ОРИГІНАЛЬНІ ДОСЛІДЖЕННЯ

ORIGINAL RESEARCHES

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Diagnosis and management of astrocytoma: a literature review

Abstract. *Astrocytoma is a form of a brain tumor that is rather prevalent. It originates in astrocytes, star-shaped cells that make up the "glue-like" or supporting tissue. Astrocytomas are classified by their nature and severity. According to the World Health Organization, there are I—IV grades of these tumours. Pilocytic astrocytoma, grade II astrocytoma, anaplastic astrocytoma, and glioblastoma multiforme are the most common types of astrocytoma. However, depending on the type, its clinical appearance and diagnosis may change. Similarly, surgical management differs depending on the type of astrocytoma. The current study aims to identify the basic characteristics of different forms of astrocytoma, better understand diagnosis and therapy, and search for publications in NCBI, PubMed, and Google Scholar databases. This article provides an overview of astrocytoma therapy based on its type; the findings greatly depend on different forms of astrocytoma, possibility to perform gross total resection, and lastly, the prognosis. Knowledge of astrocytoma types and manifestations may help in the surgical management of astrocytoma. We also presented a review of the literature on the types and diagnosis of astrocytoma and evaluated current surgical treatments and prognosis.*
Keywords: *astrocytoma; review; diagnosis; extent of resection; surgical management*

Introduction

According to Brain Tumour Charity (2018), astrocytoma is a tumour that develops from a type of brain cell called an astrocyte. Throughout the spinal cord and brain, there are nerve cells known as neurons that transmit messages to, within and from the brain. Surrounding the neurons are cells known as glial cells that support and protect the neurons by providing them with nutrients and oxygen and removing dead cells. An astrocyte secures and assists neurons which also help to pass information between neurons and it is also essential in processing the messages in brain.

Kabel et al. (2018) has stated that any tumour which emerges from brain's supportive or glial tissue is known as glioma. One type of glioma is known as astrocytoma. Astrocytomas are named after astrocytes, the star-shaped cells from which they grow. The accurate cause of astrocytoma is not known and it occurs more often in men than in women. Astrocytomas can develop both in adults and

children. The treatment methods used for astrocytomas are chemotherapy, surgery, radiation therapy or combination of treatments.

Moini and Piran (2020) have stated that the tumours which emerge from astrocytes are known as astrocytomas. The tumour may be malignant or benign and it is graded based on abnormal or normal cell qualities. The astrocytomas may exist anywhere in the central nervous system. The early symptoms of astrocytomas are seizures, headaches, memory loss and changes in behaviour. The treatments used for astrocytomas include radiation therapy, surgery, follow-up scan, survey and chemotherapy.

According to Kapoor and Gupta (2021), astrocytoma originates in astrocytes which are a type of glial star-shaped cells in the cerebrum. Astrocytoma is the most common glioma which generally affects the brain of a human being and sometimes also develops in the spinal cord. Glial tumours are the common cause of morbidity and mortality in both old

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and young age people. One of the common brain tumours is astrocytoma.

Moini et al. (2021) has mentioned that the common form of glioma is astrocytoma. The most common symptoms of astrocytomas are headache due to increased intracranial pressure, loss of memory, seizures, changes in behaviour, head tilt, neck stiffness, incoordination, vomiting, nausea, visual problems and irritability. The treatment method for astrocytomas is a combination of radiation therapy, surgery, follow-up imaging, observation, ventricular shunting and chemotherapy.

Astrocytoma types

According to the research of Hirtz et al. (2020), there are four types of astrocytoma, from grade I to grade IV. Grade I tumour is known as pilocytic astrocytoma which is always benign and can be resected. Grade II tumours are diffuse astrocytomas, low-grade or infiltrative gliomas. They develop gradually that will acquire a much aggressive phenotype over time. Grade III tumours are anaplastic astrocytomas including oligoastrocytomas and oligodendrogliomas. Grade IV tumour, glioblastoma multiforme, is characterized by a rapidly developing phenotype with the presence of necrotic areas and vascular growth.

Bikowska-Opalach et al. (2014) have described diffuse astrocytomas as grade II astrocytomas which occur in young people though they also affect senior patients and children. They may develop in any part of the brain but are most typical for hemispheres of the cerebrum. The diffuse astrocytomas tend to develop into surrounding normal tissue of brain. Headaches, weakness in one part of the body and seizures are the earliest symptoms of brain tumour.

