



Gliomatosis cerebri with favorable outcome in a child: a case report

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Abstract

Objective: To report a rare clinical case of gliomatosis cerebri with favorable outcome in a 3-year old child.

Description: A 3-year old child developed severe and progressive symptoms of gliomatosis cerebri. The initial tests were unspecific. After clinical improvement following neuroendoscopic surgery, there was a progressive decline in clinical status with development of obstructive hydrocephalus, paraparesis and difficulty in walking. The child was again submitted to surgery after disseminated injuries in the subarachnoid space were identified. She also received chemotherapy and radiotherapy. Currently, 6 years later, spinal canal and brain injuries remain unaltered, with marked syringomyelia. However, the child is clinically stable, with adequate development for her age, indicating a satisfactory response to treatment.

Comments: The child's clinical presentation and the combination of symptoms led to the diagnosis of gliomatosis cerebri. There are few descriptions of this kind of tumor in children in the literature, and none reports a favorable outcome as in the present case.

J Pediatr (Rio J). 2008;84(5):463-466. Gliomatosis cerebri, central nervous system tumor, hydrocephalus, neurooncology.

Introduction

Gliomatosis cerebri is a rare and severe central nervous system neoplasm. It is usually fatal due to its ability to infiltrate cerebral tissues, compromising the efficacy of treatment.¹ Gliomatosis cerebri is defined as a diffuse neoplasm of the glial cells, involving more than two lobes and occasionally infiltrating infratentorial structures and the spinal cord.²

A review of the literature review revealed fewer than 100 reports of this tumor in children. This paper describes a case of gliomatosis cerebri affecting a girl presenting symptoms of obstructive hydrocephalus at 3 years of age, and who later developed several other symptoms. Six years after surgery, chemotherapy and radiotherapy, the outcome is still positive.

Case report

A girl without family history of neurologic or oncologic disorders, presented strabismus at 3 years of age, followed by

symptoms of progressive intracranial hypertension, such as headaches, vomiting and seizures. Computed tomography and magnetic resonance imaging revealed obstructive hydrocephalus and probable thickening of the interpeduncular cistern. The patient then underwent neuroendoscopic third ventriculostomy, which confirmed the thickening and identified lesions in supernatant fractions of the ventricular fluid. These injuries were biopsied. The anatomical and pathological study demonstrated similarities with the encephalic fluid. Eight days after the surgery, due to new symptoms of intracranial hypertension, a ventricular-peritoneal shunt was performed. Examination of the ventricular fluid did not show any changes. The child recovered well, with adequate psychomotor development for her age and improvement in strabismus.

About a year after the first surgery, a follow-up magnetic resonance imaging exam revealed lesions scattering throughout the subarachnoid space, mainly in the posterior cranial

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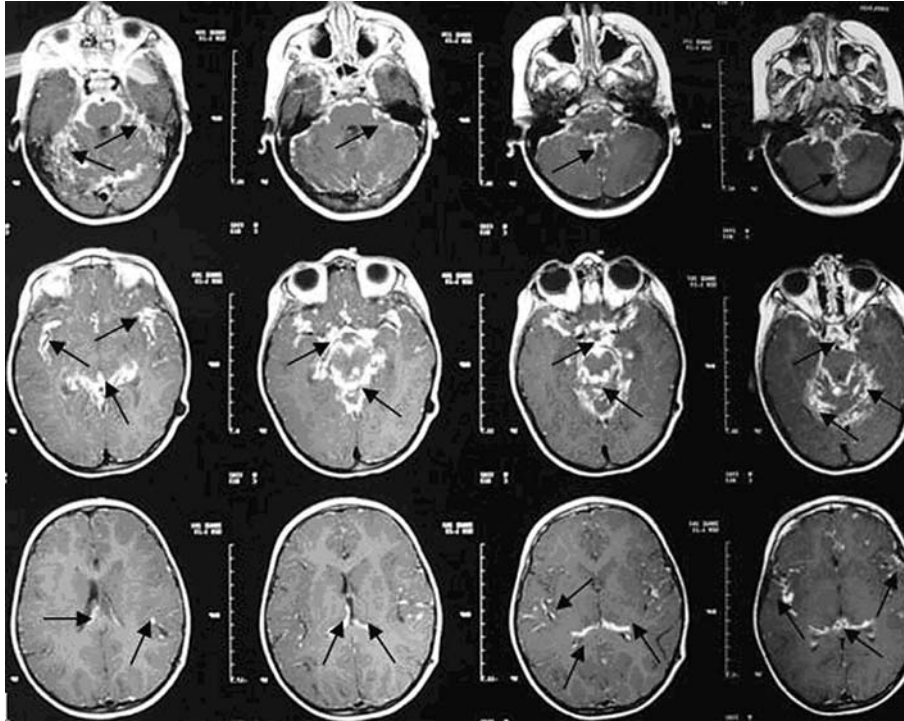


