape treatment strategies. Additionally, innovations such as artificial intelligence and mathematical modeling are supporting diagnostic and therapeutic processes.

Keywords: Brain tumors, glioblastoma, temozolomide.

Brain tumors hold a significant place among central nervous system diseases and are often associated with high mortality and morbidity rates. The complex structures of these tumors complicate the diagnosis and treatment processes, while modern imaging techniques and molecular genetic analyses have revolutionized these processes.

IMAGING TECHNIQUES AND APPLICATIONS

One of the most effective methods for diagnosing brain tumors is magnetic resonance imaging (MRI) techniques. Conventional MRI, including T1 and T2-weighted imaging, provides anatomical details of the tumors.[1] Advanced imaging techniques provide deeper insights into the biological characteristics of tumors. For example, diffusion-weighted imaging (DWI) is used to determine the degree of malignancy, while magnetic resonance spectroscopy (MRS) analyzes tumor metabolism.[2,3]

Pathological analyses play a critical role in the definitive diagnosis of tumors. According to the World Health Organization classification, different types such as gliomas, meningiomas, and metastatic tumors are defined. This classification guides treatment processes based on the molecular characteristics and genetic profiles of the tumors.[4,5] Methods such as cerebrospinal fluid (CSF) cytology can also assist in diagnosis. The CSF cytology has provided a correct diagnosis in 62% of cases of malignant tumors.[6]

Magnetic resonance imaging can be used in the diagnosis of brain tumors with both standard and advanced techniques. While conventional MRI techniques are used to assess the anatomical features of tumors, advanced techniques provide important insights into tumor biology.[1]

Among conventional MRI methods, T1-weighted imaging, with the use of contrast agents, reveals tumor vascular structure and disruptions in the blood-brain barrier. T2-weighted imaging highlights swelling and inflammation surrounding the tumor. The fluid-attenuated inversion recovery imaging technique allows for the clear visualization of small lesions and edema.[7]

Among advanced MRI techniques, DWI analyzes the movement of water molecules

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in the tissue to determine cellular density and the grade of malignant tumors. Low apparent diffusion coefficient values are commonly observed in high-grade tumors such as glioblastoma multiforme.[3]

The DWI provides microstructural mapping of white matter tracts and helps preserve critical regions during surgery.[8] Magnetic resonance spectroscopy analyzes metabolites to examine the biochemical profiles of tumors. An increase in the choline/N-acetylaspartate (Cho/NAA) ratio is particularly used as an indicator of malignant tumors in clinical applications.[9]

Magnetic resonance spectroscopy in glioblastoma

Magnetic resonance spectroscopy is an important diagnostic tool in the evaluation of brain tumors such as glioblastoma.[10] This imaging technique helps in understanding the biochemical properties of tumors by measuring the levels of specific chemicals present in the brain tissue. In a normal brain, metabolites such as NAA, creatine, and Cho are found within specific ppm (parts per million) ranges. NAA typically peaks at 2.0 ppm, creatine at 3.0 ppm, and Cho at 3.2 ppm. N-acetylaspartate is an indicator of healthy neuronal activity, creatine represents energy metabolism, and Cho plays a role in cell membrane metabolism. However, in high-grade tumors such as glioblastoma, Cho/NAA and creatine levels decrease, while Cho levels increase, reflecting cell proliferation and tumor growth. Additionally, an increase in lactate and lipid levels can be observed in tumor tissue, indicating anaerobic metabolism and cell breakdown.[11]

GLIOBLASTOMA

In the evaluation of glioblastoma, MRS not only helps determine the tumor grade but also assists in assessing treatment response and disease recurrence. For example, distinguishing between a recurrent tumor and radiation-induced tissue damage after radiotherapy can be challenging. Magnetic resonance spectroscopy can provide valuable insight by identifying changes in metabolite levels, such as increased Cho or lactate, which may indicate tumor recurrence, while radiation-induced damage may show different metabolic patterns.[12] In recurrent tumors, Cho levels are elevated, whereas in radiation damage, both NAA, creatine, and Cho levels are typically lower. In high-metabolic activity tumors like glioblastoma, these changes in metabolites serve as indicators of tumor malignancy grade and the spread of tumor cells to surrounding tissues. Elevated Cho levels suggest increased cell membrane turnover, associated with tumor cell proliferation, while decreased NAA and creatine levels reflect neuronal dysfunction and energy metabolism disruptions in the affected brain tissue.[13] This information is of great importance for accurate diagnosis and treatment planning.[11]

Genetic and molecular factors

The molecular characteristics of brain tumors play a critical role in determining treatment responses and predicting the course of the disease. Aggressive tumors, such as glioblastoma, exhibit genetic differences and molecular subgroups. A chemical alteration of the O6-methylguanine-DNA methyltransferase (MGMT) gene may serve as a marker that enhances response to temozolomide (TMZ) treatment. Isocitrate dehydrogenase mutations have a positive impact on the disease progression of low-grade gliomas and lead to metabolic reprogramming of these tumors. Additionally, tumor protein 53 mutations and epidermal growth factor receptor gene amplification are common genetic alterations found in the pathogenesis of glioblastoma.[14]

Environmental factors also play a significant role in the development of brain tumors. Ionizing radiation, particularly when exposure occurs during childhood, is a strong risk factor for gliomas and meningiomas. However, data regarding electromagnetic fields and mobile phone use are conflicting. While some studies suggest that prolonged use of mobile phones may increase the risk of gliomas, there is no definitive evidence to support this claim.[15]

