Cancer Association of South Africa (CANSA)

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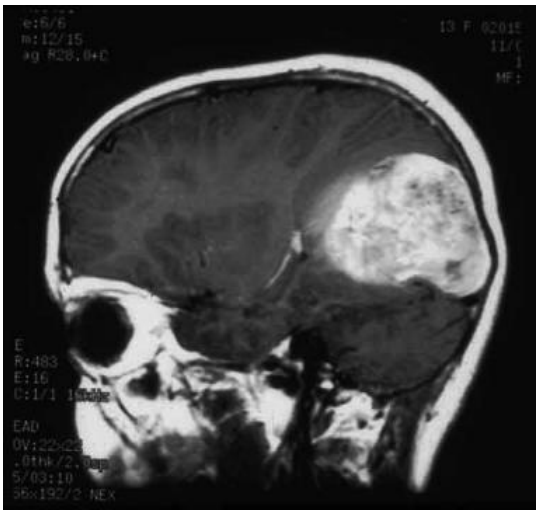
Fact Sheet
on
Childhood Astrocytoma

Introduction

Brain tumours comprise approximately 20% of all childhood malignancies, in frequency it follows second only to acute lymphoblastic leukaemia.



[Picture Credit: Paediatric Astrocytoma]

Astrocytomas comprise a wide range of tumours that differ in their location within the central nervous system (CNS), their growth potential, extent of invasiveness, features, ability tendency progression, and clinical course.

Most astrocytomas are slow to develop or heal. They are said to be low-grade tumours that predominantly arise in midline locations, such as the cerebellum and diencephalic region, including the visual pathway and hypothalamus.

Spinal cord astrocytomas are less common and may be either high-grade or low-grade.

Most cases occur in the first decade of life, with the peak age at 5-9 years. Surgical removal is often sufficient to cure most low-grade astrocytomas; however, the prognosis remains poor for high-grade astrocytomas in spite of the addition of radiotherapy and chemotherapy.

Knight, J. & De Jesus, O. 2020.

"Pilocytic astrocytoma (PA), previously known as cystic cerebellar astrocytoma or juvenile pilocytic astrocytoma, was first described in 1931 by Harvey Cushing, based on a case series of cerebellar astrocytomas. They are low-grade, and usually well-circumscribed tumors, which tend to occur in young patients. By the World Health Organization (WHO) classification of central nervous system tumors, they are considered grade I gliomas and have a good prognosis. PA can occur in the optic pathway, hypothalamus, and brainstem. They can also occur in the cerebral hemispheres, although this tends to be the case in young adults. Presentation and treatment vary for PA in other locations, and this article will discuss the PA of the cerebellum only. Glial cells include astrocytes, oligodendrocytes, ependymal cells, and microglia. Astrocytic tumors arise from astrocytes and are the most common tumor of glial origin. The WHO 2016 categorized these tumors as either "diffuse

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gliomas" or "other astrocytic tumors." Diffuse gliomas include grade II and III diffuse astrocytomas, grade IV glioblastoma, and diffuse gliomas of childhood. The "other astrocytic tumors" group include PA, pleomorphic xanthoastrocytoma, subependymal giant cell astrocytoma, and anaplastic pleomorphic xanthoastrocytoma. The above-described grading system is histological. It is worth noting that the new 2016 WHO classification gives more importance to genetic and molecular markers for categorizing gliomas."

Connors, M., Paden, W., Storm, P.B., Waanders, A.J. & Lang, S.S. 2020.
"Developmental venous anomalies (DVAs) are the most common type of cerebrovascular malformation and are considered benign. There are a few literature studies associating DVA with brain tumors, suggesting a possible underlying predisposition in these patients for tumor neogenesis. We report a 7-year-old female with a complex DVA who developed a low-grade astrocytoma in the opposite hemisphere. With analysis of a comprehensive solid tumor panel and imaging, we describe the possible association of an underlying susceptibility to neoplastic growth in the presence of a vascular malformation."

Vadhan, J.D., Eichberg, D.G., Di, L., Manzano, G., Ivan, M. & Komotar, R.J. 2020.
"An astrocytoma is a subclassification of glioma, with primary spinal manifestations accounting for less than 10% of all spinal cord tumors, with the majority encompassing low-grade features. It is even more uncommon for such lesions to demonstrate intracerebral metastasis. We report such an occurrence in a 39-year-old female who initially presented with an intramedullary and intradural mass from T10-L1, as well as secondary metastasis to the mesial right temporal lobe and cerebellum upon clinical follow-up. Surgical resection of the spine and subsequent temporal lobe biopsy confirmed high-grade glioma. Given the rarity and poor prognosis of spinal gliomas with cerebral metastasis, we also summarize all previously reported cases to date. We recommend that physicians maintain an index of suspicion for spinal gliomas in young patients with cord compression related symptoms outside the event of traumatic injury."

