Reversible Brain Atrophy after ACTH Treatment in children with continuous spike and wave during slow sleep(CSWS): Case presentation

Prof. Dr. Füsun Ferda Erdoğan

Erciyes University Faculty of Medicine, Department of Neurology , Division of Child Neurology
Erciyes University Institute of Gevher Nesibe Genome and Stemm cell, Neuroscience Department

It is well known but rare phenomenon reversible brain atrophy after ACTH treatment in children with epilpetic encephalopathy. The epileptic encephalopathies are a group of conditions in which the epileptic activity itself – ictal or interictal, clinical or electroencephalographic – contributes to a picture of severe cognitive and behavioral impairments, which are beyond what might be expected from the underlying etiology alone. In fact, under hypercortisolemia condition the brain atrophy and cognitive decline are showed in adult and children patients. The aim of this case presentation are showing a claer evidence of the formation of reversible brain atrophy related to ACTH treatment and review of the mechanism of ACTH treatment related reversible brain atrophy.

CASE PRESENTATION

A six year- old boy has suffered from frequent generalized tonic-clonic seizures during sleep. His neurologic examination, routine blood, and urine tests and cranial MRI findings were normal. Despite receiving polytherapy his seizures continued, at the same time behavioral disturbances and loss in academic skills have been observed. His sleep EEG examination showed CSWS which is a very special pattern causing a cognitive decline in children. It is known that CSWS is a very important and antiepileptic drug-resistant electrophysiological pattern. CSWS is defined as a peculiar EEG pattern with continuous epileptic activity at 2–3 Hz, predominantly in the anterior regions occupying ≥85% of nonrapid eye movement (NREM) sleep. If it can not be suppressed or eliminated it causes cognitive decline and mostly repeated seizures during its course and it can be suppressed with ACTH treatment. For this reason we applied the ACTH to this patient one year later his seizures began. The ACTH treatment had to be applied two times for 4 and 2 months respectively with a one-year interval. The seizures and CSWS pattern in EEG were resolved completely at the end of the second ACTH cure, but prominent cortical atrophy was seen in his cranial MRI. One year later ACTH cure, the cranial MRI showed resolution in cortical atrophy especially in the anterior part of the brain.

DISCUSSION

The corticosteroids most widely used in childhood encephalopathies are ACTH, hydrocortisone, prednisone and methylprednisolone. A good response to these drugs has been reported in various studies and case reports. There are several theories regarding the mechanism of action of corticosteroids in epilepsy. Adrenocorticotropic hormone can affect infantile spasms through g-aminobutyric acid [GABA(A)] receptor-mediated anticonvulsant effects or systematically through the hypothalamic-pituitary-adrenal axis, thus suppressing CRH and decreasing neuronal excitability. Possible neuromodulatory effects may include correction of deficient or dysfunctional enzymes, changes in intracellular-extracellular electrolyte ratios, correction of low intracellular glucose, reduction in cerebral water content, and modulation of intracellular adenosine and neurosteroid production. The immunomodulatory or anti-inflammatory properties of corticosteroids have been postulated to be responsible for the action of these drugs in epileptic encephalopathies with CSWS.

Since the anticonvulsant effect of corticosteroids persists after drug discontinuation, it has been suggested that in addition to allowing acute seizure control, corticosteroids may reset a deranged cerebral homeostatic mechanism, thus increasing refractoriness to seizure recurrence. Clinical and electrophysiologic peculiarities of this presented case pointed out the diagnosis of epileptic encephalopathy with CSWS. The tretment of ACTH resulted with complete resolution of CSWS pattern in the EEG and remission of the seizures both are the main goal of this treatment. One year later due to requrrence of the drug resistant seizures and CSWS pattern in EEG, treatment of ACTH repeated. At the and of first ACTH cure, brain atrophy occured and after cessation of ACTH treatment brain atrophy was resolved. We could not evaluate the effect of brain atrophy on the cognitive functions.

Brain atrophy can occur in a wide variety of conditions other than aging, and notable causes include exogenous or endogenous steroids, chronic alcohol ingestion, radiation therapy, or anorexia nervosa. Reversible brain atrophy related with ACTH treatment in children with west syndome and other epileptic encephalopathies were published.

