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OPTIC NERVE PILOCYTIC ASTROCYTOMA WITH LEPTOMENINGEAL DISSEMINATION – CASE REPORT

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Abstract: *Pilocytic astrocytoma is the most frequent type of brain tumor diagnosed during childhood. It originates from midline structures and is associated with good prognosis, with an estimated survival rate higher than 95%. We presented the case of a male patient diagnosed at the age of 6 with pilocytic astrocytoma located in the right optic nerve with associated chiasm infiltration. Incomplete resection of the tumoral process was performed, without any additional therapy, as association of chemotherapy or radiotherapy is still controversial among specialists. The patient had an unpredictable severe evolution of the disease, with associated leptomeningeal dissemination and extreme worsening of neurological and endocrinologic status. Six years after diagnosis, despite complex medical efforts the patient died.*
This article raises awareness of leptomeningeal dissemination risk, a rare evolution in cases of pilocytic astrocytoma. Early diagnosis, complete tumoral resection, tumor location and careful long-term follow up are key factors for long-term survival.

Key words: *pilocytic astrocytoma, leptomeningeal dissemination, complete resection, brain MRI, radiotherapy.*

1. Introduction

Pilocytic astrocytoma (PA) is the most frequent type of brain tumor diagnosed during childhood and is often located in the posterior fossa.

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It represents about 70-85% of all cerebellar astrocytomas and 15% of total pediatric brain tumors.

It usually originates from midline structures, the cerebellum being the most frequent location (60%). Other sites include optic pathways, brainstem, cerebral ventricles, spinal cord, cerebral hemispheres and velum interpositum [1].

Optic pathway gliomas, based on their histological analysis, are in the majority of cases pilocytic astrocytomas. They represent about 10-15% of all supratentorial tumors of children and are often associated with Type I Neurofibromatosis [2].

The origin of pilocytic astrocytoma is from astrocytes. The World Health Organization (WHO) classified astrocytomas in four grades, based on cellular reproduction speed and risk of spreading to nearby tissues. Grade I and II astrocytomas are nonmalignant tumors, classified as low-grade astrocytomas. Grade III and IV astrocytomas are malignant tumors, classified as high-grade astrocytomas.

Grade I PA are usually well-circumscribed tumors with good prognosis after proper treatment (survival rate > 95% at 5 and 10 years), surgical resection, if performed completely, being usually curative [1]. Although there is no knowledge about the exact cause of pilocytic astrocytoma, immunologic, genetic and environmental factors are considered to be involved in specific types of malignancies.

Astrocytomas are sometimes associated with rare genetic pathologies, such as tuberous sclerosis, Li-Fraumeni syndrome or Type I Neurofibromatosis, without any exact relationship being described.

There is no difference regarding gender distribution. Incidence rate is estimated at 14 new cases/ 1 million children younger than 15 years old [3].

The symptomatology associated with PA depends on the location and size of the tumor. Increased brain pressure, headache, vomiting, lethargy, hydrocephalus or changes in mental status, same as seizures, diplopia or blurred vision and progressive weakness in arms and legs are often described [3].
Optic nerve gliomas, due to their location and associated mass effects will also determine proptosis [2].

The diagnosis of pilocytic astrocytoma is based on clinical examination, imaging investigations and histopathological analysis. Confirmation of PA is based on surgical excision, biopsy and histopathological exam [3].

Computed Tomography scans (CT), although less sensitive than Magnetic Resonance Imaging (MRI) is usually the first examination performed. Imagistic findings like optic nerve enlargement, optic canal enlargement or buckling of the optic nerve are described. MRI is the best imaging technique for an appropriate evaluation of the tumor, the optic chiasm, infundibulum and hypothalamus [2].

Treatment options depend on tumor location and clinical status of the patient. In cases without extension to the optic chiasm, complete tumoral resection can be usually performed and is considered curative. In cases of tumoral extension to the chiasm, complete resection cannot be performed, but partial resection with improvement of clinical status is achieved [2].

Surgical resection remains the main therapeutic approach for this type of malignancy, considered curative in case of completely removable cerebellar tumors.

In cases of incomplete surgical excision, adjuvant therapy may be taken into consideration. Radiation therapy is very controversial due to potential side effects in pediatric population [4]. Many studies do not recommend conventional radiotherapy, due to increased radionsensitivity of pediatric population and lack of clear evidence of its advantages in preventing relapse. In case of tumoral recurrence, further surgical resection, if possible, is adopted [4].