Goodarzi, A., Garza, N., Lechpammer, M., Anthony, R. & Zwienenberg, M. 2019.
BACKGROUND: Bilateral thalamic astrocytomas in children are exceedingly rare. These highly malignant tumors seldom respond to conventional treatment strategies and carry a grim prognosis for patients. However, recent advances in molecular oncology have had a positive impact on prognostication and treatment strategies of these tumors.
CASE-BASED REVIEW: We present a new case of WHO grade III bilateral thalamic astrocytoma in a child and review the pathophysiology, molecular oncogenesis, and relevant treatment strategies for this rare disease.
CONCLUSIONS: High-grade thalamic astrocytomas affecting both thalami pose a challenge to pediatric neurosurgeons, neuro-oncologists, and neuropathologists given the lack of effective treatment strategies. Understanding recent revelations in the field of molecular oncology can assist clinicians in adequately formulating a treatment plan in this patient population.

Incidence of Childhood Astrocytoma in South Africa
The National Cancer Registry (2017) does not provide any information regarding the incidence of Astrocytoma. It only provides combined information for Brain and Central Nervous System Tumours.

Signs and Symptoms of Childhood Astrocytoma
Children with astrocytoma may experience the following symptoms or signs. Sometimes, children with astrocytoma do not show any of these symptoms. Or, these symptoms may be caused by a medical condition other than a tumour:

- Morning headache of headache that goes away after vomiting
- Nausea and vomiting
- Hearing problems
- Speech problems
- Slow speech\Worsening handwriting in children who already can write
- Weakness or change in feeling on one side of the body
- Loss of balance and trouble walking
- Unusual sleepiness or change in energy level
- Change in personality or behaviour
- Feeling tired and listless
- Seizures not related to a high fever
- Weight loss or weight gain for no know reason
- Eyesight problems, such as double vision
- Changed growth or development
- Increase in the size of the head in infants

Some tumours do not cause symptoms. Other conditions may cause the same symptoms as those caused by childhood astrocytomas. If any of the symptoms persist, the child should be referred to a doctor without delay. Symptoms may be different depending on the following:

- Where the tumour forms in the brain or spinal cord
- The size of the tumour
- How fast the tumour grows
- The child's age and development

In a baby, the only symptom may be that the head is growing too fast. An infant's skull can expand to make room for a growing tumour in the brain, so a baby with astrocytoma may have a larger than normal head.

If concerned about one or more of the symptoms or signs, please consult a doctor.

Diagnosis of Childhood Astrocytoma
Doctors use various tests to diagnose a tumour. They also need to determine whether it has spread to another part of the body, called metastasis. Imaging tests are usually used to find out whether the tumour has spread. The tests also assist in deciding on the most appropriate treatment.

For most types of tumours, a biopsy is the only way to make a definitive diagnosis.

The child's doctor may consider the following factors when choosing a diagnostic test:

- Age of the child
- General medical condition
- Type of tumour suspected
- Signs and symptoms
- Results of previous tests

In addition to a physical examination, the following tests may be used to diagnose astrocytoma:

- Computed tomography (CT or CAT) scan
- Magnetic resonance imaging (MRI)
- Biopsy. A doctor called a neurosurgeon will remove a small piece of tissue from the tumour.

Treatment Options for Childhood Astrocytomas
Children with astrocytomas should have their treatment planned by a team of health care providers who are experts in treating childhood brain tumours.

Childhood Low-Grade Astrocytomas - when the tumour is first diagnosed, fist-line treatment may be surgery. An MRI scan is done after the surgery to see if there is any remaining tumour.

If the tumour was completely removed by surgery, more treatment may not be needed and the child is closely watched to see if symptoms appear or change. This is also called watchful waiting.

If some tumour remained after surgery, treatment may include the following:

- Watchful waiting
- More surgery to remove the tumour
- Cerebrospinal fluid diversion
- Radiation therapy
- Biologic therapy
- Targeted therapy
- A clinical trial of a new treatment

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Recurrent Childhood Low-Grade Astrocytomas - before more cancer treatment is given, imaging tests, biopsy, or surgery are done to be sure cancer is present and find out how much cancer there is.

