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PILOCYTIC ASTROCYTOMA IN PRESCHOOLERS: CASE REPORT AND DISCUSSION OF PROGNOSIS DUE TO LATE DIAGNOSIS

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ABSTRACT

To report a case of pilocytic astrocytoma of late diagnosis in a preschool child. **Results:** PA is considered a Grade I tumor on the malignancy scale with low proliferative potential. It has a good prognosis and there is a possibility of cure with complete resection of the tumor. Survival can reach a rate of 94% in 10 years. The diagnostic challenge is great and sometimes late, as the report presented. 6-year-old female patient, with a history of headache that evolved for two years, associated with dizziness, photophobia and phonophobia, tremors and postural imbalance, and unable to accompany other children in collective activities in the school environment, with several preliminary diagnoses of migraine or sinusopathy, which delayed the definitive diagnosis. Finally, nuclear magnetic resonance (NMR) was performed, which found an expansive lesion in the posterior fossa topography. Microsurgery underwent resection of the intracranial tumor and posterior fossa cranioplasty, with resection of about 80% of the lesion and external ventricular drain possible. Due to the residual injury, he is undergoing cancer treatment with chemotherapy. **Final consideration:** Headache is the main symptom of neoplasms of the central nervous system, and is also very recurrent in pediatrics. However, it rarely refers to brain tumors. Primary care physicians and pediatricians must be aware of the main warning signs so that they can make an earlier diagnosis and quickly refer children with cancer to specialized centers.

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INTRODUCTION

Among all types of primary tumors of the central nervous system (CNS), the main histological type is astrocytomas (Faria, 2006). They are characterized according to their histology by low or moderate cellularity, a biphasic pattern with varied portions of compacted bipolar cells with the presence of Rosenthal fibers, and loose cells of multipolar structures with microcysts and granular bodies (Louis, 2007). The classification of brain tumors, according to the World Health Organization (WHO), refers to gliomas as low-grade tumors (grades I and II) and high-grade tumors (grades III and IV). Low-grade tumors in children have a favorable prognosis, especially when completely resected. High-grade patients, on the other hand, have a more reserved prognosis, but the tumor subtype also influences this aspect (PDQ, 2002).

The histological nature of astrocytomas together with their location determine the prognosis. Among these, those with the best prognosis are those with low grade, also known as pilocytic astrocytomas (PA) (Burkhard, 2003). According to the WHO, PA corresponds to grade I tumor, and is responsible for approximately 25% of pediatric brain tumors and 1.5 % of brain tumors in adults, with an incidence of 4.8 million cases per year (Dörner, 2007). In the case of a grade I tumor, the PA has a low proliferative potential. The cure is possible as long as there is complete resection of the tumor. As a result, it has a good prognosis with a 94% 10-year survival (Minehan, 1995). The clinical presentation of pilocytic astrocytoma varies depending on its location, as well as any CNS tumor, in addition to occurring slowly and insidiously. The clinical picture can show from headache, focal neurological deficits to more severe manifestations such as seizures and signs of intracranial hypertension due to the expansive effect or

hydrocephalus (Malheiros, 1998). Cerebellar astrocytomas usually present with ataxia, nausea, and dysfunction of the cranial pairs. When neoplasms affect the brain stem, they cause deficits related to cranial nerves (Lantos, 2002). A thorough physical examination of the patient, especially taking into account neurological and ophthalmological aspects, increases the chance of making the correct diagnosis, in addition to decreasing the diagnostic time (Allen, 1993). Children with brain tumors receive an incorrect initial diagnosis in up to 70% of cases (Abdelkhalek, 2014). On average, the diagnosis time for grade I and II tumors is around 238 days from the onset of the condition, and patients are usually seen by two doctors of different specialties (Minehan, 1995). Contrasted magnetic resonance imaging is the imaging test of choice for diagnosing the tumor, determining the extent of the disease, and detecting recurrence. Contrast computed tomography can also be used, although it is less sensitive and specific (Ruiz, 2009). The PA is considered to be a well-defined, slow-growing tumor that often contains cystic areas that can be surgically cured after total resection (Bond, 2018). This study presents the case of a 6-year-old female patient with a late diagnosis of PA.