2. Case Presentation

We present the case of a 12 years old male child who was diagnosed at the age of 6 with pilocytic astrocytoma and presented an atypical severe evolution.

The patient presented the onset of the disease at the age of 6 years old with various symptoms like nausea, headache, vomiting and vision problems and was evaluated by a multidisciplinary team.

A complex medical team, who performed both clinical and imagistic investigations (brain MRI and CT scan) raised suspicion of brain tumor, located in the right optic nerve with associated chiasm infiltration. Due to tumor location in the optic pathways with optic chiasm involvement, incomplete resection of the tumoral process was performed. Histopathological report was consistent with the diagnosis of grade I pilocytic astrocytoma. Neither chemotherapy, nor radiotherapy were further associated in this case.

The patient developed post-surgical hypothalamic-pituitary plurihormonal insufficiency, central diabetes insipidus, left spastic hemiplegia, left central facial nerve palsy, right optic nerve atrophy and symptomatic epilepsy with left motor focal crisis, with associated substitutive treatment.

Over the next 3 years, the patient referred multiple times at the Emergency Department of Targu Mures Emergency County Hospital for different respiratory, gastrointestinal and neurological intercurrences, for which he received symptomatic treatment with temporary improvement of his general condition.

In January 2018, at the age of 11 years old, the patient developed an intense episode of headache and presented again to the Emergency Department for further examination. Neurosurgical consult and medical imaging (cerebral MRI and CT scan) evidenced relapse of suprasellar tumoral process and cerebral ventriculomegaly, without radiological signs of associated active hydrocephalus.

In the summer of 2019, the patient's status worsened, developed secondary symptomatic hydrocephalus for which a ventriculoperitoneal shunt was placed.

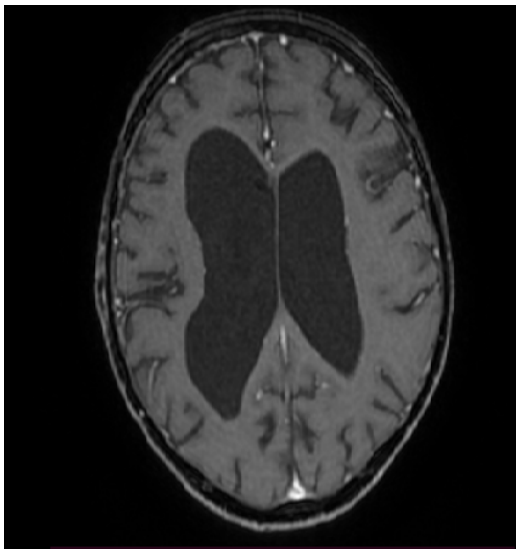

Fig 1. *Asymetric supratentorial hydrocephalus*

Brain MRI performed in October 2019 revealed leptomeningeal dissemination of the tumor, with associated worsening of neurological and biological status.

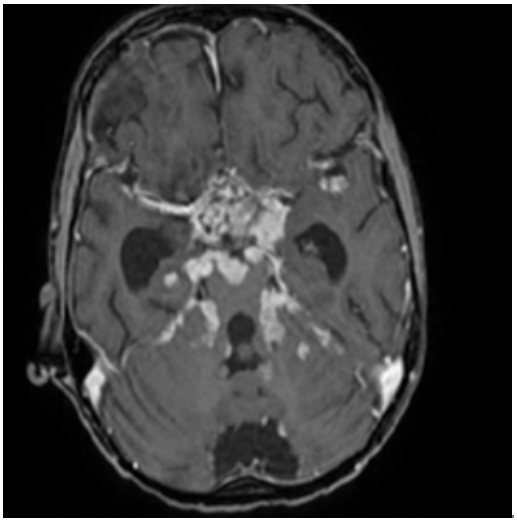

Fig 2.*Axial Brain MRI - Multiple polylobulated masses, with intense contrast enhancement – suggestive for leptomeningeal dissemination*

