Ohtahara Syndrome: A Case Report

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Abstract: Ohtahara syndrome is a rare epileptic encephalopathy in children which usually presents at early age, characterized by an abnormal EEG and intractable seizure. We reported a 18-day-old male infant with seizure frequency of 20 times a day. Physical examination showed normal vital sign and general condition. Neurological assessment revealed an increase of physiological reflexes. An electroencephalogram was performed and showed burst suppression pattern suggested Ohtahara syndrome. An abnormality was found in non-contrast brain CT scan. The patient was managed with antiseizure medication. Subsequently, the patient showed an improvement. This case report highlights the importance of early diagnosis, proper management, and prognosis of children with Ohtahara syndrome.

1 INTRODUCTION

Epileptic encephalopathy is a group of disorders wherein the abnormal epileptic electrical discharge progressively impacts the functionality of the brain. The deterioration in brain functions corresponds with alterations in brain connectivity, diminished distribution of excitatory glutamatergic receptors, and a decline in neurogenesis. Epileptic encephalopathy is often characterized by refractory epilepsy, persistent severe abnormal electroencephalogram (EEG) patterns, and cognitive dysfunction. It typically manifests in early age, with 40% of seizures occurring in first three years of life. There are 8 syndromes classified under epileptic encephalopathy, one of which is Ohtahara syndrome (Panayiotopoulos, 2005).

Ohtahara syndrome is a form of the most severe epileptic encephalopathy with the earliest onset age. It usually presents within the first 3 months of age, but 30% of cases first manifested seizures within 10 days of life. Symptoms will appear within the few hours following birth, but possible seizure activity may occur in utero. This syndrome is typically rare, with a prevalence ranging from 0.2%-4% of all epilepsies (Nieh & Sherr, 2014; Khan & Baradie, 2012). In accordance with a case report, incidents of cerebral spasms manifest in a range of 1.5–5 occurrences per 1000 newborns post-partum (Panayiotopoulos, 2005). Despite its rarity, Ohtahara syndrome is difficult to treat and continues to pose a distinct challenge in pediatric neurology. In this study, we present a case of Ohtahara syndrome that exhibited seizure improvement following the administration of pharmacological therapy.

2 CASE ILLUSTRATION

A 18-day-old male infant came to Pediatric Neurology Clinic with chief complained of tonic seizure with frequency of 20 times a day. The onset of seizure was noted on the seventh day of life. The seizure was not provoked by fever. The patient is fully breastfed, but he has not yet developed proficient sucking abilities. He was delivered via

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caesarean section at term, weighing 3300 grams, cried immediately after delivery. Antenatal scans showed no abnormalities. The mother had no medical history during pregnancy. There was no family history of seizure.

Physical examination showed normal vital sign and general condition. Neurological assessment revealed an increase of physiological reflexes. Laboratory tests showed normal result. EEG examination was performed and showed discontinuation of basic rhythm with burst attenuation pattern (Figure 1). A non-contrast brain CT scan identified a solid circular mass with a central cystic lesion in right temporal lobe suggested infection or mass, along with the presence of cavum in septum pellucidum (Figure 2).

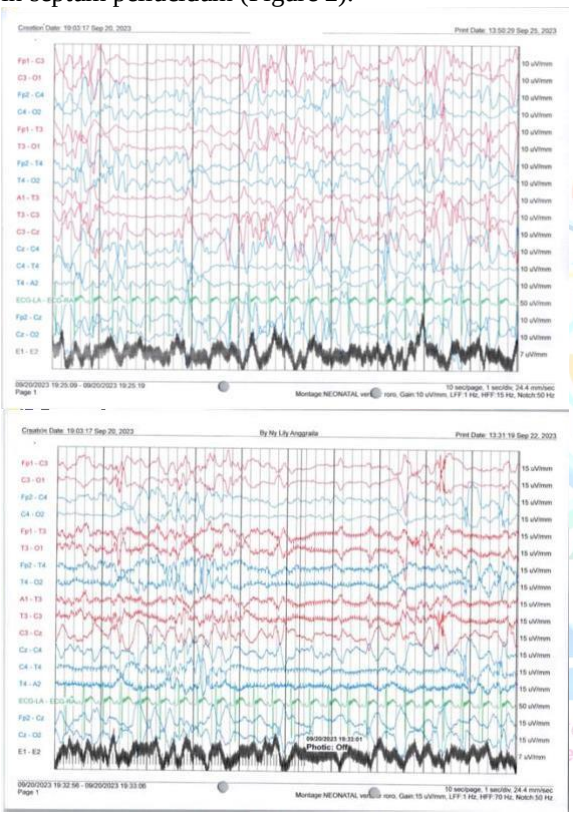

Figure 1. EEG of the patient showing abnormal rhythm and suppression burst pattern.

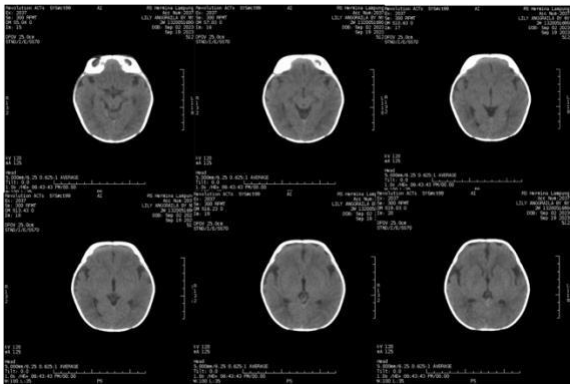

Figure 2. Non-contrast brain CT scan of the patient showing an abnormality

The patient was managed with methylprednisolone 8 mg three times a day, phenobarbital 10 mg twice a day, and levetiracetam 70 mg twice a day. He responded well to the treatment. Currently, the patient's seizure frequency has reduced to 4 times a day.