Cortical atrophy related to high serum cortisol level is a well known phenomenon in Cushing syndrome. The pathogenesis of brain atrophy in Cushing's syndrome is thought to be multifactorial, and possible explanations include loss of water content in brain tissue, catabolic effects on proteins, reduction in glucose metabolism, synaptic accumulation of glutamate, or neuronal cell death. Excess glucocorticoids cause retraction and simplification of dendrites in the hippocampus, and this morphological change probably accounts for the hippocampal volume loss. Mechanisms by which glucocorticoids affect the brain include decreased neurogenesis and synthesis of neurotrophic factors, impaired glucose utilization, and increased actions of excitatory amino acids. Anticonvulsant effects of ACTH is very well known phenomenon and it is a rescue treatment in epileptic encephalopathies in terms of control of seizures, resolution of CSWS in EEG and protection of cognitive abilities.

References

Ohara N et al. Reversible brain atrophy and cognitive impairment in an adolescent Japanese patient with primary adrenal Cushing's syndrome. Neuropsychiatric Disease and Treatment 2014:10 1763–1767

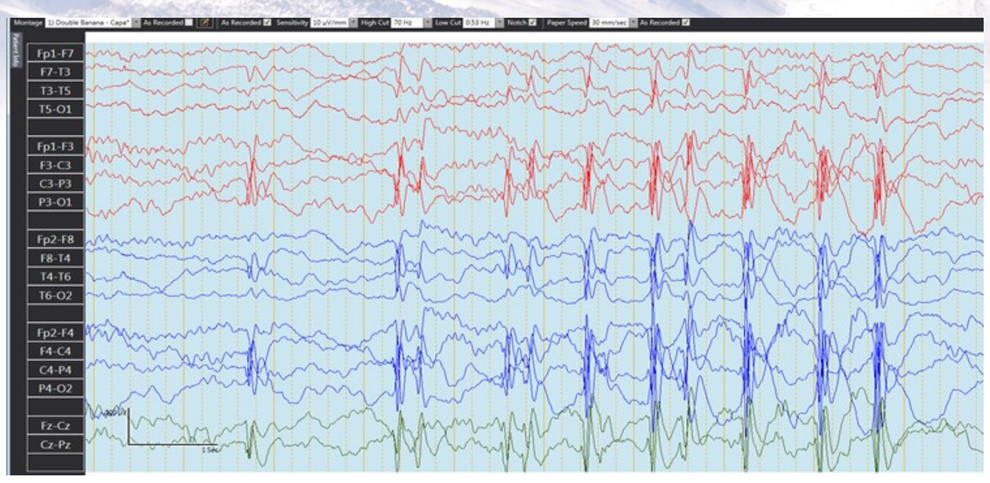
Okuno T. Et all. Cerebral Atrophy following ACTH Therapy.J Asst.Comp.Tomogrphy. 1980:40(1)20-23.

Alpietro v. Et al.Adrenal Disorders and the Paediatric Brain: Pathophysiological Considerations and Clinical Implications. International Journal of Endocrinology 2014, 282489, 15 pages

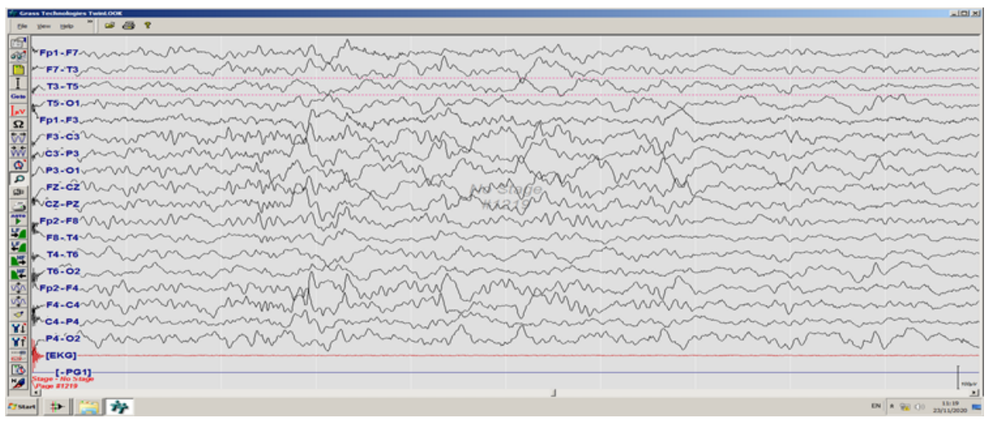
Dogan S, Dogan MS, Tutunculer F, Yapiciugurlar O, Genchellac H. Brain Atrophy and Hypomyelination Associated with Iatrogenic Cushing's Syndrome in an Infant. Iran J Child Neurol. Winter 2018; 12(1):101-104..

