Landau-Kleffnerov sindrom – prikaz bolesnika

/ Landau-Kleffner Syndrome – Case Report

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Landau-Kleffnerov sindrom je epileptički sindrom dječje dobi i sinonim je za stečenu epileptičku afaziju. Od 1957. godine kada su Landau i Kleffner opisali šestero djece s ovim stanjem do danas opisano je više od 350 djece širom svijeta s tim sindromom. Specifičnost Landau-Kleffnerovog sindroma je akutni gubitak govora i jezika u djeteta koje se do tada govorno normalno razvijalo te globalna regresija ponašanja. Rijetkost susretanja s ovim sindromom čini ga iznimno zahtjevnim za dijagnosticiranje. Potrebna je multidisciplinska obrada stručnjaka iz područja pedijatrije, neuropedijatrije, dječje psihijatrije, psihologije, logopedije, otorinolaringologije, neuroslikovnog prikaza mozga. Konačna dijagnoza postavlja se na temelju specifično epileptogeno promijenjenog nalaza EEG-a u spavanju uz uredan nalaz MR mozga, zajedno s kliničkim manifestacijama sindroma. U ovom radu opisani su prikazom bolesnika multidisciplinska obrada, započinjanje tretmana i prije samog postavljanja dijagnoze, uspostavljanje dijagnoze, daljnji tijek bolesti i liječenje.

/ Landau-Kleffner syndrome is an epileptic childhood syndrome and is synonymous with acquired epileptic aphasia. Since 1957, when Landau and Kleffner identified six children with the disorder, more than 350 cases worldwide have been reported. The specificity of Landau Kleffner syndrome is an acute loss of speech and language in a child who developed normal language and global regression of behaviour. The rarity of this syndrome makes it extremely demanding to diagnose. It requires a multidisciplinary treatment by specialists in the field of pediatrics, neuropediatrics, child psychiatry, psychology, logopedia, otorhinolaryngology, and brain imaging. The final diagnosis is based on an epileptogenically altered EEG finding during sleep with an orderly brain MRI finding, along with clinical manifestations of the syndrome. This paper describes a multidisciplinary treatment, early initiation of treatment, and further course of illness.

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UVOD

Definicija

Landau-Kleffnerov sindrom (LKS) je epileptički sindrom dječje dobi karakteriziran stečenom afazijom i epileptiformnim elektroencefalografskim (EEG) abnormalnostima tijekom spavanja. Klasificiran je među epileptičke encefalopatije i smatra se dijelom spektra idiopatskih fokalnih epilepsija. U sklopu sindroma nastupa i globalna regresija ponašanja, a karakteristično je da mu u većini slučajeva prethodi do tada normalan razvoj djeteta (1).

Etiologija

Etiologija Landau-Kleffnerovog sindroma nije poznata, ali se pretpostavlja kako je sindrom završni zajednički put višestrukih etioloških faktora, kao što su genetski i epigenetski faktori (studije blizanaca) te utjecaj okoliša. U 5-20 % obiteljskih i sporadičnih slučajeva LKS-a dokazana je mutacija GRIN2A, a etiologija poremećaja kod preostalih pacijenata ostaje nejasna (2). Druga stanja povezana s mogućom etiologijom LKS-a uključuju progresivni encefalitis, akutni diseminirani encefalomijelitis, toksoplazmozu, tumore temporalnog režnja i upalni encefalitički proces (3).

Epidemiologija

Godine 1957. Landau i Kleffner opisali su šestero djece s ovim stanjem. Od tada je više od 350 djece širom svijeta dijagnosticirano kao LKS. Procjenjuje se da je dob početka bolesti u rasponu od 2 do 8 godina, s vrhuncem između 5 i 7 godina. U rjeđim slučajevima zabilježen je i početak s 18-22 mjeseci te s 13-14 godina. Dječaci su dvostruko češće pogođeni od djevojčica (4,5).

Klinička slika

Landau-Kleffnerov sindrom je stanje s akutnim ili subakutnim gubitkom govora i jezika te globalnom regresijom ponašanja. Nakon što

INTRODUCTION

Definition

Landau-Kleffner syndrome (LKS) is an epileptic syndrome in children that is marked by acquired aphasia and epileptic electroencephalographic (EEG) abnormalities during sleep. It is defined as an epileptic encephalopathy and considered to be part of idiopathic focal epilepsy. It usually affects children with previously normal development and causes regression in all behaviours (1).