Grimm and Chamberlain (2016) have reported that anaplastic astrocytoma is a malignant, diffusely infiltrating primary brain tumour with a median onset of 41 years of age. Anaplastic astrocytoma is defined by histological features of increased cellularity, nuclear atypia, significant activity of proliferation as manifested in mitoses and lacking either necrosis or endothelial proliferation which are the two hallmarks of glioblastoma.

Singla and Gupta (2016) have described grade IV astrocytoma which is named glioblastoma multiforme. It is a malignant tumour which increasingly spreads to other brain parts. There are two types of grade IV astrocytoma, primary and secondary. Primary astrocytoma is the most common and most aggressive whereas secondary astrocytoma is a low-grade tumour that develops into grade IV tumours.

In the research of Volovetz et al. (2019), it is stated that pilocytic astrocytoma is a type of astrocytoma with specific genetic, histological and clinical features. It is the most frequent primary brain tumour which affects mainly adolescents and children though it may also present in adulthood.

Table 1 shows the reviews of the types of astrocytoma.

Diagnosis of astrocytoma

Sukheeja et al. (2015) have stated in their research that the prognosis assessment by grading astrocytoma has been challenging activity for pathologists though surgical and radiological imaging approaches have improved significantly. This research has attempted to assess tumours intraoperatively for quick diagnosis. MIB-1 labelling index was used to study their proliferative activity. Intraoperative cytology is useful and accurate in consultation of intraoperation. MIB-1 labelling index was used as a conjunct in this research for grading in little biopsies.

In the work of Matyja et al. (2016), the prognosis and behaviour of pilocytic astrocytomas correlated with location and histology of tumours. Pilomyxoid astrocytoma is a classical pilocytic astrocytoma with greater invasive development and increased risk of dissemination and recurrences. Pilocytic astrocytomas have varied histology with biphasic architecture of loose, compact and microcystic fibrillary regions. The pilocytic astrocytoma diagnosis requires careful examination of histopathological, molecular and clinical characteristics to avoid misinterpretation of benign neoplastic lesions.

The main purpose of Xia et al. (2016) study was to recognize imaging features of pilocytic astrocytomas in ventricles of the cerebrum to help radiologists differentiate pilocytic astrocytomas and other brain tumours preoperatively. The radiological and clinical records were analysed. The radiological characteristics of extraventricular and intraventricular pilocytic astrocytomas were similar to typical ones including developed nodules within cysts.

Sanju et al. (2018) have mentioned in their research that brain tumours are heterogeneous neoplasms with annual incidence of 5 to 10 % per 100,000 population in India. The tumours classification is an art of pathology to differentiate

Table 1. Reviews of the types of astrocytoma

Author	Year	Astrocytoma type	Symptoms
Hirtz et al.	2020	Pilocytic, diffuse, anaplastic astrocytoma and glioblastoma	Useful to diagnose the disease severity
Bikowska-Opalach et al.	2014	Diffuse astrocytoma	Headaches, weakness in one part of the body and seizures
Grimm and Chamberlain	2016	Anaplastic astrocytoma	Loss of sensory, weakness, language disorder, visual impairment and gait disturbances
Singla and Gupta	2016	Glioblastoma multiforme	Primary brain tumours
Volovetz et al.	2019	Pilocytic astrocytoma	Occurs as cystic tumours on imaging

malignant and benign lesions on histological basis. This research reveals that histopathology is an essential component for grading and diagnosis in some cases. Immunohistochemistry plays an essential role in critical cases where grading and diagnosis are not feasible only on the basis of histology.

Kristensen et al. (2019) propose an integrated histomolecular method which allows for an accurate diagnosis of embryonal central nervous system tumours and diffuse gliomas. This study provides an update of several essential prognostic markers and diagnostic markers for state-of-the-art identification of primary central nervous system tumours. Immunohistochemistry is a useful tool for characterizing molecules of many brain tumours.

Tian et al. (2019) have described the two most common primary brain tumours in adults, anaplastic astrocytoma and glioblastoma. The differential diagnosis is essential for prognosis and treatment suggestions. The main aim of the study is to assess the discriminative ability of texture analysis using machine learning to differentiate glioblastoma and anaplastic astrocytoma. The texture characteristics were taken from contrast-enhanced magnetic resonance imaging using the LifeX package. The results of the research show that magnetic resonance imaging using linear discriminant analysis algorithm had promising ability to distinguish glioblastoma and anaplastic astrocytoma.

Alshoabi et al. (2021) provided a case report of diffuse astrocytoma and the diagnostic dilemma in an unusual phenotype. Diffuse astrocytoma is a glioma of infiltrating type which is difficult to diagnose even with histopathology. The results of histopathology confirmed the identification of diffuse astrocytoma; the patient died postoperatively.