Figure 1 - Lesions scattered throughout the subarachnoid space, mainly in the posterior cranial fossa, diffusely covering a large part of the encephalon

fossa. These lesions diffusely covered a large part of the encephalon (Figure 1).

Some months later, the child developed paraparesis. Magnetic resonance imaging of the neural axis demonstrated disseminated injuries in the spinal subarachnoid space pressing the medullary cone (Figure 2). There were no alterations in the cerebrospinal fluid. Laminotomy and partial resection of the injury pressing the marrow were carried out. The anatomical and pathological study identified gliomatosis.

Carboplatin and vincristine chemotherapy was initiated. Eyelid ptosis developed after 10 chemotherapy sessions (approximately 3 months). Another magnetic resonance imaging exam showed persistent encephalon changes and a small decrease in the number of cervical spine lesions. After 5 months of chemotherapy, the patient presented difficulty in walking. She underwent another imaging exam which revealed no progression of gliomatosis. In spite of the combination of corticosteroid therapy and chemotherapy, the patient's state did not change. At this point, the chemotherapy drugs were replaced (cisplatin and etoposide every 21 days). The patient showed clinical improvement after the first cycle with the new chemotherapy scheme. X-rays revealed regression of the tumor started after the second chemotherapy cycle.

In the 16th month of treatment, oral chemotherapy was started with temozolomide (20 mg), five pills a day for five days with 28-day washout periods between each cycle for 14

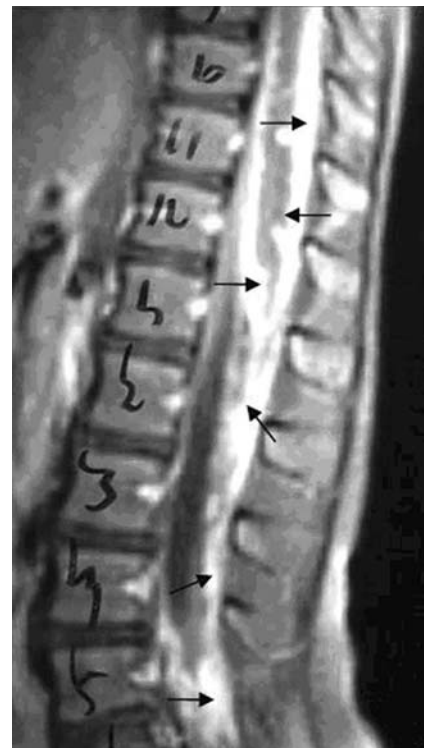


Figure 2 - Spinal subarachnoid space injury pressing the medullary cone

months. Currently, after 6 years of treatment, the child is not taking any medication and remains asymptomatic. Magnetic resonance imaging shows that the encephalon and spinal canal lesions are unaltered. The patient presents important cervical and chest syringomyelia, however still without any evident clinical signs.