Etiology

Landau-Kleffner's syndrome etiology is still unknown, but it is considered to be under the influence of many factors, such as genetics, epigenetics, and the environment. A genetic basis is still unclear, but 5-20% of families show mutations in the GRIN2A gene (2). Other conditions correlated with a possible etiology of LKS are progressive encephalitis, toxoplasmosis, temporal lobe tumour, and inflammatory encephalitis (3).

Epidemiology

Landau and Kleffner described six children with the condition in 1957. Since then, more than 350 children have been diagnosed worldwide with LKS. The onset is usually between 2-8 years of age with a peak between 5 and 7 years. In some cases, it has been reported as early as 18-22 months and as late as 13-14 years of age. Boys are affected twice as often as girls (4,5).

Clinical presentation

Landau-Kleffner syndrome is a condition with acute or subacute loss of language and global regression in behaviour. After a previously normal development, the child experiences loss of receptive and expressive language, but intelli-

je prethodno postiglo normalni napredak u razvoju jezika, dijete gubi receptivne i ekspresivne jezične vještine, ali zadržava opću inteligenciju. Pojava je popraćena abnormalnostima EEG-a, a u dijelu slučajeva i epileptičkim napadajima. Vještine se gube tijekom dana ili tjedana. Povezanost javljanja epileptičkih napadaja i gubitka jezika varira, epileptički napadaju mogu nekoliko mjeseci do dvije godine prethoditi gubitku govora te obrnuto, gubitak govora može prethoditi epileptičkim napadajima (4). LKS nije povezan s organskim oštećenjima mozga i javlja se u prethodno normalne djece koja su već razvila dobno odgovarajući govor. Međutim, postoje i izvještaji o „klinički definiranom" LKS-u u bolesnika s kongenitalnom ili stečenom lezijom mozga te u djece koja su pokazivala anomalije jezičnog razvoja prije jezične regresije (5,6). Najznačajnija odrednica sindroma je stečena afazija, zatim slijede kognitivno oštećenje i globalna regresija ponašanja. Epileptički napadaji su rijetki i nisu preduvjet za dijagnozu. Tip afazije tipično je auditorna verbalna agnozija, odnosno nesposobnost pridavanja značenja zvukovima. Djeca koja su se razvijala urednim tokom odjednom pokazuju gubitak jezika, potpunu ili djelomičnu nemogućnost prepoznavanja, procesiranja i interpretiranja verbalnih i/ili neverbalnih zvukova. Zbog toga se ovaj sindrom često zamjenjuje gluhoćom ili, ako je u kombinaciji s problemima u ponašanju, poremećajem iz spektra autizma. Važno je naglasiti da je kod Landau-Kleffnerovog sindroma slušanje očuvano (audiogram pokazuje normalnu krivulju), ali dijete ne razumije ono što čuje. Problemi s razumijevanjem govora vremenom utječu i na govornu produkciju. Nastupaju problemi s artikulacijom i prizivanjem riječi, brbljanje, perseveracije i mutizam (4). Tijek afazije progresivan je i fluktuirajući, sa spontanim poboljšanjima i pogoršanjima tijekom vremena (7). Konačna i često teška klinička manifestacija LKS-a je poremećaj ponašanja, koji se javlja kod gotovo 75 % bolesnika, u obliku značajnih deficita pažnje i koncentracije, impulzivnosti

gence remains intact. Other manifestations of LKS are EEG abnormalities and, in some cases, epileptic seizures. In the course of days, weeks, or months, those abilities are lost. Correlations between epileptic seizures and language impairments vary. Seizures can precede language impairments up to a couple of months to 2 years, and otherwise (4). As previously mentioned, LKS is not related to organic brain lesions and it affects children with previously normal development of speech. However, some authors report "clinically defined" LKS in patients with a congenital or acquired brain lesions and in children with pre-existing language difficulties (5,6). The most prominent symptom of LKS is acquired aphasia, followed by cognitive damage and global behavioural problems. Epileptic seizures are rare and not required for setting the final diagnosis of LKS. The type of aphasia is usually verbal-auditory agnosia, a failure to give a semantic significance to different sounds. Children show a sudden loss of language, complete or partial ability to recognise, process, and interpret verbal and/or non-verbal sounds. That is why LKS is commonly misdiagnosed as deafness. LKS patients have normal peripheral hearing and problems with understanding the meaning of what is said. Receptive language problems affect speech production with typical signs such as difficulties with articulation, babbling, verbal perseverations, or mutism (4). The aphasia demonstrates a progressive course with spontaneous improvements and exacerbations over time (7). Behavioural difficulties such as attentional deficits, impulsivity, and hyperactivity are common, found in 75% of patients with LKS (5,8). Behavioural disorders can occur primarily due to functional disinhibition at the limbic or diencephalic level and secondary as a result of frustration due to a loss of understanding. Periods of anger and aggression often appear unmotivated, which can be interpreted as a primary behavioural disorder, and such children are sent to a psychiatrist under

