

Seizure reduction following ventriculoperitoneal shunt surgery in an Ohtahara syndrome patient who developed hydrocephalus

Redukce záchvatů po operaci ventrikuloperitoneálního zkratu u pacienta se syndromem Ohtahara s rozvojem hydrocefalu

Dear editor,

Ohtahara syndrome, also known as early infantile epileptic encephalopathy, is a rare epileptic encephalopathy that typically manifests within the first months of life, often during the neonatal period. This syndrome is characterized by frequent recurrent tonic seizures, occurring during both sleep and wakefulness, with daily seizure frequencies ranging between 10 and 300 episodes [1]. The most notable interictal EEG finding is the burst-suppression pattern observed during both sleep and wakefulness [2]. The prognosis is poor, with more than half of the cases resulting in death, while surviving patients exhibit varying degrees of residual neurological deficits [3]. Although the frequency of seizures may decrease over time in those who survive, severe mental and motor impairments persist [4]. Here, we present a case of a male infant diagnosed with Ohtahara syndrome during the neonatal period who subsequently developed hydrocephalus.

The patient, a 3-month-old male, was referred to our department by the pediatric neurology unit due to a tense anterior fontanelle. His medical history includes parental consanguinity. The patient was born at 38+5 weeks' gestation via cesarean section to a 38-year-old mother with hypothyroidism and had Apgar scores of 8 and 9. He was admitted to the neonatal intensive care unit for 17 days due to prolonged seizures that began within 24–48 h postnatally. There was no family history of epilepsy or hydrocephalus. The patient had no history of trauma, central nervous system infection, or intracranial hemorrhage. EEG findings revealed tonic spasms accompanied by a burst-suppression pattern, leading to a diagnosis of Ohtahara syndrome. Upon physical examination, the

patient's weight was 4,100 g (below the 3rd percentile), and his head circumference was 41.2 cm (50th–75th percentile). The anterior fontanelle was assessed as tense, but other system examinations were normal. Following the diagnosis of hydrocephalus, the patient underwent ventriculoperitoneal shunt surgery. During follow-up, an increase in brain tissue thickness and a decrease in the Evans index were observed (Fig. 1). Postoperatively, the patient continued dual antiepileptic therapy, and seizure frequency decreased to once or twice per week. As of August 2024, the patient has completed 22 months of follow-up.

Seizures in Ohtahara syndrome are nearly resistant to all antiepileptic drugs. Although benzodiazepines, valproate, adrenocorticotropic hormone, and corticosteroids are commonly used, their effectiveness is limited. In some cases, thyrotropin-releasing hormone (TRH) and the ketogenic diet have shown partial efficacy [5]. Successful resections have been reported in cases with focal cortical dysplasia, resulting in relatively better outcomes post-surgery [6]. Ohtahara syndrome is a rare epileptic encephalopathy often associated with brain anomalies. The etiology is multifactorial, and in most cases, the underlying cause remains unknown. Of the 11 cases described by Clarke et al. [7], the cause was identified in three cases (asphyxia, agenesis of the corpus callosum, non-ketotic hyperglycinemia), while the remaining eight were idiopathic. In the 14 cases reported by Ohtahara et al. [8], three were idiopathic, two were associated with porencephaly, and two with Aicardi syndrome. Additionally, six cases had microcephaly or cerebral atrophy (cerebral dysgenesis), and one case exhibited subacute diffuse encephalopa-

Redakční rada potvrzuje, že rukopis práce splnil ICMJE kritéria pro publikace zasílané do biomedicínských časopisů.

The Editorial Board declares that the manuscript met the ICMJE "uniform requirements" for biomedical papers.

F. Demir¹, S. Demir¹, P. Cennetoglu², F. Baskan¹

¹ Department of Neurosurgery, Healty Sience Universty; Basaksehir Cam and Sakura City Hospital Istanbul, Turkey

² Department of Pediatric Neurology, Healthy Sience University; Basaksehir Cam and Sakura City Hospital Istanbul, Turkey



