A PECULIAR CLINICAL PROFILE OF SYMPTOMATIC EYELID MYOCLONUS AND ATONIC SEIZURES IN EARLY CHILDHOOD: A CASE REPORT

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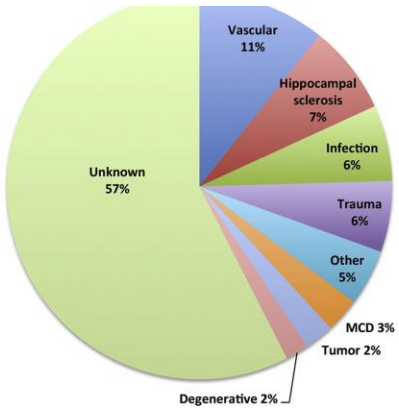
Abstract: Nowadays the development of technology in all spheres of science results in expanded and precise diagnostic possibilities in pediatric neurology. The holistic progression leads to establishing an exact diagnosis from the wide spectrum of differential diagnoses presented with symptoms which are not pathognomonic. As it is previously well elaborated in the literature, epilepsies are a broad diagnostic term and only a small proportion of them belong to ocular myoclonus, especially when symptomatic. **Materials and methods:** We present a case report of a 18-month-old female child presenting several daily unilateral eyelid myoclia followed by shortlasting self-limiting atonic seizures. After excluding ophthalmological causes, detailed neurologic physical examination and electroencephalography were performed. Due to inconclusiveness, imaging diagnostic procedures (CTm,MRim) were also performed. **Case report:** The first neurological examination takes place at the age of 16 months, with a heteroanamnesis of occasional drooping of the left eyelid, which returns to its normal state spontaneously. On several occasions the previous event is followed with vomiting and a short attention deficit episode. The neurological examination in that particular moment was unremarkable and laboratory findings showed no abnormalities. Electroencephalographic recordings showed epileptogenic activity in the occipital lobe and raised the question of differential diagnosis, considering Panayiotopoulos Syndrome- benign early onset epilepsy. It was continued with further imaging diagnostics - MRIm that revealed the existence of a solid tumor mass with a diameter of 35-40 mm that compresses the pons, mesencephalon, parahippocampal lobe and hippocampus and also involves the basilar artery. The lesion had a suprasellar extension, but no affection of the optic chiasm was visualized. **Results and therapy:** The patient underwent neurosurgical extirpation of the tumor and pathohistological tissue examination and grading and molecular diagnostic. Embryonal tumor with multilayered rosettes (ETMR), C19MC-altered (WHO grade IV) was the final diagnosis. This embryonal tumour is identified by amplification on the C19MC region on chromosome 19 (19q13. 42). It tends to be diagnosed primarily in children under 4 years old, but is so rare that no incidence statistics are available. **Conclusion:** In the pediatric neurology department, even subtle neurologic symptoms deserve extensive attention. The challenge in diagnostics is to make a differentiation from the need for extensive and expensive diagnostics when we previously have a high probability direction that indicates a benign condition. The dilemma will always remain open considering the rare situations that may not merit protocol, but they turned out to be life-saving.
Keywords: eyelid myoclonus, epilepsy, embryonal tumor, pediatric

1. INTRODUCTION

Around 85-90% of all central nervous system neoplasms are brain tumors. The specific symptomatology and clinical findings presented by pediatric patient with brain tumor varies depending on tumor location, tumor's histologic type, and the grading- rate of tumours growth. Symptoms that are found in this pathology, and are not pathognomonic, include signs of increased intracranial pressure and focal neurologic signs. In more than 35% of the pediatric population with an expansive process in the central nervous system, epileptic seizures occur as a clinical manifestation, in fact, children acquire symptomatic epilepsy due to the existing tumor.

Figure 6. Etiology of Epilepsy



Although in the etiology of epilepsy, brain tumor as a cause is represented in less than 2%, in the inverse situation, seizures are a common complication of the expansive processes in the brain and occur in