METHODS

The present study is a case report whose bibliographic research used the descriptors (MeSH Terms) *tumors of the central nervous system, astrocytoma, infantile pilocytic astrocytoma, late diagnosis, pediatrics*. The research was carried out through the study of digital articles and virtual books attached to the PubMed, Embase, Ovid, Cochrane Library, Web Of Science, ScienceDirect Journals, Scopus, academic Google, in database platforms such as Scientific Electronic Library Online (SCIELO), PubMed, and in scientific repositories, following the rules of systematic review - PRISMA (Transparent reporting of systematic reviews and meta-analyzes-https: //www.prisma-statement.org/). Used as the main data sources, the most relevant works wereselected for the theme for synthesis and presentation of information, excluding references that diverged from the purposes covered here.

Case Report: The present study was elaborated according to the rules of CARE case report (https://www.care-statement. org/) [13].

Patient Information and Clinical Findings: A.J.C, 6 years old, female, born in Tupã, São Paulo. She was referred to the Pediatrics Service of Santa Casa de Misericórdia de Marília, with a history of headache for two years, associated with dizziness, photophobia and phonophobia, tinnitus, tremors, and postural imbalance, needing to rely on furniture and unable to accompany others. Children in collective activities in a school environment. Several outpatient pediatric consultations were held, and as the most prevalent complaint was a headache, it was clinically interpreted as migraine or sinus disease, and the patient was treated for two years for migraine, which delayed her definitive diagnosis. As the condition evolved, the mother reported emotional dullness, social isolation, and hypersomnia from the child. She had an acute headache in the last two months before the diagnosis, with night awakening due to pain. Upon neurological physical examination, she was conscious, oriented, with photoreactive isochoric pupils, terminal nuchal rigidity, axial ataxia with no apparent motor focus. The presence of diplopia was also elucidated by the neurologist. Magnetic resonance imaging (NMR) was performed, which found an expansive lesion in the topography of the posterior fossa, with compression of the cerebellar vermix and brain stem, large-volume obstructive hydrocephalus, and signs of CSF transudation into the parenchyma.

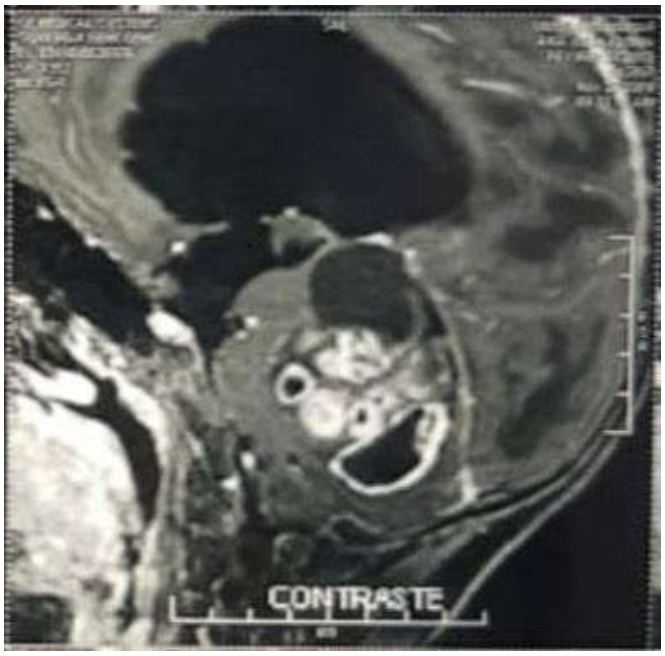

Figure 1. Post-contrast sagittal NMR, showing an expansive lesion in the posterior fossa with compression of the cerebellar vermix and brain stem

Timeline: Four weeks after the first hospitalization, the patient returned to the service to undergo microsurgery for resection of the intracranial tumor and posterior fossa cranioplasty. After 30 days of microsurgery for tumor resection, a CT scan showed an increase in bilateral subdural collection (hygroma) due to hyperfunctioning ventriculo-peritoneal shunt (VPS). The patient was released to perform daily activities 90 days after microsurgery.