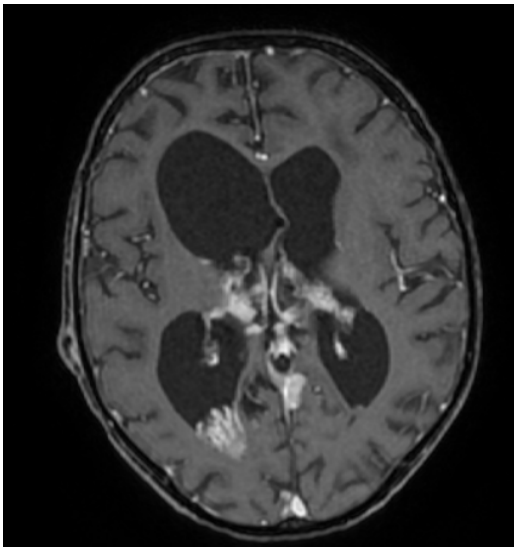

Fig 3. *Brain MRI - Polylobulated mass at the level of ventricular ependymal lining – suggestive for leptomeningeal dissemination*

Despite complex diagnostic and therapeutic medical efforts, this case was classified as recurrent astrocytoma with leptomeningeal spreading and unpredictable severe evolution.

Palliative care was indicated as the last option for this patient.

Two months later, the patient was again referred at the Emergency Care Unit for vomiting, vicious position of the head, incapacity of oral alimentation and multiple severe tonic-clonic seizures.

Unfortunately, despite extreme medical efforts, the patient developed severe bradycardia, asystole and cardiac arrest.

3. Discussions

The particularity of this case was represented by the aggressive, unpredictable evolution of this grade I pilocytic astrocytoma, with leptomeningeal spreading and intense neurologic and endocrinologic involvement, as this tumor is usually considered a low-grade, nonmalignant tumor, which usually do not spread to the surrounding brain tissue [3].

Leptomeningeal spreading is rarely associated, being atypical for PA [5], [6] and leads to a less favorable prognosis [7]. Leptomeningeal dissemination is more often present in case of high-grade tumors like glioblastoma, ependymoma and medulloblastoma and until 2013, only 60 cases of PA with leptomeningeal spreading were described in literature [8].

The prognosis of PA with associated leptomeningeal dissemination is more favorable than for diffuse astrocytomas [9], with a 5-year survival rate reaching 55%. Only few cases had longer survival rates which may reach even 20 years [10], [11].

The most frequent location of PA is the cerebellum, whereas our patient was diagnosed with pilocytic astrocytoma located in the right optic nerve with associated infiltration of optic chiasm, which made total resection impossible. This location is considered to be frequently associated with Type I Neurofibromatosis, but no evidence of Type I Neurofibromatosis was identified in this case.

Another important topic to discuss is related to additional therapy if surgical resection of the tumor is incomplete, as it was the case of our patient. Complete surgical resection is the standard approach in the management of pilocytic astrocytomas and for reducing the risk of leptomeningeal dissemination [12], [13].

Incomplete resection and need for additional therapies remains controversial among clinicians. Some studies suggest that associated radiotherapy may improve progression-free survival rate, but has little effect on the overall survival rate.

Radionsensitivity of pediatric patients must be also considered. In order to minimize the risk of long-term brain sequelae, radiotherapy is usually not favored in young patients [9], [14] being reserved only for unresectable tumors in which multiple chemotherapy strategies have failed [15].

Long time prognosis is apparently the same with or without any adjuvant treatment [16].

Common differential diagnosis of pilocytic astrocytoma include ependymoma, medulloblastoma, hemangioblastoma, choroid plexus papilloma and difuse pontine glioma [4].

4. Conclusion

We presented the case of a male patient diagnosed at the age of 6 with pilocytic astrocytoma, a tumor classified by WHO as grade I, with associated good prognosis and outcome.

Leptomeningeal dissemination appeared five years after diagnosis, associating worsening of neurological status and overall clinical condition, classified this case as one of the minority of cases of PA with an aggressive unpredictable evolution.

The patient died at the age of 12 years old, despite all medical efforts.

Our article raises awareness of leptomeningeal dissemination risk which requires close monitoring and is associated with less favorable prognosis.

Early diagnosis, tumor location, complete tumoral resection and close long-term follow-up with brain MRI are key factors for long-term survival.

Optimal treatment in case of incomplete tumoral resection remains an open topic, further studies being necessary in order to properly clarify the best therapeutic approach of difficult cases of PA.

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