Firat Demir, MD

Department of Neurosurgery

Healthy Sience University

Basaksehir Cam and Sakura

City Hospital Istanbul

Basaksehir Olympic Boulevard Road

34480 Basaksehir Istanbul

Turkey

e-mail: dr.demir@hotmail.com

Accepted for review: 1. 9. 2024

Accepted for print: 14. 5. 2025

thy. The etiology of Ohtahara syndrome remains uncertain, and although hydrocephalus is not commonly associated with this condition, our patient presented with both. He had a documented history of perinatal asphyxia, and comprehensive investigations excluded other potential etiologies, including structural malformations, genetic abnormalities, metabolic disorders, and central nervous system infections. Perinatal

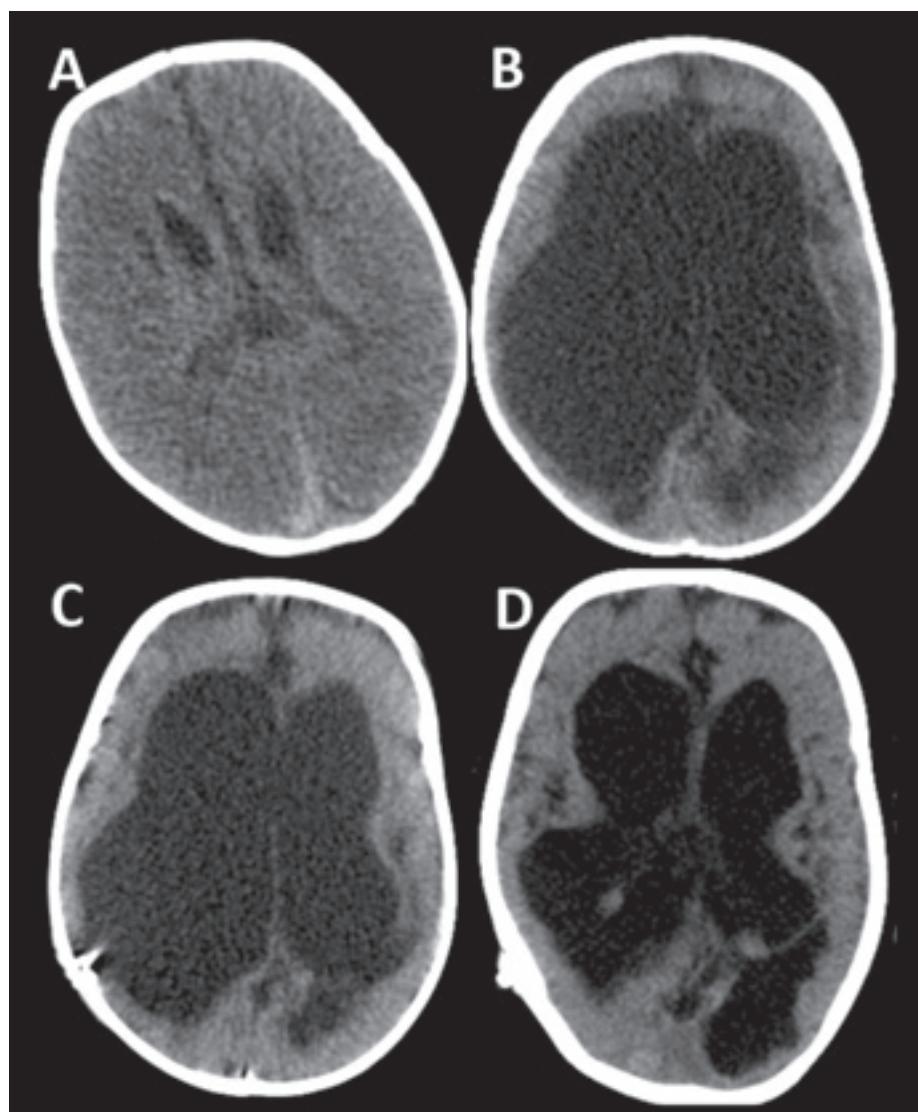


Fig. 1. Brain CT (axial view). (A) At 1 month of age: a bifrontal index of 37.1%, frontal tissue thickness of 20 mm, and an Evans index of 33.7%. (B) At 3 months of age: significant enlargement of the lateral ventricles and a reduction in tissue size; the bifrontal index was measured at 73%, frontal tissue thickness at 11.96 mm, and the Evans index at 63.3%. (C) At postoperative month 1: a bifrontal index of 70%, frontal tissue thickness of 12.06 mm, and an Evans index of 59.8%. (D) At postoperative month 21: a bifrontal index of 65.9%, frontal tissue thickness of 17.82 mm, and an Evans index of 57.7%.