Treatment of recurrent childhood low-grade astrocytoma may include the following:

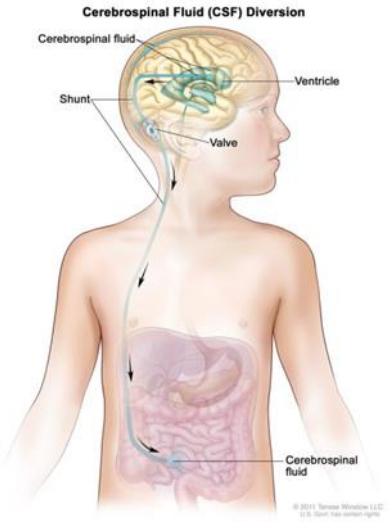
- More surgery to remove the tumour
- Radiation therapy to the tumour
- Surgery, chemotherapy, and/or radiation therapy
- A clinical trial

Childhood High-Grade Astrocytomas - treatment may include the following:

- Surgery, chemotherapy, and radiation therapy
- A clinical trial

Recurrent Childhood High-grade Astrocytomas – treatment of childhood high-grade Astrocytoma may include the following:

- Surgery
- High-dose chemotherapy with possible stem cell transplant
- A clinical trial



[Picture Credit: Cerebrospinal Fluid Diversion]

Cerebrospinal fluid diversion –
cerebrospinal fluid diversion is a method used to drain fluid that has built up around the brain and spinal cord. A shunt (long, thin tube) is placed in a ventricle (fluid-filled space) of the brain and threaded under the skin to another part of the body, usually the abdomen. The shunt carries excess fluid away from the brain so it may be absorbed elsewhere in the body.

Cerebrospinal fluid (CSF) is the fluid that flows in and around the hollow spaces of the brain and spinal cord, and between two of the meninges (the thin layers of tissue that cover and protect the brain and spinal cord).

Childhood Astrocytomas Treatment (PDQ®). 2019. Patient Version. PDQ Pediatric Treatment Editorial Board. Published online: August 20, 2019.

Newly Diagnosed Childhood Low-Grade Astrocytomas

When the tumour is first diagnosed, treatment for childhood low-grade astrocytoma depends on where the tumour is, and is usually surgery. An MRI is done after surgery to see if there is tumour remaining.

If the tumour was completely removed by surgery, more treatment may not be needed and the child is closely watched to see if signs or symptoms appear or change. This is called observation.

If there is tumour remaining after surgery, treatment may include the following:

- Observation.
- A second surgery to remove the tumour.
- Radiation therapy, which may include conformal radiation therapy, intensity-modulated radiation therapy, proto beam radiation therapy, of stereotactic radiation therapy, when the tumour begins to grow again.
- Combination chemotherapy with or without radiation therapy.
- A clinical trial of targeted therapy with a combination of BRAF inhibitors in patients with mutations in the BRAF gene

In some cases, observation is used for children who have a visual pathway glioma. In other cases, treatment may include surgery to remove the tumour, radiation therapy, or chemotherapy. A goal of treatment is to save as much vision as possible. The effect of tumour growth on the child's vision will be closely followed during treatment.

Children with neurofibromatosis type 1 (NF1) may not need treatment unless the tumour grows or signs or symptoms, such as vision problems, appear. When the tumour grows or signs or symptoms appear, treatment may include surgery to remove the tumour, radiation therapy, and/or chemotherapy.

Treatment of childhood high-grade astrocytoma may include the following:

- Surgery to remove the tumor, followed by chemotherapoy and/or radiation therapy
- A clinical rial of a new treatment.
- A clinical trial of targeted therapy with a PARP inhibitor combined with radiation therapy and chemotherapy to treat newly diagnosed malignant glioma that does not have mutations (changes) in the BRAF gene