i hiperaktivnosti (5,8). Smetnje u ponašanju mogu nastupiti primarno zbog funkcijske dezinhibicije na limbičkoj ili diencefaličkoj razini i sekundarno kao posljedica frustracije zbog gubitka razumijevanja. Često se nemotivirano javljaju izljevi bijesa i agresije, koji se mogu tumačiti kao primarni poremećaj u ponašanju te se takva djeca pod pogrešnom uputnom dijagnozom pošalju psihijatru (9). Robinson i suradnici u svom radu (10) opisuju tri faze razvoja sindroma. Prva faza je faza akutnog propadanja jezičnog razumijevanja najčešće praćeno pogoršanjem u jezičnoj proizvodnji. Problemi u ponašanju su blagi i povezani s frustracijom oko komunikacijskih teškoća, a neverbalne vještine ostaju očuvane. Prva faza obično traje nekoliko tjedana nakon čega prelazi u drugu fazu. Druga faza je faza kroničnog pogoršanja u kojoj se nastavljaju abnormalnosti EEG-a. Kod težih slučajeva gubi se razumijevanje zvukova iz okoline, dijete potpuno gubi govor (mutizam) i nastupaju ozbiljni problemi u ponašanju. Djeca mogu postati agresivna i destruktivna, a njihova je pažnja značajno narušena. Ponekad su agresivnost i udaljavanje toliko izraženi da izgledaju kao psihotični poremećaj. Druga faza se javlja između prve i sedme godine života. U trećoj fazi nastupa spontani oporavak, prosječno 5,2 mjeseci nakon normalizacije EEG-a i prestanka epileptičkih izbijanja. Problemi u ponašanju nestaju prvi. U lakšim slučajevima jezično razumijevanje se generalno poboljšava, govor se počinje prepoznavati te se odbacuju sredstva alternativne komunikacije. Kod težih slučajeva prvo se oporavlja sposobnost razumijevanja neverbalnih zvukova iz okoline, a postupno i razumijevanje govora.

Dijagnoza

Postavljanju dijagnoze prethodi multidisciplinska obrada stručnjaka iz područja pedijatrije, neuropedijatrije, dječje psihijatrije, psihologije, logopedije, otorinolaringologije. Osnovna dijagnostička metoda je elektroencefalogra-

an incorrect referral diagnosis (9). In their paper, Robinson and associates (10) described the evolution of LKS through three stages. The first stage is acute deterioration of receptive language followed by deterioration in expressive language. Behavioural difficulties are usually mild and linked to communication frustration. The duration of the first stage is usually a few weeks. The second stage is chronic deterioration with continuation of EEG abnormalities. In more severe cases, the understanding of the sounds from the environment is lost, the child completely loses speech (mutism), and experiences serious behavioural problems. Children can become aggressive and destructive, and their attention is significantly disrupted. Sometimes aggression and distress are so pronounced that they look like a psychotic disorder. The second phase occurs between 1 and 7 years of age. In the third stage, spontaneous recovery occurs, averaging 5.2 months after EEG normalization and epileptic outbreaks. Behavioural problems disappear first. In the milder cases, language understanding is generally improved, speech is beginning to be recognized and alternative means of communication are rejected. In more severe cases, the ability to understand non-verbal sounds from the environment is first recovered, followed by gradual understanding of speech.

