



A rare central nervous system anomaly in a tuberous sclerosis case with gelastic seizures: Corpus callosum agenesis

Jelastik nöbet ile gelen tüberosklerozlu bir olguda nadir bir santral sinir sistemi anomalisi: Korpus kallosum agenezisi

Sedat IŞIKAY

Clinic of Pediatric Neurology, Gaziantep Children's Hospital, Gaziantep, Turkey

ABSTRACT

Gelastik seizures are associated with hypothalamic hamartomas in general. Herein, we report a patient with gelastic seizures who was diagnosed with tuberous sclerosis complex and corpus callosum agenesis in the absence of hypothalamic hamartomas. As all these rare conditions were together in this patient, tuberous sclerosis presented with gelastic seizures in the presence of corpus callosum agenesis without hypothalamic hamartomas, this case was regarded as valuable to be reported in the light of recent literature.

Keywords: *Tuberous sclerosis, gelastic seizure, corpus callosum agenesis, child*

ÖZ

Jelastik nöbetler genellikle hipotalamik hamartomlar ile ilişkilidir. Biz burada tüberoskleroz ve korpus kallosum agenezi tanıli hipotalamik hamartomsuz jelastik nöbetleri olan bir olguyu sunuyoruz. Tüm bu nadir hastalıkların bu hastadaki birlikteliği gibi tüberoskleroz hipotalamik hamartom olmaksızın korpus kallosum agenezisi varlığında jelastik nöbetler ile prezante olabilir. Bu olgu güncel literatür ışığında kaydedeğer görülebilmektedir.

Anahtar Kelimeler: *Tüberoskleroz, jelastik nöbet, korpus kallosum agenezisi, çocuk*

INTRODUCTION

Tuberous sclerosis complex (TSC) is an autosomal dominant, neuro-cutaneous genetic disorder associated with multiple benign tumors (hamartomas) most commonly in the brain, kidney, lungs, and skin (1). Tuberous sclerosis complex was recognized to be a genetic disease with the discovery of the two causative genes, TSC1 and TSC2 (2). Common symptoms of TSC include seizures, skin lesions such as macules and fibromas, and neurocognitive impairments (3). Epilepsy is the most prevalent clinical manifestation of TSC and reported in 70-80% of cases almost all subtypes of seizures (simple partial, complex partial and generalized tonic-clonic) are reported in patients with TSC (3). The major brain lesions associated with TSC include cortical tubers, radial white matter bands, subependymal nodules, and subependymal giant cell astrocytomas;

while parenchymal cysts, cortical calcifications and other cortical dysplasias have rarely been reported (4).

Gelastik seizures (GS) involve sudden outburst of unpleasant, sardonic laughter or crying without an apparent cause, usually lasting for less than a minute (5). They are rarely reported and often have a high frequency, occurring several times daily, and may accompany other seizure types. Brandberg and colleagues estimated the prevalence of this syndrome among Swedish children to be 0.5 in 100.000 (6). In fact GS have been associated to hypothalamic hamartomas in general; however they were also described in several different conditions such as brain tumors, lesions, dilated temporal horns, atrophy, tuberous sclerosis, post infectious foci and cortical dysplasia (7).

Corpus callosum agenesis (CCA) is a rare congenital cerebral malformation with an incidence ranging from

Yazışma Adresi/Correspondence: Sedat IŞIKAY

Gaziantep Çocuk Hastanesi, Çocuk Nöroloji Kliniği, Gaziantep, Türkiye
Telefon/Tel: +90 342 3606060 • **E-posta/E-mail:** dr.sedatisikay@myynet.com

Geliş Tarihi/Received: 15.01.2015 • **Kabul Ediliş Tarihi/Accepted:** 25.07.2015

0.7% to 5.3% that often manifests as complex partial seizures, intellectual impairment and psychosis. The deficit may be complete or partial and it is usually observed in conjunction with other brain anomalies such as interhemispheric cysts with hydrocephalus, Dandy-Walker syndrome and neuronal migrational disorder (8).

Herein, we will report a patient with gelastic seizures who was diagnosed with TSC and corpus callosum agenesis in the absence of hypothalamic hamartomas. Though there are some corpus callosum agenesis cases with gelastic seizures reported before; they all have accompanying hypothalamic hamartomas. To the best of our knowledge, this is the first tuberous sclerosis case presented with gelastic seizures in the presence of corpus callosum agenesis without hypothalamic hamartomas in literature.