Obr. 1. CT mozku (axiální řez). (A) Ve věku 1 měsíce: bifrontální index 37,1 %, tloušťka frontální tkáně 20 mm a Evansův index 33,7 %. (B) Ve věku 3 měsíce: významné zvětšení laterálních komor a zmenšení velikosti tkáně; bifrontální index byl změřen na hodnotu 73 %, tloušťka frontální tkáně byla 11,96 mm a Evansův index 63,3 %. (C) Jeden měsíc po operaci: bifrontální index 70 %, tloušťka frontální tkáně 12,06 mm a Evansův index 59,8 %. (D) 21 měsíců po operaci: bifrontální index 65,9 %, tloušťka frontální tkáně 17,82 mm a Evansův index 57,7 %.

hypoxic-ischemic injury is a well-recognized cause of early infantile epileptic encephalopathies and may impair inhibitory neuronal circuits involved in seizure generation, particularly in subcortical structures. Given the early onset of seizures and absence of

alternative explanatory factors, we consider perinatal asphyxia the most plausible underlying etiology in this case, in line with previous reports implicating hypoxic events in the pathogenesis of Ohtahara syndrome [9]. In addition, cranial imaging did not reveal

any findings suggestive of previous intracranial hemorrhage or post-infectious changes such as ventriculitis or ependymal enhancement. There was also no clinical history of neonatal sepsis, meningitis, or neurological deterioration consistent with CNS infection. While these differential diagnoses were considered, they were ultimately not supported by clinical or radiological evidence.

We have not found any reported cases in the literature of Ohtahara syndrome patients developing hydrocephalus during follow-up. Therefore, we believe that patients with Ohtahara syndrome should be closely monitored for the development of hydrocephalus. Timely treatment of hydrocephalus could potentially improve the prognosis of these patients. In our case, the frequency of seizures significantly decreased following shunt surgery. Further research is needed to better understand the neurodevelopmental impacts and underlying causes of Ohtahara syndrome.

Conflict of interest

The authors declare they have no potential conflicts of interest concerning drugs, products, or services used in the study.

References

- Yamatogi Y, Ohtahara S. Early-infantile epileptic encephalopathy with suppression-bursts, Ohtahara syndrome; its overview referring to our 16 cases. *Brain Dev* 2002; 24(1): 13–23. doi: 10.1016/s0387-7604(01)00392-8.
- Roessler E, Muenke M. Holoprosencephaly: a paradigm for the complex genetics of brain development. *J Inher Metab Dis* 1998; 21(5): 481–497. doi: 10.1023/a:1005406719292.
- Komárek V. Léčba epileptických syndromů u dětí. *Cesk Slov Neurol N* 2007; 70/103(5): 473–485.
- Karagöl BS, Özkan M Okumuz N et al. Erken infantile epileptik encefalopati ve izlemede west sendromu gelişen bir yenidoğan olgusu. *İstanbul Tip Derg – İstanbul Med J* 2012; 13(2): 89–92.
- Ishii Mtamai K, Sugita K, Tanabe Y. Effectiveness of TRH analog in a case of early infantile epileptic encephalopathy. *No to Hattatsu* 1990; 22(5): 507–511.
- Pedes pan JM, Loiseau H, Vital A et al. Surgical treatment an early epileptic encephalopathy with suppression-bursts and focal cortical dysplasia. *Epilepsia* 1995; 36(1): 37–40. doi: 10.1111/j.1528-1157.1995.tb01662.x.
- Clarke M, Gill J, Noronha M et al. Early infantile epileptic encephalopathy with suppression burst: Ohtahara syndrome. *Dev Med Child Neurol* 1987; 29(4): 520–528. doi: 10.1111/j.1469-8749.1987.tb02512.x.
- Ohtahara S, Ohtsuka Y, Yamatogi Y et al. The early-infantile epileptic encephalopathy with suppression-burst: developmental aspects. *Brain Dev* 1987; 9(4): 371–376. doi: 10.1016/s0387-7604(87)80110-9.
- Pavone P, Spalice A, Polizzi A. Ohtahara syndrome with emphasis on recent genetic discovery. *Brain Dev* 2012; 34(6): 459–468. doi: 10.1016/j.braindev.2011.09.004.