Diagnosis

LKS requires an interdisciplinary assessment of different specialists – a pediatrician, neuropediatrician, child psychiatrist, psychologist, speech and language pathologist, and an otolaryngologist. The basic diagnostic method is electroencephalography. Increased epileptiform activity can be confirmed by polysomnographic recording. As soon as a child falls asleep, CSWS occurs (Continuous Spike and Wave During Slow Sleep), mainly at 1.5-2.5 Hz, which lasts throughout all stages of slow sleep. In 70-80% cases of LKS, epileptic seizures of

fija. Prisutna povećana epileptiformna aktivnost može se potvrditi polisomnografskim cjelonoćnim snimanjem. Čim dijete zaspi javlja se CSWS - kontinuirano izbijanje šiljak-val kompleksa za vrijeme spore faze spavanja (od engleskog termina *Continuous Spike and Wave During Slow Sleep)*, uglavnom na 1,5-2,5 Hz, koje traje u svim fazama sporog spavanja. U 70-80 % slučajeva javljaju se i epileptički napadaji niske učestalosti. U ostalim slučajevima (20-30 %) epileptički napadaji se nikada ni ne pojave unatoč značajnim elektroencefalografskim abnormalnostima. Epileptogena izbijanja su pretežito unilateralna ili jasno lateralizirana. Kada su prisutni, napadaji su rijetki i uglavnom jednostavni za kontrolu i liječenje. Oni mogu biti parcijalni kompleksni, parcijalni klonički, generalizirano toničko-klonički i atonički napadaji (5). U sklopu diferencijalne dijagnoze mogu se učiniti nalazi cerebrospinalnog likvora, CT snimanje (kompjutorizirana tomografija) i MR snimanje (magnetska rezonancija) mozga koji su obično uredni i bez specifične patologije. U rjeđem broju slučajeva zabilježeni su blagi porast proteina u likvoru, promjene na bijeloj tvari i strukturna lezija. Moguć je pronalazak blagog povećanja ili asimetrije temporalnih rogova, moguće kao posljedica dugotrajnih epileptičkih napadaja. Nije pronađena povezanost afazije i hipometabolizma glukoze temporalnog režnja, jer su slični nalazi opaženi i kod djece s epilepsijom koja nemaju smetnje govora (3). Mikroskopski pregled kirurških uzoraka mozga pokazao je minimalnu gliozu, ali za sada bez dokaza za encefalitis (9).

Diferencijalna dijagnoza

Iako postoje znatna preklapanja u kliničkoj slici LKS-a i autizma, postoje i razlike. Velika većina djece s autizmom pretrpi jezičnu regresiju prije dobi od 3 godine, u usporedbi s prosječnom dobi jezične regresije u LKS-u od 5-7 godina. Samo u 10 % djece s LKS-om jezična regresija nastupi prije 3. godine. Kako se regresija u au-

low frequency occur. In other cases (20-30%), epileptic attacks never occur, despite significant electroencephalographic abnormalities. Epileptogenic outbreaks are predominantly unilateral or clearly lateralized. When present, seizures are rare and mostly simple to control and treat. They can be partially complex, partially clonic, generalized tonic-clonic, and atonic seizures (5). As a part of the differential diagnosis, cerebrospinal fluid, CT scans (computerized tomography), and MR (magnetic resonance) brain scans can be performed, which are usually normal and without a specific pathology. In a small number of cases there is a slight protein increase in cerebrospinal fluid, changes in white matter, and structural lesions. It is possible to find a slight increase or asymmetry of temporal horns, possibly due to long-lasting epileptic seizures. No association of aphasia and glucose hypometabolism of temporal lobe was found, as similar findings have been observed in children with epilepsy with no speech difficulties (3). The microscopic examination of surgical brain patterns showed a minimal gliosis, but for now without evidence of encephalitis (9).

Differential diagnosis

Although there are significant overlaps in the clinical course of LKS and autism, there are also differences. The vast majority of children with autism suffer from language regression before the 3rd year of age, compared to the average age in LKS of 5 to 7 years. In only 10% of children with LKS the speech regression appears before 3 years of age. As regression in autism occurs early, there usually appears a loss of individual words, as compared to more drastic changes in children with LKS that are typically older and have more developed vocabulary and language. LKS does not have a behavioural profile with core changes in autism as specific abnormalities of social functioning and stereotypical patterns of interest and behaviour. Children with severe