Geramizadeh et al. (2021) presented a study on a simple panel of isocitrate dehydrogenase 1 (IDH1) and P53 in differential diagnosis of low-grade astrocytoma and reactive gliosis. Reactive gliosis is a glial tissue response to various types of injury namely trauma, abscess, neoplastic or haemorrhage process of the brain. In certain situations, particularly when the biopsy of tissue is small, there may be difficulty to discriminate the reactive condition with low-grade diffuse astrocytoma by hematoxylin and eosin slides, so some molecular and immunohistochemical markers have been introduced for differential diagnosis. In this research, the authors evaluated P53 and IDH1 mutation by immunohistochemistry as a highly sensitive, easy and specific approach to distinguish reactive gliosis and low-grade astrocytoma. The combination of IDH1 and P53 as an immunohistochemical panel reveals 91% sensitivity and 96% specificity for differential diagnosis of low-grade astrocytoma and reactive gliosis. These two markers can be useful for differential diagnosis.

Table 2. Reviews of diagnosis of astrocytomas

Author	Year	Type of diagnosis	Results of diagnosis
Sukheeja et al.	2015	Histopathology and intraoperative cytology	Helps in providing accurate planning and diagnosis for better management of patients
Matyja et al.	2016	Histology diagnosis of pilocytic astrocytomas	Needs careful examination of histopathological, molecular and clinical characteristics to avoid misinterpretation of benign neoplastic lesions
Xia et al.	2016	Radiology and pathology	Diagnose pilocytic astrocytomas and developed nodules within cysts properly
Sanju et al.	2018	Histopathological diagnosis and immunohistochemistry	Essential for accurate subtyping, grading and diagnosis of tumours
Kristensen et al.	2019	Immunohistochemistry and molecular pathology	Provides effective and specific therapeutic methods for tumour patients
Tian et al.	2019	Differential diagnosis	Assess the discriminative ability of texture analysis using machine learning to differentiate glioblastoma and anaplastic astrocytoma
Alshoabi et al.	2021	Histopathology diagnosis	Confirms the diagnosis of diffuse astrocytoma; the patient died postoperatively
Geramizadeh et al.	2021	Immunohistochemistry diagnosis	Differential diagnosis of gliosis and gliomas using P53 and IDH1 to confirm the results of immunohistochemistry with molecular approaches
Madabushi et al.	2021	Immunohistochemistry diagnosis	Overcomes the diagnostic difficulties since accurate histologic diagnosis helps in predicting the clinical outcomes in different brain tumours
Mubarak and Naeem	2021	Histopathology diagnosis	Makes the diagnosis of pilocytic astrocytoma challenging

In the research of Madabushi et al. (2021), central nervous system tumours comprise 1 to 2 % of all tumours which pose diagnostic difficulties because various histogenesis of tumours reveals different overlap and differentiation in morphological characteristics. The results of the research show that astrocytomas in adults were most common followed by nerve sheath tumours, meningiomas, metastatic deposits, gliosarcomas and glioblastomas. Tumour grading was performed as per revised criteria of the World Health Organization (WHO). Immunohistochemistry results were studied in selective cases. This research highlights the immunohistochemistry utility as an adjunct in histologic diagnosis of brain tumours in critical cases.

Mubarak and Naeem (2021) reviewed five cases in patients with histopathological diagnosis of pilocytic astrocytoma. Pilocytic astrocytoma is a low-grade glial tumour which occurs commonly in paediatric population. It is rare in adults and usually has better prognosis. These tumours have various locations in the central nervous system including the fourth ventricle, cerebellum, optic chiasm, suprasellar area, brain stem and cerebral hemisphere in different patients. Pilocytic astrocytoma has a wide spectrum vast set of neuroradiological presentation. Besides its classical existence as low-grade glioma, a more typical presentation makes the diagnosis challenging.

Table 2 shows the reviews of diagnosis of astrocytomas.

Treatment of astrocytoma

Barker et al. (2014) describe survival of patients treated with radiation therapy for anaplastic astrocytoma. Anaplastic astrocytomas make up 7 % of primary brain tumours in adults. This study assessed the association of patient-, treatment- and tumour-related factors with survival in astrocytoma. Medical records of patients with astrocytoma who underwent radiotherapy between 1987 and 2007 were reviewed. In this study, the classification of Radiation Therapy Oncology Group recursive partitioning analysis correlated with survival.