Discussion

Neoplasms are the second cause of death in children between the ages of 1 to 15 years in most of the world. They are surpassed only by trauma injuries. In childhood, leukemia is the most common cancer, followed by brain tumors, lymphomas, sarcomas and neuroectodermal tumors.³

Gliomatosis is rare among the brain tumors. It diffusely affects several parts of the central nervous system which are permeated by tumor cells filling the intra-axial subarachnoid spaces and potentially covering the encephalon as a whole. The affected parts are typically augmented, resulting in "pseudohypertrophy." However, the central nervous system's anatomical and neural structures are preserved and intra-axial tumors cannot be identified. The process may be extremely diffuse. Since its onset, it involves both brain hemispheres, the brain stem and even the spinal cord.^{4,5}

Until some years ago, gliomatosis was diagnosed strictly in autopsy studies. Currently, technological innovations, especially in magnetic resonance imaging, and more precise surgical techniques, allow earlier diagnosis. The analysis of biopsy material usually shows diffusely infiltrative glioma, usually fibrillary astrocytoma.⁴

It is important to highlight that gliomatosis cerebri is neither a single cytogenetic entity nor a state diagnosed solely for its histologic or citologic characteristics. The majority of the samples presents astrocyte characteristics, however oligodendrogliomas and even pure oligodendrogliomatosis have been described to take part in the process. Although elongated nuclear profiles and a tendency to subpial, perivascular and circumneuronal cellular aggregation are often described as typical findings, there are no specific findings or morphologic characteristics that are typical of gliomatosis cerebri.⁴

As a diffuse tumor, surgical treatment is usually not recommended, and radiology over extensive areas may cause serious toxicity. Early chemotherapy results in clinical or radiologic improvement of approximately 30%.⁶⁻⁸ Temozolomide is well tolerated and seems to be a good substitute for procarbazine - lomustine (CCNU) - vincristine, mainly for cases of slow growth and low grade gliomatosis cerebri.⁶

Recent studies show that the young males are more affected by oligodendroglial gliomatosis, but they also have a better prognosis than the females. Survival (14.5 months on average) is also longer for young patients with low grade oligodendroglial gliomatosis.^{6,9}

The clinical course of gliomatosis cerebri is slow and long, especially when the neoplastic infiltrate is of low histological grade. However, prognosis is poor, and the disease is often fatal. Local or multicentric progression to anaplastic astrocytoma is observed in many cases.⁴ Patients of all ages are affected, but it mostly affects the age group between 50 and 60 years. The clinical course is variable and includes pyramidal deficit, dementia, headache, cranial nerve changes, intracranial hypertension, and others. As in the case described above, its infiltration capacity is ill-proportioned in comparison to the level of differentiation.¹⁰

Only a few gliomatosis cerebri cases are described in the literature, and most refer to adults.^{11,12} Cases of child gliomatosis in children are rare, and no descriptions of favorable outcome were found. In 2007, Malton et al. described epilepsy surgery with improvement in children with intractable crises. The retrospective study interval was 16 years, and the study was carried out in an international excellence center (The Brain institute, Miami Children's Hospital). Out of 741 children with intractable seizure crises, only four had gliomatosis cerebri (0.5% in a group of sick children), which reinforces the rarity of this disease.¹³ In 2001, the case of a 10-year-old child was described. This child had symptoms of intracranial hypertension, progressing with pressure on the spinal cord, nervous central system decay and death. The diagnosis of gliomatosis cerebri was only reached through autopsy.¹⁴ The difficulties to diagnose gliomatosis cerebri during life are described in the literature, and relate to the injury's histological characteristics.¹⁵

In the case described here, the illness shows an atypical outcome, with good response to the treatment (surgery, chemotherapy and radiotherapy). Because the course of the disease is slow, long and often fatal, follow-up is always required, and a favorable outcome cannot be considered to be definitive. Nevertheless, the fact that our patient remains asymptomatic 6 years after the diagnosis and 1 year and a half after the interruption of chemotherapy should be seen as positive, even if radiological studies show diffuse gliomatosis cerebri and syringomyelia.

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