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Astrocytoma: Insights into Risk Factors, Pathogenesis, Diagnosis and Management

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Abstract Astrocytoma is one of the most common types of brain tumors. It arises from astrocytes—star-shaped cells that make up the "glue-like" or supportive tissue of the brain. There are different types and severities of Astrocytomas. According to (WHO),It can be classified into grades from I to IV. The most frequently diagnosed types of astrocytoma are pilocytic astrocytoma, grade II astrocytoma, anaplastic astrocytoma and glioblastoma multiforme. They may or may not be cancerous. The exact cause of astrocytoma is unknown. Astrocytomas occur slightly more often in men than in women. They are slightly more common in Caucasians. Astrocytomas can develop in both children and adults. The diagnosis of astrocytoma is based on a thorough clinical evaluation, characteristic physical findings, a careful patient history, and specialized tests. Astrocytomas may be treated with surgery, radiation therapy, chemotherapy or a combination of treatments.

Keywords: *Astrocytoma, tumor, pathogenesis, diagnosis, management*

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1. Introduction

Any tumor that arises from the glial or supportive tissue of the brain is called a "glioma.". One type of glioma is the astrocytoma. Astrocytomas are named after astrocytes, the star-shaped cells from which they grow [1]. The World Health Organization (WHO) classifies astrocytomas into four grades depending on how fast they are growing and the likelihood that they will spread (infiltrate) to nearby brain tissue. Non-infiltrating astrocytomas usually grow more slowly than the infiltrating forms [2]. Astrocytomas can appear in various parts of the brain and nervous system, including the cerebellum, the cerebrum, the central areas of the brain, the brainstem, and the spinal cord [1]. Neurologic symptoms from astrocytoma development depend foremost on the site and extent of tumor growth in the CNS and may include altered mental status, cognitive impairment, headache, nausea and vomiting, visual disturbances, motor impairment, seizures, sensory anomalies and ataxia [3]. The diagnosis of astrocytoma is based on a thorough clinical evaluation, characteristic physical findings, a careful patient history, and specialized tests [4].

There is no accepted standard of treatment for low-grade or anaplastic astrocytoma. Treatment decisions are generally best made through a team approach, including input from the involved neurosurgeon, radiation oncologist, and medical oncologist or neurologist [3].

2. Risk factors of astrocytoma

The exact risk factors for astrocytomas have not been identified. Some studies suggest the following risk factors increase your chance of this tumor [5]:

2.1. Envirmontal Risk Factors

Researchers suspect that exposure to certain chemicals may increase the risk of astrocytoma in developing babies during pregnancy or infancy. Such chemicals include pesticides, formaldehyde, vinyl chloride, phenols, acrylonitrile, N-nitrosos compounds, polycyclic aromatic hydrocarbons, lubricating fluids, and organic solvents. People may be exposed to these chemicals at certain jobs [7].

2.2. Genetic Disorders Risk factors

Neurofibromatosis, Neurofibromatosis is an inherited disorder that causes a type of noncancerous tumor called a neurofibroma to form on peripheral nerves in the body, brown spots on the skin, and tissue and bone deformities andTuberous sclerosis, Li-Fraumeni syndrome, Nevoid basal cell carcinoma syndrome, Turcot syndrome [5,6].

3. Pathophysiology

The diffuse astrocytoma (grade II) is the earliest stage of infiltrating astrocytic tumors. No premalignant stage of this tumor has been recognized. A high percentage of diffuse astrocytomas and anaplastic astrocytomas exhibit a characteristic mutation in the codon 132 of one copy of the IDH gene, with the most common mutation resulting in the substitution of histidine for arginine, [8] and the acquired ability of the enzyme to catalyze the nicotinamide adenine dinucleotide phosphate (NADPH)-dependent reduction of alpha-ketoglutarate to R(-)-2-hydroxyglutarate (2HG). The accumulation of 2HG has been demonstrated in individuals with an inherited error in 2HG metabolism, a disease which is also associated with an increase in gliomas [9].

4. Clinical Presentation

Clinical symptoms of diffuse astrocytomas are the result of brain irritation (e.g., seizures), increased intracranial mass (e.g., headache), or brain invasion (e.g., hemiparesis, dysphasia). Tumoral progression from lower to higher grades is associated with a concomitant lower incidence of seizures and a higher incidence of focal neurologic deficits. Tumors originating in clinically silent areas of the brain may be quite extensive at diagnosis but present with only signs of raised intracranial pressure, including headaches, nausea, diplopia, personality changes, and lethargy [10]. Inheritable brain tumor syndromes that have an association with a propensity to form astrocytomas includes Li-Fraumeni Syndrome (TP53 mutation syndrome), Turcot-Lynch syndrome (DNA mismatch repair loss), and neurofibromatosis type 1. Rare familial astrocytomas clusters have also been described [11].