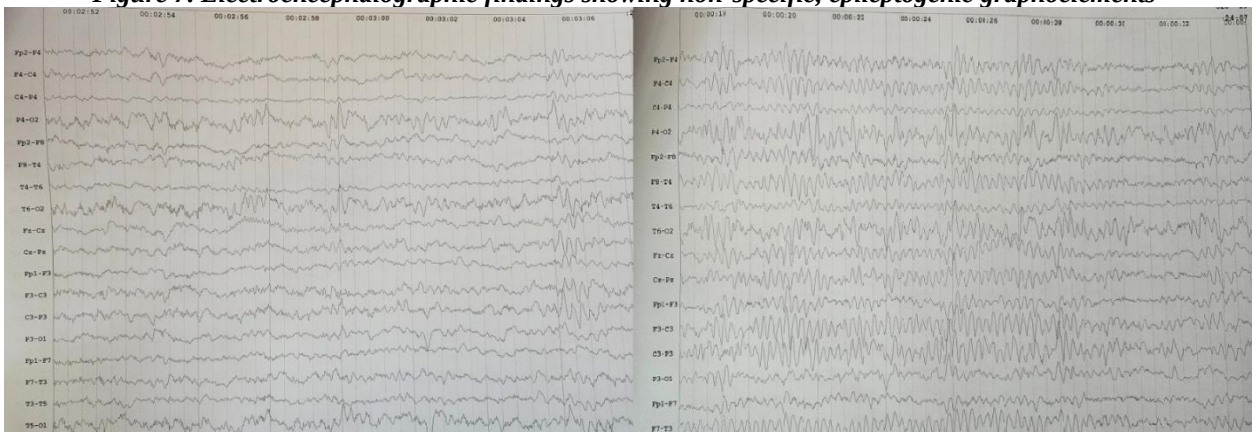
approximately 70% of patients. In the pediatric population, very rarely symptomatic epilepsy is due to a brain tumor. What makes it worth investigating is the necessity for early diagnosis in order to improve the outcome, which is otherwise characterized by poor prognosis and high mortality. In this age group idiopathic epilepsy or fever are the most common causes of seizures. On the other hand, seizure occurring for the first time in adults is probably caused by brain neoplasm. Age increases the risk of epilepsy being caused by a tumour. Seizures are more commonly seen in specific pediatric brain tumor types, often termed LEATs. Although LEATs are usually of low grade and have low mortality rates, our case witnesses for it's exclusion rule. The interictal electroencephalographic (EEG) results in pediatric brain tumors lack specificity and may not reliably indicate the tumor's location. They can suggest different locations, or even appear within the normal range, even in patients experiencing seizures. According to the latest literature reviews of presenting signs and symptoms of pediatric brain tumors, seizures ranked as the fifth most common clinical presentation. The seizures were surpassed in frequency only by headache, nausea and vomiting, abnormal gait or coordination, and papilledema. However, when specifically examining supra-tentorial tumors, seizures emerged as the second most common clinical presentation, with only symptoms of increased intracranial pressure occurring more frequently.

The likelihood of a brain tumor causing seizures is influenced by various factors, including its histology and location within the brain. It has been statistically proven in the literature that the low-grade tumors are more likely to trigger seizures, possibly due to extended survival, which provides a longer timeframe for epilepsy to develop. Within the same pediatric studies , tumors located in the cerebral cortex are associated with a higher incidence of seizures compared to midline and infratentorial tumors. Even though infratentorial tumors are less frequently linked to seizures compared to supratentorial tumors, seizures can still occur due to mass effect, hydrocephalus, or metastases.