Forst et al. (2014) have mentioned in their study that low-grade gliomas are a diverse group of primary brain tumours that emerge in healthy patients and have an indolent course with higher survival compared to high-grade gliomas. The treatments include surgery, observation, chemotherapy, radiation or combination method and the management depends on tumour location, molecular profile, histology and patient characteristics. This study reviews current strategies for low-grade gliomas such as radiotherapy, chemotherapy and surgery.

Pace et al. (2014) have stated that patients with brain tumour differ from other cancer populations due to complexity of supportive care requirements, disease course, short life expectancy and resulting need for a particular palliative method. This research proposed a pilot model of palliative care for brain tumour patients.

According to Walbert and Chasteen (2015), brain tumour diagnosis is a life-changing situation for families and patients. This study discusses screening tools specific for symptoms and validates global symptom assessments to recognize distressing symptoms. Fatigue, seizure, anxiety and depression are common symptoms throughout the disease and must be managed properly.

Narita (2018) et al. proposed chemotherapy treatment for adults with diffuse astrocytoma. The chemoradiotherapy or chemotherapy efficiency in diffuse astrocytoma has been largely unknown until recently. However, a randomized controlled study revealed that addition of CCNU, vincristine and procarbazine chemotherapy to fractioned radiotherapy in patients with high-risk WHO grade II gliomas, including those with diffuse astrocytoma, has essential positive effect on overall and progression-free survival. Temozolomide efficiency in low-grade gliomas was reported and a randomized phase III study that compares fractioned radiotherapy alone or in combination with temozolomide in unresectable diffuse astrocytoma is ongoing presently.

The research of Wang and Li (2018) presents synthesis of the most recent evidence of surgery and its efficacy in the treatment of astrocytoma patients. The findings of this study provide useful reference for the complications and efficiency of surgery in astrocytoma patients to future researchers and clinicians.

According to Wahner et al. (2020), current guidelines suggest maximal safe resection followed by chemotherapy and radiotherapy for anaplastic astrocytoma patients. They have a limited life expectancy despite this multimodal treatment method. In this study, variables related to the overall survival were identified and a score was built to find the overall survival of anaplastic astrocytoma patients at primary diagnosis stage. Implementing molecular markers into the classification of the World Health Organization raised queries about the importance of clinical trials and grading revealed advantages of overall survival for combined radiochemotherapy.

Table 3 shows the reviews of the treatment types for astrocytoma.

Reviews on astrocytoma studies

Hervey-Jumper and Berger (2014) have stated that central nervous system tumour is a major cause of mortality and morbidity in the US. Outside of brain metastasis high- and low-grade gliomas are the most common intrinsic brain tumours. High-grade gliomas are aggressive with the vast majority of patients facing recurrence and a median survival of one to three years.

Xia et al. (2018) have mentioned in their research that resection is essential to conduct a pathological biopsy and to achieve intracranial pressure reduction in patients with low-grade gliomas. The main purpose of the study is to determine whether a greater extent of resection would improve the 5- and 10-year overall survival of these patients.

Patel et al. (2019) presented a study on the extent of surgical resection in lower-grade gliomas with differential impact based on molecular subtype. The diffuse low-grade gliomas are classified into molecular subtypes.

Wang et al. (2019) performed a systematic review on the advance of extent of resection in glioblastoma surgical treatment. This study summarizes and reviews the history of surgical resection for glioblastoma.

Table 3. Reviews of the treatment types for astrocytoma

Author	Year	Treatment for astrocytoma	Advantage of treatment
Barker et al.	2014	Radiation therapy	Improves the survival in patients with glioblastoma (type of astrocytoma)
Forst et al.	2014	Radiotherapy, chemotherapy and surgery	Improves the quality of life of a patient and ability to tolerate ongoing chemotherapy
Pace et al.	2014	Palliative and supportive care	Protects patients dying from brain tumour and helps develop care for them particularly at this stage of disease
Walbert and Chasteen	2015	Palliative and supportive care	Improves the quality of life of patients, symptom burden and survival in glioma patients
Narita et al.	2018	Chemotherapy treatment	Increases effectiveness of astrocytoma treatment
Wang and Li	2018	Surgery treatment	Assesses the surgery efficacy for the treatment of astrocytoma patients
Wahner et al.	2020	Chemotherapy and radiotherapy	Effective in treating patients with diffuse gliomas and astrocytoma
Steidl et al.	2021	Radiochemotherapy	Increases maximum time to treatment failure in oligodendrogliomas