Tekgül H. Et al.Electrical status epilepticus in sleep (ESES)/continuous spikes and waves during slow sleep (CSWS) syndrome in children: An electroclinical evaluation according to the EEG patterns. Epilepsy & Behavior 61 (2016) 107–111

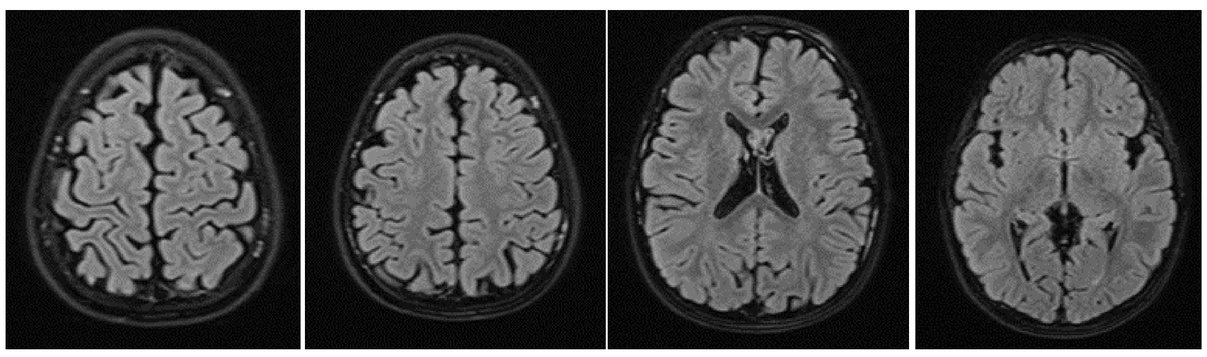
EEG 2017- Before ACTH Treatment



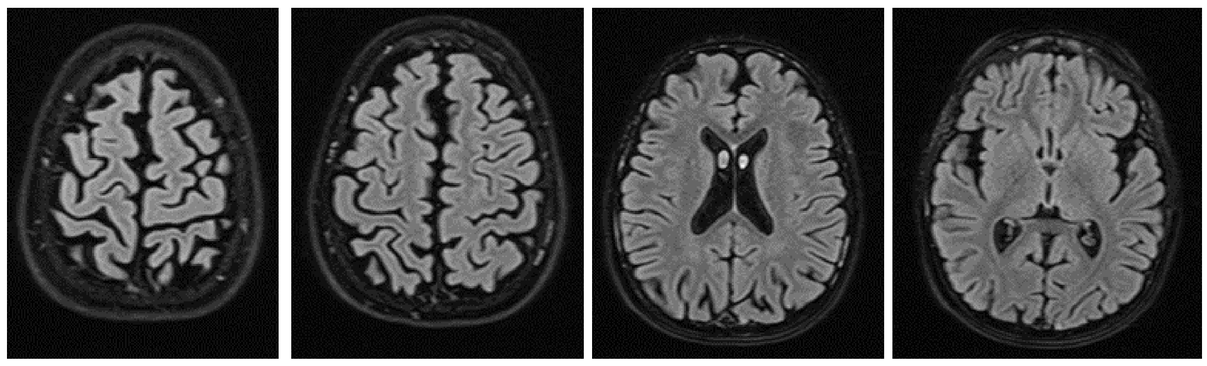
EEG 2018-After ACTH Treatment



Cranial MRI 2017- Before ACTH Treatment



Cranial MRI 2018-Immediatelly After ACTH Treatment



Cranial MRI-2019-1 year later first cure of ACTH