2. CASE PRESENTATION

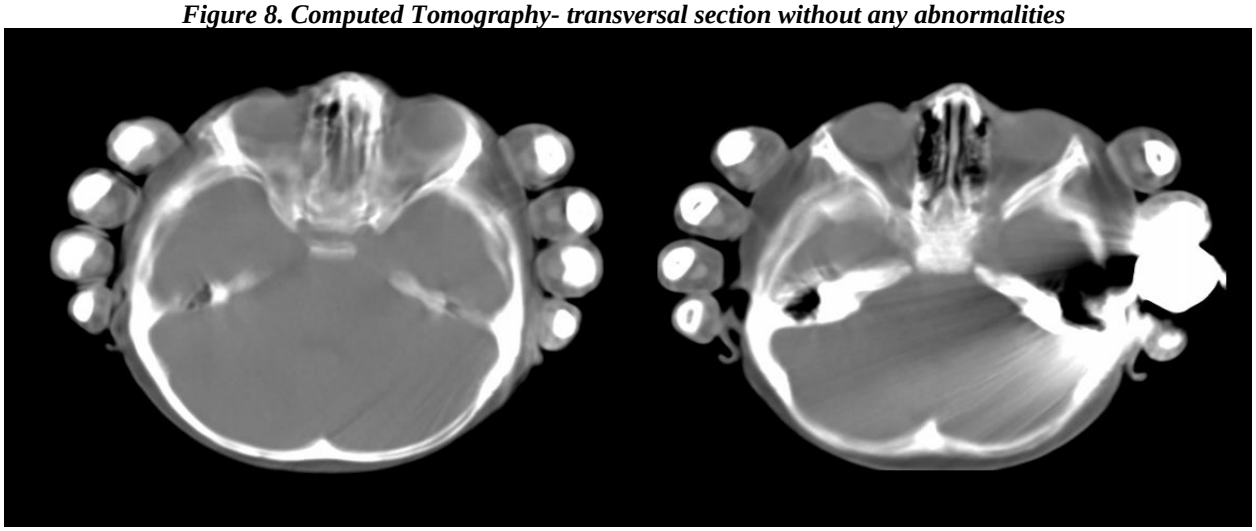
The case is about a child from pregnancy with uneventful perinatal and postnatal course. The mother passed away few months postpartum due to venous sinus thrombosis. The first neurological examination of the child takes place at the age of 16 months, with a heteroanamnesis of occasional drooping of the left eyelid, which returns to its normal state spontaneously. On several occasions the previous event is followed with vomiting and a short attention deficit episode, and after the ocular symptoms follows an episode with generalized relaxation of the whole body- described as an atonic seizure and an impression of a transient loss of consciousness. The neurological examination in that particular moment was unremarkable- cranial nerves innervate properly, muscle strength and tone were regular and deep tendon reflexes were evoked symmetrically and adequately. Laboratory findings showed no abnormalities, including referent ranges of inflammatory markers. Further investigations were made after admission in University Children's Hospital, Skopje. Previous electroencephalographic recordings showed epileptogenic activity in the occipital lobe and raised the question of differential diagnosis, considering Panayiotopoulos Syndrome- benign early onset epilepsy. Control electroencephalography while asleep revealed physiological baseline brain activity with symmetric sleep spindles and K-complexes. Generalized burst of slow theta waves were also noted.

Figure 7. Electroencephalographic findings showing non-specific, epileptogenic graphoelements



Computed Tomography of the skull did not show any deviations from normal bone structures, but knowing that it is insufficient diagnostic tool for soft tissue, magnetic resonance was also performed.

Figure 8. Computed Tomography- transversal section without any abnormalities



It was continued with further imaging diagnostics – MRI of the brain that revealed existence of a infratentorial solid tumor mass with a diameter of 35-40 mm that compresses the pons, mesencephalon, parahippocampal lobe and hippocampus and also involves the basilar artery. The lesion had a suprasellar extension, but no affection of the optic chiasm was visualized.

Figure 9. Transverse and Coronal section of the brain revealing expansive process that compresses the pons, mesencephalon, parahippocampal lobe and hippocampus.

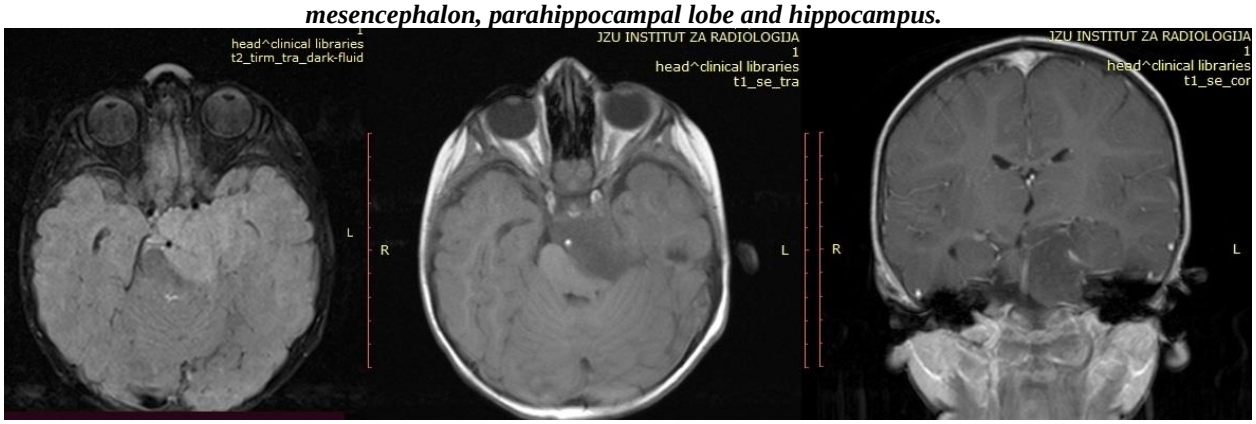
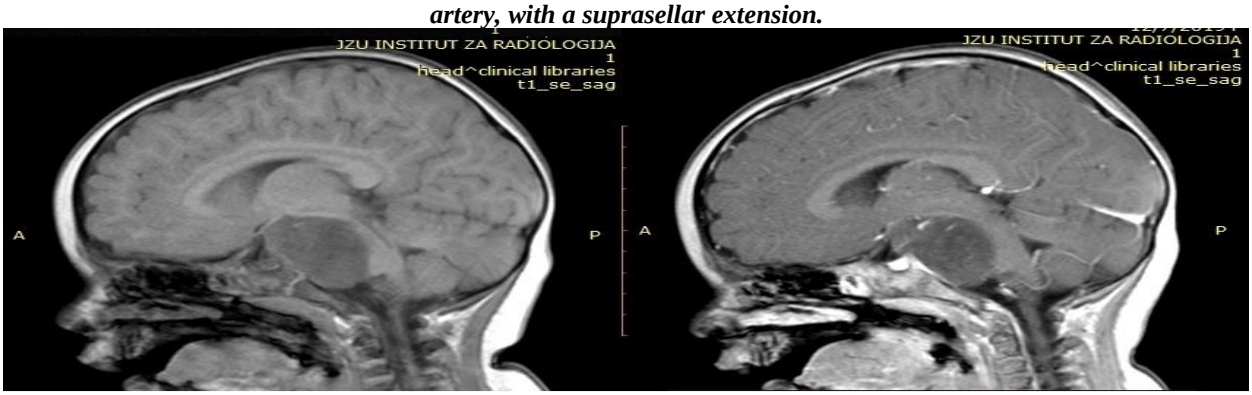