CASE REPORT

An 8-years-old boy was admitted to our outpatient clinic with intermittent, uncontrollable laughter and giggling during the day and night for last 3-4 months. The patient was the first child of healthy parents with a non-consanguineous marriage, and was born uneventfully by a normal vaginal delivery without any perinatal problems. He was having a healthy brother. His family history was negative for epilepsy. The neuro-psychomotor development of the patient was not normal. Although he had walked at the age of 18 months and acquired verbal language at the age of 24 months; he still was not knowing the colors or counting. He first had a seizure by the age of seven months, as contractions around the mouth and eyes for just once. He was under phenobarbital treatment for two years, in another hospital at that period. From then on, he did not have any controls or medications. The gelastic seizures were occurring 4-10 times per day and were lasting shorter than a minute in last six months.

In physical examination; mental retardation has been determined; he was scared, frightening of everything and there were many (> 20 in number) hypopigmented macules larger than 5 mm in diameter in different parts of his body. Electroencephalography (EEG) revealed slowing in the left hemisphere with frequent sharp waves. He was then admitted for a 24 hour video EEG monitoring, which revealed several bursts of generalized high-amplitude spike and wave activity with frontotemporal predominance for five to 10 seconds provoked by 'deep belly' laughing. Brain magnetic resonance imaging (MRI) revealed that 'third and both lateral ventricles are larger than normal; posteriorly due to the volume loss in neural parenchyma, occipital horns of lateral ventricle are colpocephalic in appearance, in this region,

hyperintensities compatible with the marked gliosis in periventricular white matter, and subcortical tubers are observed; corpus callosum is agenetic in appearance (Figure 1) and an arachnoid cyst of right temporal type with the dimensions of 2 x 4 x 3.5 cm is also observed'. His routine blood laboratory tests and abdominal ultrasound revealed nothing abnormal. The patient was diagnosed with tuberous sclerosis, mental retardation and gelastic seizures and carbamazepine treatment has been started. However, he still had an average of 1 to 3 seizures per day despite 1 month of carbamazepine

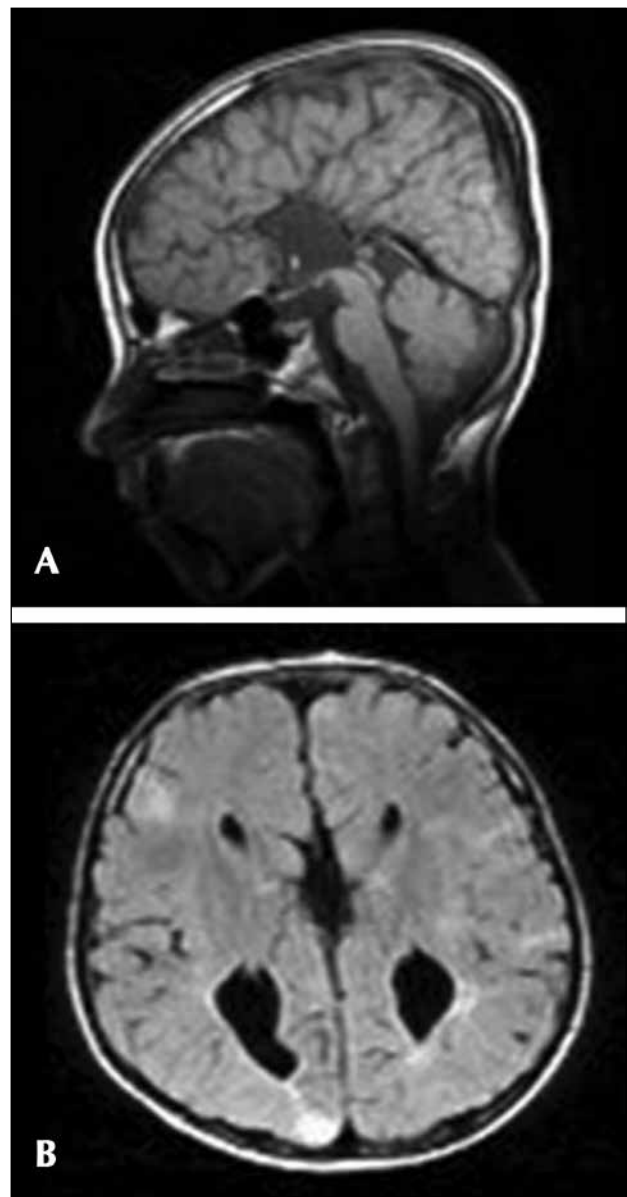


Figure 1. Axial T2-FLAIR (B) and sagittal T1-weighted (A) images show corpus callosum agenesis. Third and both lateral ventricles are larger than normal and cortical tubers are observed in the subcortical areas (A).