tizmu pojavljuje rano, obično dolazi do gubitka pojedinačnih riječi, u usporedbi s drastičnijim promjenama kod djece s LKS-om koji su tipično stariji i imaju razvijeniji vokabular i jezik. LKS ne sadrži profil ponašanja koji obuhvaća jezgrovne promjene u autizmu kao specifične abnormalnosti socijalnog funkcioniranja i stereotipne obrasce interesa i ponašanja. Djeca s teškom fokalnom epilepsijom od statičnih oštećenja mozga koji uključuju jezični korteks mogu imati epizodičnu iktalnu afaziju ili status epileptikus i postati trajno afazični (3). Rane faze LKS-a s hiperkinezijom i blagom auditorno verbalnom agnozijom mogu se zamijeniti s hiperkinetičkim poremećajem. Diferencijalna dijagnoza također uključuje gluhoću, selektivni mutizam i akutne psihijatrijske poremećaje.

Liječenje LKS-a

Ne postoji međunarodna usuglašenost u pogledu liječenja LKS-a. Što ranije započinjanje farmakoterapije pokazalo se blagotvornim za kasniju prognozu. Dugotrajna epileptička aktivnost povećava težinu bolesti i u progresiji bolesti ima veće značenje od dobi nastanka. Dugoročni cilj liječenja je normaliziranje jezičnih poremećaja. Konvulzije su obično blage, rijetke i reagiraju na antiepileptike, međutim često je potrebna dugogodišnja terapija održavanja. Od antiepileptika se najčešće koriste valproati, klobazam, levetiracetam, etosuksimid i sultiam (4). Općenito se preporučuje izbjegavanje drugih antiepileptika kao što su fenitoin, fenobarbital, karbamazepin, okskarbazepin, lamotrigin i topiramat jer su povezani s pogoršanjem epileptičkih pražnjenja (5). Učestalost i vrsta napadaja nemaju utjecaj na prognozu. Liječenje antikonvulzivnom monoterapijom općenito je učinkovito za kontrolu napadaja, ali ne i za afaziju (3). Ako epileptička aktivnost i jezični problemi nisu poboljšani antiepilepticima tijekom nekoliko tjedana, preporučuje se upotreba kortikosteroida (4). Intravenski imunoglobulini pokazali su obećavajuće rezultate u nekim

focal epilepsy resulting from brain damage of linguistic cortex may have episodic ictal aphasia or status epilepticus and become permanently aphasic (3). Early LKS phases with hyperkinesia and mild auditory-verbal agnosia may be mistaken by a hyperkinetic disorder. The differential diagnosis also includes deafness, selective mutism, and acute psychiatric disorders.

Treatment of LKS

There is no international agreement on the treatment of LKS. The earlier start of pharmacotherapy proved to be beneficial to the later prognosis. Long-term duration of epileptic activity increases the severity of the disease and appears to have a more adverse effect than the earlier age onset. The long-term goal of treatment is improving language difficulties. Convulsions are usually mild, rare, and respond well to antiepileptics, however, long-term therapy is often required. Valproate, clobazam, levetiracetam, ethosuximide, and sulthiame are most commonly used in antiepileptics (4). It is generally recommended to avoid other antiepileptics such as phenytoin, phenobarbital, carbamazepine, oxcarbazepine, lamotrigine, and topiramate as they are associated with worsening of epileptic discharges (5). Frequency and type of seizure have no effect on the prognosis. Anticonvulsant monotherapy treatment is generally effective for seizure control but not for aphasia (3). If epileptic activity and language problems are not improved with antiepileptics over a few weeks, corticosteroids are recommended (4). Intravenous immunoglobulins have shown promising results in some cases of LKS. Ketogenic diet and vagus nerve stimulation have led to clinical improvement in some patients (5). Surgical treatment in the form of multiple subpial transections was performed in a limited number of children, with the aim of stopping the spread of epileptiform activity. Improvements were described in individual cases. Such type of treatment is reserved for those children

slučajevima LKS. Ketogena dijeta i stimulacija vagusnog živca doveli su do kliničkih poboljšanja kod pojedinih pacijenata (5). Kirurško liječenje u obliku višestrukih subpijalnih transekcija provedeno je u ograničenom broju teško pogođene djece, u svrhu sprječavanja širenja epileptiformne aktivnosti. Opisana su poboljšanja u pojedinačnim slučajevima. Takva vrsta liječenja rezervirana je za onu djecu kod koje su prisutni ustrajna afazija i napadaji rezistentni na lijekove (4,9). Drugi oblik liječenja, presudan za odnos djeteta s okolinom, ponašanje i psihosocijalno funkcioniranje, održavanje je komunikacije putem govorno jezične terapije. Uvode se mjere u obliku učenja znakovnog jezika i drugih oblika potpomognute komunikacije s istovremenim osposobljavanjem slušanja, što pozitivno pridonosi intelektualnoj stimulaciji i razvoju (4). Pojedina djeca s dugogodišnjom auditornom verbalnom agnozijom uspješno su integrirana u škole za gluhe (3).