CLINICAL SYMPTOMS AND EPIDEMIOLOGICAL FINDINGS

Brain tumors can occur across all age groups, from childhood to adulthood. In children, brain tumors account for approximately 20% of

solid tumors, while in adults, glioblastoma is the most common malignant tumor.[16,17] In children, tumors such as medulloblastomas are more common, while in adults, gliomas and metastatic brain tumors are more prevalent. During pregnancy, hormonal changes can lead to an increase in tumor size, which can complicate diagnosis and treatment.[18]

The symptoms of brain tumors vary depending on the location, size, and growth rate of the tumor. Common signs include headaches, nausea, vomiting, papilledema, and seizures.[19] Frontal lobe tumors are associated with personality changes and cognitive impairments, temporal lobe tumors with memory loss and partial seizures, and parietal lobe tumors with loss of spatial awareness.[20]

In advanced stages, tumors can also cause psychiatric symptoms, which further complicates the diagnostic process.[19,21,22]

The symptoms of brain tumors depend on factors such as the size, location, and growth rate of the tumor. Common symptoms include headaches, nausea, vomiting, papilledema (swelling of the optic disc due to increased intracranial pressure), and seizures. Morning headaches that worsen may indicate increased intracranial pressure.[23] Seizures are common, especially in slow-growing tumors like low-grade gliomas. These tumors may cause seizures due to their gradual development, which can affect brain function and lead to electrical disturbances. Symptoms vary depending on tumor localization. Tumors in the frontal lobe are associated with personality changes and impairments in motor function. Tumors located in the temporal lobe can cause memory loss and partial seizures. Parietal lobe tumors lead to sensory deficits and loss of spatial awareness, while tumors in the occipital lobe are characterized by visual field loss.[19]

Epidemiological data show that the incidence of malignant tumors is higher in men compared to women, while benign tumors are more common in women. During childhood, medulloblastomas are the most common malignant tumors. High-grade tumors such as glioblastoma, with an average age of diagnosis of 59, are typically seen in older age groups.[2]

Treatment approaches and innovations

In the treatment of brain tumors, surgical interventions, chemotherapy, radiotherapy, and immuno-oncological approaches are utilized in combination. Surgical methods aim to physically remove the tumor, while technological advancements focused on preserving surrounding tissues have gained significant importance.[24] For example, laser interstitial thermal therapy and intraoperative fluorescence-guided surgery have improved surgical success rates.[25]

The chemotherapy agent TMZ is used as a first-line treatment for glioblastoma, while MGMT gene methylation plays a critical role in determining the response to therapy.[14] Radiotherapy is tailored to the histopathological type of the tumor. In particular, the side effects of craniospinal irradiation should be carefully considered in younger age groups.[26]

Immuno-oncological therapies hold promise in the treatment of resistant tumors such as glioblastoma. T cell-based therapies, oncolytic viruses, and vaccines targeting the immune system are among these therapeutic approaches.[27]

Surgery, radiotherapy, and chemotherapy stand out as the main approaches in the treatment of brain tumors.[28] Surgery aims to achieve complete tumor removal whenever possible, but preserving surrounding structures is crucial. Robotic surgery and laser interstitial thermal therapy are effective alternatives in cases where traditional surgery is limited.[25] Intraoperative fluorescence-guided surgery enhances precision in defining tumor boundaries and increases surgical success rates.[22]

In the field of chemotherapy, TMZ is used as a first-line agent in the treatment of glioblastoma.[29] The MGMT gene methylation status is a key determinant of the response to TMZ treatment. Additionally, targeted radiotherapy minimizes damage to healthy tissues by enabling radioactive molecules to bind specifically to tumor cells.[30]

The mechanism of action of temozolomide

Temozolomide inhibits the proliferation of cancer cells by adding methyl groups to DNA.[31] This methylation primarily occurs at the guanine base of DNA and complicates DNA repair during cell division. If the cells are unable to repair the damage, tumor cells either die or lose their capacity to grow.[32]

Effect of temozolomide on DNA repair

The effect of TMZ depends on the activity of the MGMT enzyme. If the MGMT enzyme is low or suppressed, the damage caused by TMZ to the DNA cannot be repaired, leading to the death of cancer cells.[33] However, when MGMT is active, cells can repair the DNA damage, leading to resistance to TMZ treatment. Therefore, MGMT gene methylation is an important biomarker for the efficacy of TMZ.[34]

Artificial intelligence and mathematical modeling

In recent years, artificial intelligence and computer-assisted systems have revolutionized the diagnostic processes of brain tumors. Explainable convolutional neural networks enhance diagnostic accuracy by analyzing MRI images, providing valuable support to doctors.[35] Additionally, mathematical modeling methods are used to predict tumor growth. For example, modeling has been done using one-dimensional boundary value problems, and nonlinear equations have been solved using the Newton-Raphson method.[36]

Psychosocial effects and patient care

Brain tumors affect patients' quality of life not only physically but also psychologically and socially.[37] Psychiatric symptoms, particularly in advanced stages, are common and can interfere with patients' daily activities. Counseling services help patients adapt more easily to treatment while also contributing to the development of their ability to function independently in daily life.[38-40]

In conclusion, advancements in the methods used for the diagnosis and treatment of brain tumors offer significant potential to improve patients' lifespan and quality of life. Artificial intelligence, genetic analyses, and multidisciplinary approaches have made this process more effective. However, further research is needed on issues such as the limitations of gene therapy, improving diagnostic accuracy, and managing psychosocial impacts.

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