treatment and Levetiracetam and valproic acid were also added for recurrent seizures in first month control. In first year follow-up, the recurrent seizures were under control with carbamazepine, valproic acid and levetiracetam treatments and the drugs are planned to be lessened one by one.

DISCUSSION

Herein, we have presented a tuberous sclerosis case with gelastic seizures. Our case is unique, since his MRI revealed corpus callosum agenesis in the absence of hypothalamic hamartomas accompanying these seizures. Gelastic seizures, described usually as a manifestation of hypothalamic hamartomas, are characterized by inappropriate, stereotypical attacks of uncontrolled laugh. These seizures have associated signs compatible with seizure, and ictal or interictal abnormalities. It is a rare condition, representing less than 1% of all epilepsies (9). It can also accompany other seizure types including tonic-clonic, atonic seizures, strange eye movements, lip-smacking and giggling. The corpus callosum is a white matter structure connecting the cerebral hemispheres and its main function is the coordination of information and bilateral exchange of sensory stimuli. Depending on the stage of development, corpus callosum agenesis may be complete or partial. Clinically, isolated agenesis of the corpus callosum may be completely asymptomatic; however patients with agenesis of the corpus callosum may have neurological problems, such as seizures (60%), intellectual impairment (70%), and psychosis (8). In fact; it has been believed that the clinical picture is determined by the associated abnormalities rather than CCA alone. Byrd et al. (10) had studied 105 children with CCA and reported that; 85% of these cases were symptomatic; and macrocephaly with hydrocephalus and seizures were the most common symptoms. In literature, to the best of our knowledge, there are three cases of gelastic seizures accompanied by corpus callosum agenesis, all of which also had hypothalamic hamartomas. In 1998, Alikchanov et al. (11) described a boy who had gelastic epilepsy, precocious puberty, hypothalamic hamartoma, and agenesis of the corpus callosum. Later, Chen et al. (12) reported a boy presented with mental retardation, aggressive behavior, and generalized tonic-clonic and gelastic seizures and his cranial imaging studies had revealed hypothalamic hamartoma and agenesis of the corpus callosum. Very recently, Cheng et al. (13) have described another case with gelastic seizures, followed by complex partial and tonic-clonic seizures whose MRI revealed a rare combination of hypothalamic hamartoma

and partial agenesis of the corpus callosum. This patient was operated and interestingly following resection of the hypothalamic hamartoma, the seizures were reduced, but not fully controlled, with medication at the first year follow-up. In that case, it was considered to be likely that the seizures following surgery were due to secondary epileptogenesis or partial agenesis of the corpus callosum, or both (14). After operation, continuing symptoms of this patient may resemble our patient; since the etiology of these ongoing seizures may be CCA alone. Although the cause of the gelastic seizures in our case was not clear exactly, the etiology of these seizures may also be the cortical dysplasia in different areas reported on the MRI of the patient since there were no epileptic foci.

Interestingly in 1992, DeMarco described three cases of children, all young male patients, who suffer from tuberous sclerosis and corpus callosum agenesis together with Lennox-Gastaut syndrome (LGS). The CCA was total in two cases and partial in the third. All cases showed mental retardation with different degrees and in all subjects tonic and atonic seizures were frequent. Antiepileptic therapy improved the clinical picture in only one case (15). The clinical pictures of those cases resembled our case.

In prenatal period subependymal nodules and giant cell astrocytoma or cardiac rhabdomyoma are suggestive of TSC (15). Although prenatal sonographic diagnosis of agenesis of the CC is difficult; magnetic resonance imaging should be considered a part of CCA assessment, in order to clarify the diagnosis and accompanying abnormalities (16). In fact, since gelastic seizures are rare, their togetherness with tuberous sclerosis is also an occasional condition. In fact, in literature there are only three reported tuberous sclerosis cases with gelastic seizures (14). Since all these rare conditions were together in our patient, tuberous sclerosis presented with gelastic seizures in the presence of corpus callosum agenesis without hypothalamic hamartomas, we determined this case as valuable for reporting.