5. Grades of Astrocytoma

Astrocytomas are one of the most lethal and difficult to treat tumors among neuroepithelial neoplasms [12]. According to the 2007 World Health Organization (WHO) classification of tumors of the central nervous system, astrocytomas can be classified into grades I-IV [13].

Because exact grading was obtained by pathologists through examining tissue section slides, and malignancy grading of astrocytomas is fundamentally important due to its effects on accurate treatment planning and patient management, it is important to assess tumor grading before operation [12,14,15].

The World Health Organization (WHO) scheme is based on the appearance of certain characteristics: atypia, mitoses, endothelial proliferation, and necrosis. These features reflect the malignant potential of the tumor in terms of invasion and growth rate. Tumors without any of these features are classified as grade I. Tumors with cytological atypia alone are considered grade II (diffuse astrocytoma). Those that show anaplasia and mitotic activity in addition to cytological atypia are considered grade III (anaplastic astrocytoma) and those who exhibit all of the previous features as well as microvascular proliferation and/or necrosis are considered grade IV [16].

5.1. Grade I Astrocytoma (Pilocytic astrocytomas)

Pilocytic astrocytomas are slow growing tumors with an expansile growth pattern and little propensity to disseminate resulting, overall, in an excellent prognosis, as represented in the WHO grade (grade I). These tumors primarily arise in children and young adults but may remain asymptomatic until later in life. Clinically, the tumors are most commonly associated with either headaches or seizures and rarely present with focal deficits, except when they occur in the optic pathway.

Of clinical importance is the occurrence of these tumors in the brainstem, where they may be mistaken for a diffusely infiltrating fibrillary astrocytomas. In contrast to the fibrillary astrocytomas, the prognosis of the brightly enhancing, exophytically growing pilocytic astrocytoma is much better [17,18,19]. Pilocytic astrocytoma is the most common intracranial tumor in patients with neurofibromatosis type I, and these lesions are largely confined to the optic nerve [20].

5.2. Grade II Astrocytoma (Diffuse astrocytoma)

Diffuse astrocytoma typically arises in young adults, although they are also found in children and senior citizens. They may be found anywhere in the brain, but are most common in the cerebral hemispheres – the “thinking” part of the brain. As the name implies, the borders of a diffuse astrocytoma tend to grown into surrounding normal brain tissue. Seizures and headaches are very often the earliest signs of this tumor; weakness on one side of the body (hemiparesis) is also common [21].

5.3. Grade III Astrocytoma (Anaplastic Astrocytoma)

Anaplastic astrocytomas are lesions with imaging appearances and prognosis between those of diffuse low grade astrocytomas (WHO grade II) and glioblastomas (WHO IV). On imaging, these tumours share common features with diffuse low grade astrocytomas. However, they tend to present with contrast enhancement. Anaplastic astrocytomas occur in adulthood with peak incidence between 40 and 50 years of age, which is older than low grade astrocytomas and younger than glioblastomas [22].

5.4. Grade IV Astrocytoma (Glioblastoma)

Composed of a heterogeneous mixture of poorly differentiated neoplastic astrocytes, glioblastomas primarily affect adults, and they are located preferentially in the cerebral hemispheres. Much less commonly, glioblastoma multiforme can affect the brainstem (especially in children) and the spinal cord. These tumors may develop from lower-grade astrocytomas (World Health Organization [WHO] grade II) or anaplastic astrocytomas (WHO grade III), but, more frequently, they manifest de novo, without any evidence of a less malignant precursor lesion [23,24,25].

6. Prevention

There are no prevention guidelines since the exact cause of astrocytoma is not known [5].

7. Diagnosis

7.1. Laboratory Studies

No laboratory studies are diagnostic of astrocytoma. Baseline laboratory studies that may be obtained for general metabolic surveillance and preoperative assessment include: basic metabolic profile, Complete blood cell count (CBC), Prothrombin time (PT), Activated partial thromboplastin time (aPTT).