Silva da Costa, M.D., Camargo, N.C., Dastoli, P.A., Nicácio, J.M., Benevides Silva, F.A., Sucharski Figueiredo, M.L., Chen, M.J., Cappellano, A.M., Saba da Silva, N. & Cavalheiro, S. 2020.
Objective: Tumors of the CNS are the main causes of childhood cancer and have an incidence that exceeds that of leukemia. In addition, they are the leading causes of cancer-related death in childhood. High-grade gliomas account for 11% of such neoplasms and are characterized by aggressive clinical behavior and high morbidity and mortality. There is a lack of studies focusing on the factors that can prolong survival in these patients or guide therapeutic interventions. The authors aimed to investigate the factors related to longer survival durations, with a focus on reoperation for gross-total resection (GTR).
Methods: In this retrospective cohort study, the authors analyzed 78 patients diagnosed with high-grade gliomas occurring across all CNS locations except diffuse intrinsic pontine gliomas. Patients 0 to < 19 years of age were followed up at the Pediatric Oncology Institute. Overall survival (OS) and progression-free survival (PFS) were analyzed in the context of various prognostic factors, such as age, sex, histology, extent of tumor resection, reoperation for GTR, adjuvant treatment, and treatment initiation from 2010 onward.
Results: With a mean age at diagnosis of 8.7 years, 50% of the patients were female and approximately 39% underwent GTR at some point, which was already achieved in approximately 46% of them in the first surgery. The median OS was 17 months, and PFS was 10 months. In terms of median OS, the authors found no significant difference between those with reoperation for GTR and patients without GTR during treatment. Significant differences were observed in the OS in terms of the extent of resection in the first surgery, age, sex, Ki-67 expression, adjuvant treatment, and treatment initiation from 2010 onward. Furthermore, the PFS values significantly differed between those with GTR in the first surgery and Ki-67 expression ≥ 50%.
Conclusions: This study demonstrates the importance of GTR for these neoplasms, highlights the role of surgeons in its achievement in the first attempt, and questions the role of reoperation for this purpose. Finally, this study further supports the use of combined adjuvant treatment for the improvement of OS and PFS.

Standard Treatment Options for Childhood Astrocytomas

Treatment Group	Standard Treatment Options
Childhood low-grade astrocytomas:	
Newly diagnosed childhood low-grade astrocytomas	Observation without intervention
	Surgery
	Adjuvant therapy (for tumors that are incompletely resected):
	—Observation after surgery
	—Chemotherapy
	—Radiation therapy
	—Targeted therapy
Progressive/recurrent childhood low-grade astrocytomas	Second surgery
	Radiation therapy
	Chemotherapy
	Targeted therapy with or without chemotherapy
Childhood high-grade astrocytomas:	
Newly diagnosed childhood high-grade astrocytomas	Surgery
	Adjuvant therapy:

Treatment Group	Standard Treatment Options
	—Radiation therapy
	—Chemotherapy
Recurrent childhood high-grade astrocytomas	Surgery (not considered standard treatment)
	High-dose chemotherapy with stem cell transplant (SCT) (not considered standard treatment)
	Radiation therapy (not considered standard treatment)
	Targeted therapy with a BRAF inhibitor, for patients with a *BRAF* V600E mutation (not considered standard treatment)

PDQ Pediatric Treatment Editorial Board

Maharaj, A., Manoranjan, B., Verhey, L.H., Fleming, A.J., Farrokhyar, F., Almenawer, S., Singh, S.K. & Yarascavitch, B. 2019.

PURPOSE: The present study aims to determine the tumor-related, clinical, and demographic factors associated with extent of resection (EOR) and post-operative outcomes in JPA patients.

METHODS: All patients with JPA, identified from a single-center brain tumour data base, were included in this retrospective analysis. Pre-operative MRI scans were reviewed by a single neurosurgeon blinded to the EOR. JPA cases that exhibited no residual tumor post-operatively were assigned to the GTR group, all other tumors were assigned to the <GTR group. Tumor-related, clinical and demographic variables as well as perioperative morbidities were compared between both groups.

RESULTS: Of the 28 patients included, 15 had a GTR (46% male; median age: 7.5 years; range: 1.16-14.9) and 13 had <GTR (69.2% male; median age: 10.6 years; range: 0.66-17.68). Tumor location reached statistical significance, as there were significantly more cerebellar tumors in the GTR group (86.7%) compared to the <GTR group (38.5%) ($p = 0.016$). GTR cases had a significantly longer average follow-up interval (6.6 months) than <GTR cases (4.5 months) ($p = 0.031$). All demographic variables, clinical variables and tumor-related factors showed no significant differences between the two groups. There were no differences between GTR and <GTR cases in terms of perioperative outcomes.

CONCLUSIONS: This study shows other than location of the lesion in the cerebellum, demographic, clinical and tumor-related variables are not associated with EOR in children with JPA. GTR was associated with an extended follow-up interval but not with increased perioperative morbidities compared to those with <GTR.

About Clinical Trials

Clinical trials are research studies that involve people. They are conducted under controlled conditions. Only about 10% of all drugs started in human clinical trials become an approved drug.

Clinical trials include:

- Trials to test effectiveness of new treatments
- Trials to test new ways of using current treatments
- Tests new interventions that may lower the risk of developing certain types of cancers
- Tests to find new ways of screening for cancer

The South African National Clinical Trials Register provides the public with updated information on clinical trials on human participants being conducted in South Africa. The Register provides information on the purpose of the clinical trial; who can participate, where the trial is located, and contact details.

For additional information, please visit: www.sanctr.gov.za/

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