Diagnostic Assessment: The patient was hospitalized on the same day to collect preoperative exams for urgent **e**xternal ventricular drain (EVD), as well as CSF collection for chemocytology and neoplastic cell research. The derivation was performed in the right frontal region, maintaining a height of 12 cm from the acoustic meatus in the postoperative period. Thus, 57 mL of cerebrospinal fluid was drained, which resulted in the absence of signs of neoplastic cells on anatomopathological examination. She was transferred to the pediatric ICU and progressed uneventfully, with clinical improvement of signs of intracranial hypertension (ICH). In the third postoperative period, with the patient stable, we opted for the removal of the EVD and placement of a ventriculo-peritoneal shunt **(**VPS). The procedure was carried out without complications. Diet was released, analgesia was maintained on schedule and postoperative cefazolin was prescribed for 24 hours. He evolved without complications in the immediate postoperative period, without signs of ICH, with an improvement of headache and diplopia. In the postoperative room, he developed a stable, conscious, active neurological condition. She was discharged with an outpatient return.

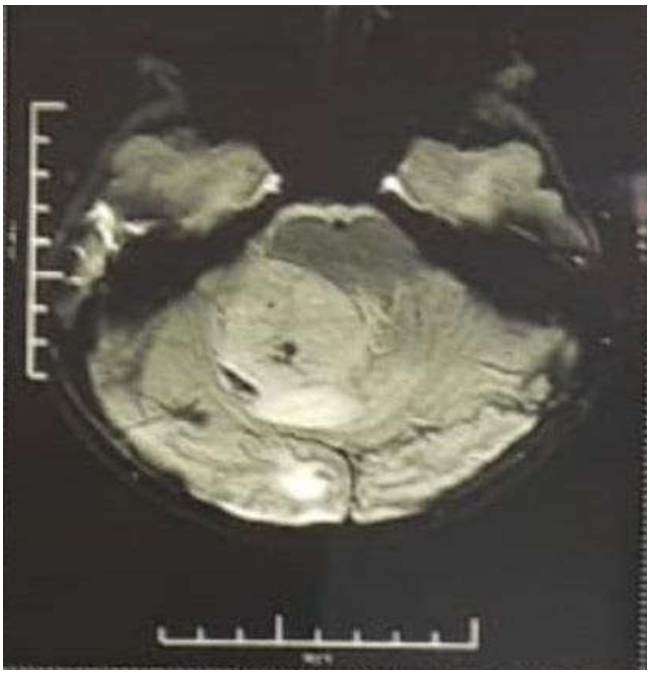

Figure 2. Axial, post-contrast NMR showing an expansive lesion in the posterior fossa with compression of the cerebellar vermix and brainstem

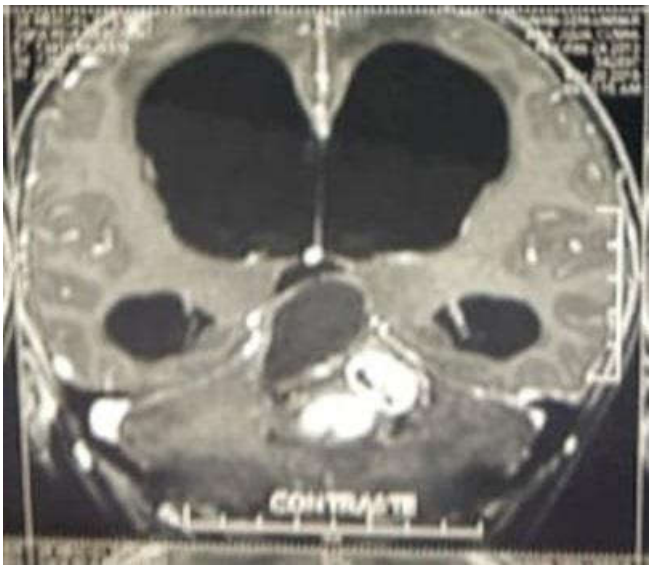

Figure 3. Coronal plane NMR, post contrast, showing an expansive lesion in the posterior fossa with compression of cerebellar vermix and brain stem