Table 4. Reviews of astrocytoma studies

Author	Year	Findings of the study
Hervey-Jumper and Berger	2014	Greater extent of resection in low-grade glioma patients not only improves survival but also helps control seizure
Xia et al.	2018	The relation between prognosis and extent of resection provide a basis for the development of evidence-based medicines in low-grade glioma patients
Patel et al.	2019	The extent of surgical resection influences overall survival in patients with IDH-mutant low-grade gliomas, especially in those with IDH mutant-noncodeleted low-grade glioma
Wang et al.	2019	Maximize the resection using developed techniques; focus on microenvironment of glioblastoma multiforme therapy remains challenging
Choi et al.	2020	Clinical trials using the adjuvant therapy for low-grade gliomas must be stratified by molecular subtype and extent of resection
Mao et al.	2020	Survival in gross total resection was greater compared to not attempted or unsuccessful gross total resection; therefore, several patients are motivated to undergo gross total resection to improve the cancer specific survival and overall survival
Laurent et al.	2020	Extent of resection is not related to increased risk of hospital-acquired conditions and patient safety indicators
Karschni et al.	2021	Categories is used as a factor of stratification for future clinical trials
Motomura et al.	2021	Extent of resection is not related to progressive free survival in patients with aggressive IDH-wild type of anaplastic and diffuse astrocytoma
Revilla-Pacheco et al.	2021	A weak correlation is found between the overall survival and extent of surgical resection with a reduced level of evidence

Choi et al. (2020) evaluated prognostic factors in adult low-grade gliomas according to the 2016 World Health Organization classification. Records of 153 patients diagnosed with WHO grade II low-grade glioma between 2003 and 2015 were reviewed retrospectively.

Laurent et al. (2020) carried out a retrospective analysis to assess the relationship between extent of resection and the occurrence of hospital-acquired conditions and patient safety indicators. The extent of resection is well established as correlating with overall survival in patients with glioblastoma.

The study of Mao et al. (2020) examines the relationship between survival results and surgical approaches in astrocytoma patients. People diagnosed with astrocytoma between 2004 and 2015 were identified using the Surveillance, Epidemiology and End Results database.

Karschnia et al. (2021) developed evidence-based expert recommendations on the types for extent of resection. Surgical resection is the standard of care in diffuse gliomas and more extensive tumour resection seems to be associated with favourable outcomes.

The main purpose of Motomura et al. (2021) study is to assess the impact of the extent of tumour resection on survival in patients with lower-grade gliomas who underwent awake brain mapping.

Revilla-Pacheco et al. (2021) proposed a systematic review and meta-analysis on extent of resection and survival in patients with glioblastoma multiforme. Glioblastoma multiforme has an ominous prognosis with overall survival of 14 months. The extent of surgical resection is one of the factors associated with better prognosis.

Table 4 shows the reviews of studies conducted on astrocytoma.

Conclusions

With the present growth in the treatment of brain astrocytoma, it is debated highly whether the extent of resection influences the survival. The maximum extent of resection must be tried safely while reducing the surgically-induced neurological risk. Genetics is the upcoming sector for brain tumour therapies. Various treatment methods are used to cure astrocytoma. Thus, it can be summarized that astrocytoma can be managed with greater quality clinical trials prospectively.

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Діагностика і лікування астроцитоми: огляд літератури

Резюме. Астроцитома є досить поширеною формою пухлини головного мозку. Вона розвивається з астроцитів — зіркоподібних клітин, що утворюють «клейоподібну» або підтримуючу тканину. Астроцитоми класифікують за характером і тяжкістю. За даними Всесвітньої організації охорони здоров'я, виділяють I—IV ступені цих пухлин. Пілоцитарна астроцитома, астроцитома II ступеня, анапластична астроцитома і мультиформна гліобластома є найпоширенішими видами астроцитоми. Однак залежно від виду клінічні прояви і діагноз можуть змінюватися. Хірургічне лікування теж відрізняється залежно від типу астроцитоми. Мета цього дослідження: визначити основні характеристики різних форм астроцитоми, краще зрозуміти діагностику і терапію, а також провести пошук публікацій у базах даних NCBI, PubMed та Google Scholar. У статті наведено огляд лікування астроцитоми на основі її типу; результати значною мірою залежать від різних форм астроцитоми, можливості виконати тотальну резекцію і, нарешті, прогнозу. Знання типів астроцитоми і проявів може допомогти при хірургічному лікуванні. Ми також представили огляд літератури щодо типів і діагностики астроцитоми та оцінили існуючі хірургічні методи лікування та прогноз.

Ключові слова: астроцитома; огляд; діагностика; обсяг резекції; хірургічне лікування