Gelastic epilepsy is a rare condition but can also be reported in some disorders like tuberous sclerosis other than hypothalamic hamartomas. Moreover, corpus callosum agenesis may also accompany and may be the cause of these seizures occasionally. Clinicians should be aware of these rare conditions and each patient should be evaluated individually for the togetherness of them in the presence of any suspicion. Etiogenic areas should be focused in patients with gelastic seizures and further studies are warranted to elucidate the relationship of gelastic seizures and tuberous sclerosis.

REFERENCES

1. Northrup H, Krueger DA. International Tuberous Sclerosis Complex Consensus Group. Tuberous sclerosis complex diagnostic criteria update: recommendations of the 2012 International Tuberous Sclerosis Complex Consensus Conference. *Pediatr Neurol* 2013; 49(4):243-54.
2. vanSlegtenhorst M, deHoogt R, Hermans C, Nellist M, Janssen B, Verhoef S, et al. Identification of the tuberous sclerosis gene TSC1 on chromosome 9q34. *Science* 1997;277(5327):805-8.
3. de Vries PJ, Prather PA. The tuberous sclerosis complex. *N Engl J Med* 2007;356(1):92.
4. Christophe C, Sekhara T, Rypens F, Zierysen F, Christiaens F, Dan B. MRI spectrum of cortical malformations in tuberous sclerosis complex. *Brain Dev* 2000;22(8):487-93.
5. Zenteno JFT. Gelastic seizures associated with hypothalamic hamartomas. An update in the clinical presentation, diagnosis and treatment. *Neuropsychiatr Dis Treat* 2008;4(6):1021-31.
6. Brandberg G, Raininko R, Eeg-Olofsson O. Hypothalamic hamartoma with gelastic seizures in Swedish children and adolescents. *Eur J Paediatr Neurol* 2004;8(1):35-44.
7. Chai Y, Adamolekun B. Cryptogenic gelastic epilepsy originating from the right temporal lobe. *Med Princ Pract* 2010;19(2):153-8.
8. Singh S, Garge S. Agenesis of the corpus callosum. *J Pediatr Neurosci* 2010;5(1):83-5.
9. Douglas R, Nordli Jr. Hypothalamic hamartoma with gelastic seizures atlas of epilepsies. 2010;1(1):931-4.
10. Byrd SE, Radkowski MA, Flannery A. The clinical and radiological evaluation of absence of the corpus callosum. *Eur J Radiol* 1990;10(1):65-73.
11. Alikchanov AA, Petrukhin AS, Mukhin KYu, Nikanorov Ayu. Gelastic epilepsy, hypothalamic hamartoma, precocious puberty, and agenesis of the corpus callosum: a new association. *Brain Dev* 1998;20(4):239-41.
12. Chen CC, Lin YT, Chang WC, Hsieh LC, Liang JS. Rare combination of gelastic epilepsy, agenesis of the corpus callosum, and hamartoma. *Pediatr Neurol* 2011;45(4):265-7.
13. Cheng B, Sun C, Li S, Gong Q, Lui S. Gelastic epilepsy in combination with hypothalamic hamartoma and partial agenesis of the corpus callosum: A case report and review of the literature. *Exp Ther Med* 2013;6(6):1540-2.
14. Cook T, Joshi C. Gelastic seizures in tuberous sclerosis complex: case report and literature review. *J Child Neurol* 2011;26(1):83-6.
15. DeMarco P. Tuberous sclerosis, agenesis of the corpus callosum and Lennox-Gastaut syndrome: mere chance or a new syndrome? *Clin Electroencephalogr* 1992;23(1):7-9.
16. Santo S, D'Antonio F, Homfray T, Rich P, Pilu G, Bhide A, et al. Counseling in fetal medicine: agenesis of the corpus callosum. *Ultrasound Obstet Gynecol* 2012;40(5):513-21.

How to cite:

Işııkay S. A rare central nervous system anomaly in a tuberous sclerosis case with gelastic seizures: corpus callosum agenesis. *Gaziantep Med J* 2016;22(2):102-105.