Therapeutic Intervention and Follow-up: Four weeks after the first hospitalization, the patient returned to the service to undergo microsurgery for resection of the intracranial tumor and posterior fossa cranioplasty. The surgery lasted approximately 12 hours and occurred without complications. There was resection of about 80% of the lesion, with residual lesion covering the brain stem floor, left Luschka foramen, and left cerebellar peduncle. The anatomopathological examination by freezing revealed a pilocytic astrocytoma. A control CT was performed, with the patient still unconscious, which showed mild to moderate edema at the operative site, presence of air in the previous, inferior and superior cystic lesions, and hyper-functioning EVD, maintaining bilateral hygroma. In the first postoperative period, the patient had a feverish peak, laboratory tests and chest X-rays were collected. There were no significant changes, except for the culture of tracheal secretion, which resulted from pneumonia associated with mechanical ventilation (VAP), caused by *Streptococcus sp*. alpha-hemolytic. During hospitalization, the patient evolved uneventfully, awakened, collaborative, Glasgow 15, bilateral axial and appendicular ataxia preserved cranial pairs and without meningeal signs.

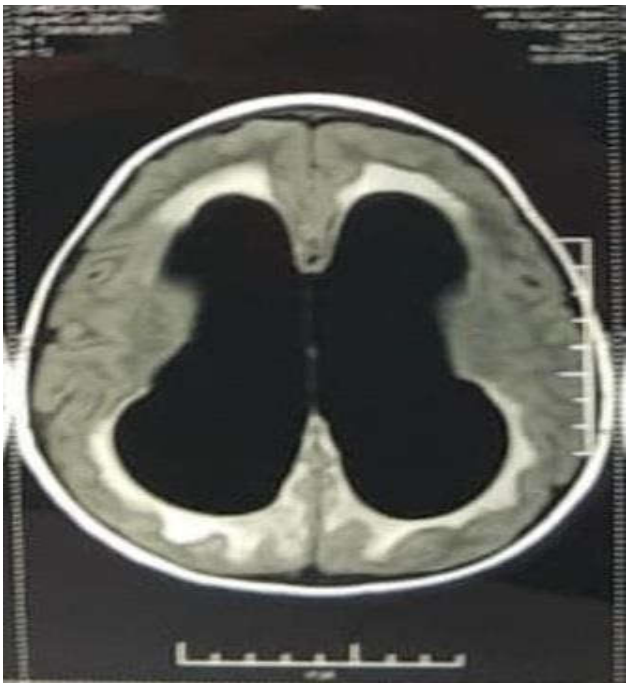

Figure 4. NMR showing large-volume obstructive hydrocephalus and signs of cerebrospinal fluid transudation

On the sixth postoperative day, he was discharged with outpatient follow-up. After 30 days of microsurgery for tumor resection, a CT scan showed an increase in the bilateral subdural collection (hygroma) due to hyper-functioning EVD. Therefore, it was decided to replace the conventional EVD with an adjustable pressure one, with an anti-siphon mechanism. A new control CT was performed 60 days after microsurgery and already with the new VPS, showing subdural hygroma with a great decrease in its volume, this being laminar. The patient was released to perform daily activities 90 days after microsurgery. Currently, he has a stable neurological condition, maintaining mild axial ataxia and with no other deficits found. However, due to the residual injury, cancer treatment was started with chemotherapy with Vinblastine 6mg/m² of body surface per week (1x/week), Carboplatin 175 mg/m² of body surface per week (1x/week), and Vincristine 1.5 mg/m² of body surface per week (1x/week). So far nine cycles of Vinblastine and six cycles of Carboplatin and Vincristine have been performed. With adjuvant chemotherapy, the patient presents with good evolution, noticing a reduction of the tumor verified by tomography.

Informed Consent: Those responsible for the patient signed the consent form.

