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Landau-Kleffner Syndrome: Case Report

Landau-Kleffner Sendromu: Olgu Sunumu

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ABSTRACT

Landau-Kleffner syndrome (LKS) is acquired aphasia circumstance with loss of gained language ability and epileptiform electroencephalography or clinical seizure described first in 1957 by Landau and Kleffner. Expressive aphasia starts commonly among children of 3 to 8 age group and verbal auditor agnosia are other clinical features of LKS. Patients have difficulty in understanding what they are being told and respond to visual as well as auditory arousals. Seizure is seen in 70% of the cases. Patients with LKS usually develop normally, but it has been reported that about 13% of the cases had speech ability problem previously. Due to resemblance of symptomatology, causals such as audition loss, deafness, psychiatric disorders, progressive encephalopathy, "Childhood Rolandic Epilepsy" should be considered as differential diagnoses of LKS. We have briefly discussed the clinical progress of an 8-year-old male child who was followed with prediagnosis of major depression by child psychiatry department because of agression, relationship problems with his friends and regression in his speech. His behavior problems and absence of seizures had delayed obtaining an EEG in the early period. Seizures started two years after the behavior problems and loss of speech. Thus, we suggest that if a child with normal language development starts to regress, Landau-Kleffner syndrome must be considered in the differential diagnosis even in the absence of epileptic seizures. *The Journal of Pediatric Research 2015;2(1):42-5*

Key words: Landau-Kleffner syndrome, autistic disorder, acquired epileptiform aphasia, pervasive developmental disorders

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ÖZET

Kazanılmış dil becerilerinin kaybıyla birlikte edinsel afazi ve epileptiform elektroensefalografi ya da klinik nöbetlerle seyreden Landau-Kleffner sendromu (LKS) ilk olarak 1957'de Landau ve Kleffner tarafından tanımlanmıştır. Genellikle 3 ila 8 yaş grubu arası çocuklarda başlayan ifade afazisi ile verbal işitsel agnozi LKS'nin diğer özellikleridir. Hastalar ne anlatıldığını anlamakta ve görsel ile işitsel uyarılara cevap vermekte zorluklar yaşamaktadırlar. Nöbet olguların %70'inde görülmektedir. LKS hastaları genel olarak normal gelişim göstermektedir fakat olguların %13'ünün daha öncesinde konuşma yetisi problemleri oldukları belirtilmiştir. Semptomatoloji benzerliği sebebiyle, işitme kaybı, sağırlık, psikiyatrik hastalıklar, ilerleyici ensefalopati, "Çocukluk Çağı Rolandik Epilepsisi" gibi nedenler LKS'nin ayırıcı tanısında gözden geçirilmelidir. Biz kısaca saldırganlık, arkadaş ilişkilerinde sorunlar konuşmasında gerileme sebebiyle çocuk psikiyatrisi tarafından major depresyon öntanısıyla izlenen 8 yaşında erkek hastanın klinik gidişatını tartıştık. Hastanın davranış sorunları ve nöbetlerinin olmayışı erken dönemde EEG çekilmesini geciktirmişti. Antiepileptik tedavi almasına rağmen nöbetler davranış değişikliklerinden ve konuşmanın kaybından iki yıl sonra başlamıştı. Böylelikle normal dil gelişimi olan bir çocuk gerileme gösterirse, Landau Kleffner sendromu epileptik nöbet olmasa dahi ayırıcı tanıda gözden geçirilmelidir. *The Journal of Pediatric Research 2015;2(1):42-5*

Anahtar Kelimeler: Landau-Kleffner sendromu, otistik bozukluk, kazanılmış epileptiform afazi, yaygın gelişimsel bozukluklar

Çıkar Çatışması: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemiştir.

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Introduction

In this case report, we aimed to discuss; pre-and post-diagnosis process, treatment period and differential diagnosis of an 8 years old boy who did not have any sign of the autism disorder and LKS previously but later on behavioral alterations and loss of speech ability came out. Developmental milestones are usually normal in LKS cases but 13% of them may have speech problem and expressive aphasia as well as verbal/auditory agnosia are other clinical features (1-4).

Case Report

Eight years old boy patient was referred to our clinic by child psychiatry due to symptoms of aggression, regression in speech and attention deficit which may presumably arise from medical reasons. It is understood from anamnesis, his problems started firstly at 6 years of age with loss of speech. Aggressiveness, impairment in friendships, self-destruction, violent behaviors, micturition in inappropriate places were emerged later on. We learned that patient was referred to child psychiatrist before admission, fluoxetine and atypical antipsychotic drug was started due to depressive symptoms and conduct disorder but the drugs were stopped because of adverse effect of agitation. His complaints relapsed after termination of medication. We cleared that levetiracetam was started at that time due to right-sided partial seizure which occurred 1 year before our examination however this drug was discontinued a few weeks later by parents due to increased self-destructive and violence behavior. Sodium valproate regimen was given for epilepsy instead of levetiracetam. His auditory examination was normal, risperidone and imipramine were initiated by child psychiatrist for severe aggressiveness symptom. In spite positive effect of those psychiatric drugs parents discontinued both of risperidone and imipramine. Patient was referred to our clinic by child psychiatrist due to increased seizure frequency, new-onset autism like symptoms which were not in usual pattern. Special education discussion were delayed beyond neurological examination.