Figure 10. Sagital section of the brain revealing existence of a infratentorial solid tumor mass with a diameter of 35-40 mm, compressing the pons, mesencephalon, parahippocampal lobe and hippocampus, involving the basilar artery, with a suprasellar extension.



Additional diagnostics were necessary in order to be conclusive about the most adequate option for further therapeutic treatment. Questions were raised whether the tumor is primary, the pathohistological type of the tumor and its stage. Multidisciplinary approach with a neurosurgeon, a pathohistologist and a pediatric oncologist was conducted. The patient underwent neurosurgical extirpation of the tumor, consequent pathohistological tissue examination/grading and molecular diagnostic. Embryonal tumor with multilayered rosettes (ETMR), C19MC-altered (WHO grade IV) was established to be the final diagnosis. This embryonal tumour is identified by amplification on the C19MC region on chromosome 19 (19q13. 42). It tends to be diagnosed primarily in children under 4 years old, but is so rare that no incidence statistics are available.

4. DISCUSSION

In the 2016 revision of the WHO Classification of Central Nervous System Tumors, the designation "CNS embryonal neoplasm" refers to a diverse collection of extremely aggressive and malignant tumors. These tumors consist of primitive cells with specific morphological and molecular characteristics. ETMR is one of the rarest members in this group and can have three different subtypes according to histological features. As previously mentioned in our case, for one of the subtypes was discovered the unique ETMR C19MC amplification in a subset of CNS primitive neuroectodermal tumors with aggressive behavior. The diagnosis can be established if this amplification is present, even if multilayered rosettes are not observed. In situations where molecular testing is not feasible, the mandatory requirement shifts to the presence of multilayered rosettes. In such cases, the diagnosis should be categorized as embryonal tumors with multilayered rosettes, specifically as "not otherwise specified" (NOS).

Experiences in described the literature are consistent with our case and claim that, the majority of these tumors occur in the first 2 years of life. They can involve any part of the CNS but over two-thirds occur in the supratentorial region, that is, in the cerebral hemispheres. In contrast to the majority of described cases, in our case we describe an infratentorial tumor but with a tendency for supratentorial extension. Symptoms depend on the areas of the brain affected by the tumor. However, hydrocephalus, nausea and vomitus are the most common symptoms, that are also present in our case.

5. CONCLUSION

An expansive process can be hidden behind any apparently benign epilepsy in childhood. Subtle neurological deficits in childhood should not be underestimated and must be followed up with a comprehensive diagnostic protocol. The prognosis for C19MC-altered ETMR remains devastating, but the first step to a better tomorrow is an enriched literature that will serve for the further development of science in the direction of finding a curative treatment.

AUTHOR CONTRIBUTIONS

TS had a main contribution in literature search, writing and drafting the manuscript. LAA contributed in the diagnosing, treatment, and follow-up of the patient. LAA and TS edited the manuscript and approved the final version.

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