DISCUSSION

According to the WHO, the AP is considered a Grade I tumor on the malignancy scale, that is, with low proliferative potential. It has a good prognosis and there is a possibility of cure with complete resection of the tumor. Survival can reach a rate of 94% in 10 years (Faria, 2006). Pilocytic astrocytomas

often affect young patients. According to Rosemberg (2005) the most affected age group is between 2 and 5 years. As it presents a very nonspecific clinical picture and is present in other common diseases within pediatrics, the diagnostic challenge is great and sometimes late, as the report presented. A thorough physical examination during the patient's admission, with special attention to the neurological and ophthalmological, decreases the chance of errors regarding the diagnosis and, consequently, decreases the delay in treatment (Allen, 1993). The fundus examination may demonstrate papilledema and signs of intracranial hypertension, and the neurological examination may suggest the location of the lesion (Coelho, 2015). At the time of the first visit, the child had a headache as the main complaint. However, some misdiagnoses have been made, such as sinusopathy and migraine. In up to 70% of cases of brain tumors in children, the initial diagnosis is incorrect.

The diagnostic delay tends to be greater when more doctors are consulted (Haimi, 2004), in addition, it reflects the professionals' lack of preparation to recognize the warning signs for the diagnosis of patients with tumors of the central nervous system. Dorner et. al (2007) described, after the evaluation of 50 children with a tumor in the posterior fossa, that the signs and symptoms of intracranial hypertension syndrome were initially diagnosed as gastrointestinal tract infections, appendicitis, psychological problems, torticollis, and others. The average diagnosis time for grade I and II tumors is around 238 days from the onset of the condition (Minehan, 1995). In this case, the patient was seen at several services and the period from the first symptom to the discovery by NMR was 730 days. The delay in diagnosis, with the subsequent delay in instituting appropriate treatment, can lead to numerous unfavorable consequences for children and adolescents, such as the need for more aggressive treatment, less chance of cure, and a greater possibility of late sequelae, with negative impact quality of life. Total or subtotal surgical removal is the treatment of choice for pilocytic astrocytomas (Forsyth, 1993). The indication for adjuvant radiotherapy or chemotherapy only occurs in cases in which total tumor resection is not possible (Forsyth, 1993). In the case reported in question, it was necessary to resort to adjuvant chemotherapy, since the delay in diagnosis caused the tumor to grow sufficiently to prevent its total resection. Radiotherapy was not considered to not affect the patient's pituitary gland and cause multiple endocrinological disorders.

Final Considerations

Headache is the main symptom of neoplasms of the central nervous system and is also very recurrent in pediatrics. However, it rarely refers to brain tumors. However, in cases of tumors, headache is chronic and progressive associated with complaints such as visual changes (diplopia), vomiting, behavioral disorders, personality changes, school difficulties, among others (Nishio, 1989). The delay in diagnosing cancers, in general, is related to fundamental factors such as children under the age of five, parents with low education, and poor socioeconomic status, the latter being the most relevant (Abdelkhalek, 2014). Factors related to the child's parents are not the only ones responsible for delaying the diagnosis. The failure to recognize early symptoms that may indicate a possible neurological deficit and the integration of medical care in the various services consulted are also factors that are part of this delay (INSTITUTONACIONAL DO CÂNCER, 2019 and Wilne, 2010). Several elements influence the patient's survival when dealing with pediatric cancer. Among them are the sex, age, location, extension, and type of the tumor (Macdonald, 1994). The diagnosis of brain tumors becomes a challenge in children due to nonspecific symptoms and few clinical signs. The pediatrician must be very attentive to the slightest alterations in the clinical examination since, in pediatrics, semiology is hampered by the patient's inability to express his symptoms clearly (Coelho, 2015). Therefore, medical knowledge is essential, and that it values the physical examination of the child, so that there is the possibility of an early diagnosis and treatment, aiming to improve the survival and quality of life of the affected population (Coelho, 2015). Most tumors of astrocytic lineage do not respond to chemotherapy, especially in cases of tumors with a low degree of malignancy (Michalowski, 2012). In cases of more aggressive tumors in children, the aim is to avoid radiotherapy due to its deleterious effects in the long term, using various chemotherapy schemes, which have been reported to date without success (Malheiros, 1998). Therefore, it is essential that primary care physicians and pediatricians are aware of the main warning signs so that they can make an earlier diagnosis and quickly refer children with cancer to specialized centers. Thus, there will be better chances of cure and a better quality of life for these children.

Patient Perspective: Those responsible for the patient in the present study have the perspective that the interaction of a multidisciplinary medical team will favor the resolution of illnesses and the progression to a stable condition of the patient.

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Declaration of conflicts of interest: The authors declare nothing.

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