Parents have first degree cross-cousin marriage and the case have possessed normal psychomotor development. He could not understand meaning of words and was speaking senseless. Excessive hyperactivity, self-destructive behaviors were raised concern during our outpatient clinic examination. Disorganized behaviors such as trying to eat inedible objects, micturition in inappropriate places in his daily life were detected. Deep tendon reflexes were normal; pathological reflexes were not detected. "Expressive type" speech disorder and "auditory agnosia" were determined. Routine hemogram, biochemistry panel, blood and urine organic acids, Tandem mass spectrometry were normal. Cranial magnetic resonance imaging was normal. Sleep EEG (electroencephalography) determined sharp waves and spike and wave complexes occurred in left hemisphere, they sometimes spread synchronously to symmetrical contralateral areas.

Due to clinical history and process and EEG findings patient was accepted as Landau-Kleffner syndrome. We found LKS deficit score 16 in his first hospitalization. Sodium valproate treatment proceeded in same dosage. We noticed moderate decrease in aggressiveness, increase in speaking effort in outpatient clinic follow-up. Ankara Development Screening Inventory was performed: chronologic age was 8 years and 2 months; general developmental score: 14-16 months, cognitive language score: 12-14 months, fine motor score: 2 years 11 months, social and self-help score: 12-14 months.

Due to increased seizures, control EEG was performed. Sleep EEG displayed continuous spike and wave discharging in left frontotemporal region and spreading to whole left hemisphere during 85% or more of the spike and wave sleep (Figure 1).

Clobazam treatment was added, and oral steroid was continued and valproic acid dosage was titrated up to 40 mg/kg/day. Seizures were lasted and recovery in speaking and behavioral problems was noticed during follow-up. He retrieved his ability in perception and comprehension. We assumed that the patient had benefit from the treatment. His EEG findings partially recovered. His LKS deficit score was 5. Special education was not needed. His child psychiatry examination was "almost-normal" when compared to initial one.

Discussion

LKS which is acquired epileptic aphasia disorder is situated in international epilepsy syndrome classification since 1985. Loss of speaking ability is commonly first symptom among patients (5). Patient's language development is usually normal before the illness. Although rarely expressive impairment occurred firstly, in most cases expressive impairment follows receptive language failure, spontaneous and verbal expression get lost later on (6). The view which suggests verbal auditory may cause speech problem is being accepted. Besides non-verbal auditory agnosia which means other sounds except speaking voices becomes senseless was stated in literature (7,8). Among 50% of the cases; language problems are the first symptoms. Impairment in language and speech may show wavy changes and recurrences in follow-up. Speech properties of those patients could be classified as;

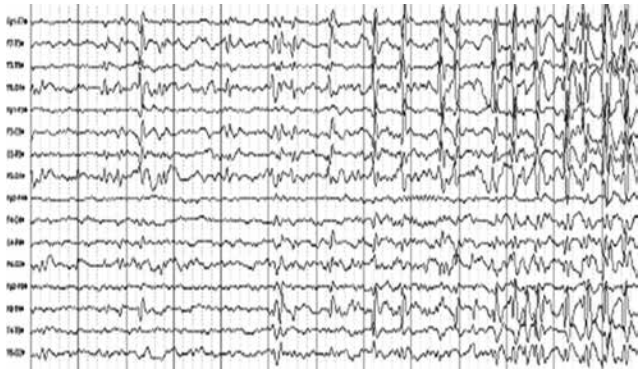

Figure 1. Electroencephalography of the patient
Fp: Frontoparietal, T: Temporal, C: Central, O: Occipital

jargon, paraphasia, mutism, anomia, in syntax impairment, perseveration, expressing themselves with gestures, baby talk and pronunciation deficit (9). We detected impairment in speaking ability and behavioral changes in our patient firstly. Our patient's speech features were jargon, aphasia, impaired syntax and pronunciation deficit. However his speaking was normal previously.

After clinical properties emerge in LKS patients receptive type speech deficit occurs. Further cases could be misdiagnosed as deafness during this period. Therefore otorhinolaryngology polyclinics may be the first admission point. Cases cannot response loud-voice arousals and may be misdiagnosed as loss of audition. But objective auditory assessments can obtain responses from patients (10,11). In our patient auditory examination was normal. The pathophysiology of LKS is not well understood yet. Some authors report that an autoimmune mechanism might be involved in the pathogenesis in some of the cases (12,13). The diagnosis of LKS is often delayed for many reasons. The clinical features of auditory agnosia may be subtle at the beginning or the cases may be misdiagnosed with psychiatric disorder.