7.2. Imaging Studies

Computed tomography (CT) and magnetic resonance imaging (MRI) grading, and pathophysiological evaluation of astrocytomasare helpful in the diagnosis. [3]

7.3. Biopsy

Biopsy will help differentiate tumor from other types of masses, such as infection. The microscopic structure of the tumor will be important in grading the tumor [26].

7.4. Other Tests

Electroencephalography (EEG) may be employed to evaluate and monitor epileptiform activity in patients with seizures associated with astrocytoma. Radionuclide scans, such as positron emission tomography (PET), single-photon emission tomography (SPECT), and technetium-based imaging, can permit study of tumor metabolism and brain function; PET and SPECT may be used to distinguish a solid tumor from edema, to differentiate tumor recurrence from radiation necrosis, and to adjacent structures. Metabolic activity determined by radionuclide scans can be used to determine the grade of a lesion; hypermetabolic lesions often correspond to higher-grade tumors. An electrocardiogram (ECG) and chest radiograph are indicated to evaluate operative risk.

7.5. Procedures

Lumbar puncture (LP) should be approached with extreme caution in patients with cerebral astrocytomas, because of the risk of downward cerebral herniation secondary to elevated intracranial pressure [3].

8. Management of astrocytoma

Treatment options in astrocytomas include operative intervention and the use of chemotherapy and radiation therapy. Treatment decisions are generally best made by a team approach, including input from the involved neurosurgeon, radiation oncologist, and medical oncologist or neurologist. Generally, care is primarily directed by a neurologist or specialist in neurooncology. A study found that adjuvant radiotherapy for pilocytic astrocytoma significantly prolonged progression-free survival (PFS) at both 5 years and 10 years compared with observation alone. However, the overall survival was equivalent [27].

8.1. Chemotherapy

Chemotherapy is the use of drugs to destroy tumor cells, usually by stopping the tumor cells' ability to grow and divide. Chemotherapy is given by a medical oncologist, a doctor who specializes in treating a tumor with medication, or a pediatric oncologist. Systemic chemotherapy gets into the bloodstream to reach tumor cells throughout the body. Common ways to give chemotherapy include an intravenous (IV) tube placed into a vein using a needle or in a pill or capsule that is swallowed (orally) [28].

For low-grade astrocytomas that are inoperable because of location or have demonstrated early recurrence or progression, chemotherapy with carboplatin and vincristine has been successfully used in prepubertal children in an effort to avoid or delay irradiation. Other drug regimens may also be effective [29]. High-grade astrocytomaChemotherapy has little impact on the overall survival of patients with high-grade tumors despite several regimens showing significant tumor response rates [30].

8.2. Surgical Treatment

Surgery is the removal of the tumor and some surrounding healthy tissue during an operation. It is the most common treatment for astrocytoma. During surgery, a neurosurgeon removes as much of the tumor as possible. Sometimes, a tumor is inoperable, meaning it cannot be reached by surgery because of its location. However, even for inoperable tumors, a surgical biopsy can usually still be done to find out the type and grade of the tumor [28].

Surgical resection is the primary treatment modality. If feasible, a complete resection is the goal of surgery in order to minimize the risk of local recurrence. However, long-term progression-free intervals may ensue even after partial resection. Low-grade tumors that recur or progress may be re-resected, and patients can undergo observation without further treatment if the risk of neurologic impairment from further growth is low and the tumor has undergone a significant interim period of dormancy [30].

8.3. Radiation Therapy

Radiation therapy is the use of high-energy x-rays or other particles to destroy tumor cells. A doctor who specializes in giving radiation therapy to treat a tumor is called a radiation oncologist. The most common type of radiation treatment is called external-beam radiation therapy, which is radiation given from a machine outside the body. When radiation treatment is given using implants, it is called internal radiation therapy or brachytherapy. A radiation therapy regimen usually consists of a specific number of treatments given over a set period of time [28].

9. Prognosis

As most diffuse astrocytomas are often treated, the natural history of these lesions is not easily discerned. The available literature does indicate that even the seemingly indolent tumors have a potentially ominous future, with most sources indicating a 6-8 year survival. [30,31] The location and physical association of these tumors clearly alters the therapeutic options and ultimate prognosis [32]. In general, the survival of patients with anaplastic astrocytoma is 2.5 years [33,34].

10. Conclusion

Astrocytomas are one of the most lethal and difficult to treat tumors among neuroepithelial neoplasms but it may be treated with surgery, radiation therapy, chemotherapy, or a combination of treatments.

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