3 DISCUSSION

Ohtahara syndrome is a complex condition that manifest in infancy, thus also known as early infantile epileptic encephalopathy (EIEE). Ohtahara syndrome may arise from brain structural malformations, although in some cases, it may be caused by genetic mutations or abnormal metabolic conditions. Several genetic mutations associated with the occurrence of this syndrome including aristaless-related homeobox (ARX), STXBP1, and SCN2A (Nieh & Sherr, 2014). The underlying pathophysiology of Ohtahara syndrome involves abnormalities in the catecholaminergic and serotonergic systems (Panayiotopoulos, 2005).

Early onset seizure constitutes the main clinical manifestation of Ohtahara syndrome. Tonic spasms are the most frequent seizure type, characterized by tonic flexion lasting 1-10 seconds, either singularly or in prolonged clusters of 10-300 times within a 24-hour period. Seizures manifest as either generalized and symmetrical or lateralized, occurring both during sleep and wakefulness. Other seizure types that may occur include tonic/clonic, clonic myoclonic, atonic, absence, partial, and Jacksonian seizures. The seizure types may exhibit variability over time. Symptoms associated with Ohtahara syndrome also encompass developmental delays, intellectual disabilities, and other neurological abnormalities (Nieh & Sherr, 2014; Panayiotopoulos, 2005; Beal et al., 2012).

EEG examination serves as the key diagnostic tool for Ohtahara syndrome. However, a thorough medical history, physical examination, and comprehensive neurological evaluation are crucial to detect other causes of seizure. Brain imaging such as brain MRI or CT scans may show abnormalities and cortical malformations. Metabolic evaluation can be done to explore potential etiological sources if brain imaging shows no abnormality [Panayiotopoulos, 2005; Moumen, 2023).

EEG findings in Ohtahara syndrome reveal a pathognomonic feature of suppression burst pattern. The bursts are characterized by high-amplitude spikes lasting 2-6 seconds. The suppression period lasts for 3-5 seconds. The interval between two bursts within the range of 5-10 seconds. The occurrence of bursts is synchronous with the tonic spasm. This electrographic pattern is observed during both wakefulness and sleep (Khan & Baradie, 2012; Panayiotopoulos, 2005; Beal et al., 2012).

To date, there is no curative therapy for Ohtahara syndrome. Treatment is primarily supportive, aimed at controlling seizures and addressing underlying comorbidities. Although seizures in Ohtahara syndrome are generally drug-resistant, optimized dosages or combination of anticonvulsant drugs can still be utilized. Interventions such as ketogenic diet, vagus nerve stimulation (VNS), and invasive surgical procedures such as partial or complete hemispherectomy, may be considered when pharmacological interventions fail to adequately control seizures. Medical rehabilitation, such as physiotherapy and occupational therapy, can be implemented to enhance motor skills development, which often limited in patients with Ohtahara syndrome (Khan & Baradie, 2012).

The prognosis for Ohtahara syndrome is generally poor. Half of the patients died within weeks to months after onset, while others experience significant neurological deficits (Moumen, 2023). Psychomotor functions in affected patients may gradually decline with conditions such as spastic diplegia, hemiplegia, tetraplegia, ataxia, or dystonia (Panayiotopoulos, 2005). In some cases, within a few months following the onset of Ohtahara syndrome, the EEG patterns are likely to evolve into West syndrome, characterized by the transition from suppression burst to hypsarrhythmia. Some cases may transform into Lennox-Gastaut syndrome if the patients reach the age of 2-3 years, marked by a slow spike-wave pattern (Panayiotopoulos, 2005; Beal et al., 2012). Patients with Ohtahara syndrome who do not develop West syndrome or Lennox-Gastaut syndrome may exhibit a slightly better psychomotor development (Khan & Baradie, 2012).

4 CONCLUSIONS

Ohtahara syndrome represents a rare and severe form of epileptic encephalopathy in infancy. Its hallmark diagnostic features include early-onset seizures, developmental delays, and a distinctive EEG pattern. Despite the generally unfavorable prognosis, ongoing research and therapeutic advancements offer optimism for improved outcomes in the future.

REFERENCES

Panayiotopoulos, C. P. (2005). Epileptic Encephalopathies in Infancy and Early Childhood in Which the Epileptiform Abnormalities May Contribute to Progressive Dysfunction. In: Panayiotopoulos CP. The Epilepsies: Seizures, Syndromes and Management. Oxfordshire (UK): Bladon Medical Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK2611/

Nieh, S. E., Sherr, E. H. (2014). Epileptic encephalopathies: New Genes and New Pathways. Neurother. 11:796-806

Khan, S., Baradie, RA. (2012). Epileptic Encephalopathies: An Overview. Epilepsy Res Treat. ;2012:403592.

Panayiotopoulos, C. P. (2005). Neonatal Seizures and Neonatal Syndromes. In: Panayiotopoulos CP. The Epilepsies: Seizures, Syndromes and Management. Oxfordshire (UK): Bladon Medical Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK2599/

Beal, J. C., Cherian, K., Moshe, S. L. (2012) Early-onset epileptic encephalopathies: Ohtahara syndrome and early myoclonic encephalopathy. Pediatr Neurol. 47(5):317-23.

Moumen, A. E. 2023. Ohtahara Syndrome: Case Report and Literature Review. Sch J Med Case Rep.11(4): 594-596.