EEG may be accepted as most objective diagnostic test in LKS but EEG changes may vary. Electroencephalographic findings during wakefulness may be bilateral centrotemporal, posterior temporal, and parieto-occipital spikes and waves. Sleep EEG may reveal continuous and diffuse slow spikes and waves, mainly at 1.5–2.5 Hz, persisting through all the slow-sleep stages. This pattern of continuous spikes and waves during slow sleep (CSWS) or electrical status epilepticus in sleep (ESES) in patients with Landau-Kleffner syndrome tends to be unilateral or clearly lateralized (14). Our patient's EEG pattern was similar to those features. Seizures may occur in 70% of the cases, %30 of the patients do not have any. Partial seizure emerged in our patient 1 year after the initial symptoms (15). Seizure properties are stated as generalized, tonic-clonic or complex partial types. There is frequently good response to medical treatment for seizure control, but refractory cases were indicated also.

The patients may apply to hospital with behavioral changes firstly. This circumstance frequently occurs due to secondary language and speech impairments, but sometimes behavioral and emotional changes may be seen unbound to language impairment (16). There are LKS cases who can be presented as autistic spectrum disorder in child psychiatry clinics. LKS patients with autism-like acts, introverted behaviors, echolalia, echopraxia, hyperlexia, and psychotic symptoms can be seen in literature (17,18). For those of reasons Pervasive Developmental Disorders may take place in differential diagnoses. According to ICD-10, Pervasive Developmental Disorders must be ruled out to make diagnosis of LKS (19). In our case, even though social and language development was normal till 3rd year of his life; impairment in language, retarded verbal expression with behavioral changes and introvert mood emerged later on. This symptoms were misunderstood by family members as jealousy to the other siblings and made them admit to child psychiatrist. His clinical picture was not conformed to ordinary depression and autism spectrum disorder pattern and even supplementary drugs were initiated the case was consulted with child neurology clinic. Early on-set of disorder, EEG findings, respond to anti-epileptics, recurring and fluctuating process are helpful indications for LKS.

There could be seen various pharmacological treatments and surgical approaches in literature but still there is not any certain approach (20-27). Although Bharni and colleagues reported total recovery of clinical and EEG findings in a 8-years old case who was diagnosed as LKS and treated with 30 mg/kg valproic acid; reports could be found in literature which state inefficacy of anti-epileptic drugs (20,23,24,28). In our case we did not obtain sufficient recovery from monotheraphy of valproic acid. Alternative treatment option corticosteroids and ACTH used in 1990 firstly, and it is stated that they are beneficial in case of usage in early stage of disorder (23). Tsuru and colleagues stated apparent recovery with high-dosage methylprednisolone in 2 cases in their research (24). Lerman and colleagues indicated 3 months-long corticosteroid treatment resulted with significant recovery of clinical and EEG findings in 4 cases who were 3, 5, 7 and 9 years old, respectively (29). In another assessment Guevara and colleagues detected significant recovery in both EEG and clinical findings in 10 cases who were treated with 1 U/kg/day ACTH (30). In our case, after 30 mg/kg/day iv methylprednisolone, 2 mg/kg/day maintenance was performed. Partial response was obtained from the first intervention but sufficient response was acquired after the second pulse methylprednisolone treatment. Researches which indicate efficacy of clobazam can be found in literature. Marescaux and colleagues performed clobazam treatment in 3 LKS cases for 3 to 8 weeks in their study, and observed significant response in 2 cases but there was not any change in other patient (23). We added 10 mg/kg/day clobazam during the follow-up period due to inadequate recovery and after that we observed the improvement in language skills, reduction in behavioral problems and seizures. During the course, sulthiame was the most effective drug in our case. It had a positive effect both on EEG and language difficulties.

Consequently there is not treatment consistence in LKS patients. Treatment achievement rates can be different due to the time of diagnosis, time to start treatment and necessity of behavioral-educational support beside drug approaches. Early diagnosis and treatment is very important in those patients. Especially, cases under 3 years of age who have impairments in speech ability and behavioral problems are being admitted to child psychiatry clinics firstly and may be followed for a while as Pervasive Developmental Disorder or Disruptive Behavioral Disorders. For that reason, these kind of cases should be thought from the point of LKS. It is important to evaluate EEG in these cases for differential diagnosis. It is also apparent that those patients may be admitted to otolaryngology clinics for the reason of acquired auditory loss, speech impairment and auditory agnosia prior than pediatric neurology clinics. Besides it is a necessity for those patient to be examined by otolaryngologist to make differential diagnose of LKS and to get required auditory tasks. In addition, reviewing researches and case reports

regarding LKS in literature and generating meta-analysis about Landau-Kleffner syndrome may light the way of recognize LKS better by the other specialists and be helpful for gaining a clear understanding of this disorder.

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