Prognoza

Na prognozu može utjecati koliko varijabli: dob početka, obrazac jezičnog deficita, učestalost i topografija EEG pražnjenja, trajanje epilepsije, učinkovitost i nuspojave antiepileptika. Nepovoljni prognostički faktori su pojava LKS-a prije četvrte godine života, trajanje afazije dulje od jedne godine, trajanje i kontinuitet CSWS-a (3). Epileptički napadaji imaju tendenciju smanjivanja i obično nestaju do 15. godine života. Opća inteligencija je najčešće sačuvana (4). Prognoza za poremećaje govora i jezika varira od potpunog i djelomičnog oporavka do trajnog oštećenja verbalne komunikacije. Za potonju skupinu važno je uspostaviti komplementarne i alternativne metode komunikacije što je prije moguće. Brzi početak liječenja lijekovima pokazao se važnim za prognozu. Dugotrajnost epileptičke aktivnosti pogoršava prognozu i čini se da ima veći nepovoljni utjecaj od ranije dobi javljanja sindroma. Učestalost i vrsta epileptičkih napadaja ne utječe na prognozu kognicije i jezičnog razvoja.

with persistent aphasia and drug resistant seizures (4,9). Another type of treatment, crucial to the relationship of the child to the environment, behaviour, and psychosocial functioning, is maintaining communication through speech therapy. Measures are introduced in the form of sign language learning and other forms of assisted communication, which positively contributes to intellectual stimulation and development (4). Some individuals with long-term auditory-verbal agnosia have successfully integrated into schools for deaf children (3).

Prognosis

Several variables can affect the prognosis: age, the form of language deficit, frequency, and topography of EEG discharges, the duration of epilepsy, efficacy, and side effects of antiepileptics. Unfavourable prognostic factors are the occurrence of LKS prior to the fourth year of life, duration of aphasia for longer than one year, duration and continuity of CSWS (3). Epileptic seizures tend to decrease and usually disappear up to 15 years of age. General intelligence is most often preserved (4). Prognosis for speech and language disorders varies from total and partial recovery to permanent damage of verbal communication. For the last group it is important to establish complementary and alternative communication methods as soon as possible. The rapid onset of drug treatment proved to be important for the prognosis. Long-term epileptic activity exacerbates the condition and appears to have a more adverse effect than the earlier age onset. Frequency and types of epileptic seizures do not affect the prognosis of cognition and language development.

CASE REPORT

In May 2017, a boy aged 4 years and 8 months reported to a child and adolescent psychiatrist at the recommendation of a speech therapist,

PRIKAZ BOLESNIKA

U svibnju 2017. g. dječak u dobi od 4 godine i 8 mjeseci doveden je na pregled dječjem psihijatru, po preporuci logopeda, u sklopu specifičnog poremećaja razvoja govora i jezika.

U obitelji postoji pozitivan psihijatrijski hereditet na shizoafektivni poremećaj po ocu i depresivni poremećaj po majci. Dječak je rođen iz prve majčine trudnoće održavane mirovanjem zbog insuficijencije cerviksa. Majka hospitalizirana 2 tjedna prije poroda, koji je bio prirodnim putem, zadržan 5 dana zbog simptomatskog liječenja novorođenačke žutice. Urednog ranog psihomotornog razvoja, prohodao u dobi od 12 mjeseci, sfinktere kontrolirao u dobi od 2,5 godine, prve riječi sa značenjem s godinu dana, spajao rečenice u dobi od 2 godine. Ne pohađa vrtić. Odrasta u narušenim obiteljskim odnosima, izložen roditeljskom neslaganju, roditelji su se razveli no zbog nepovoljne financijske situacije žive na istoj adresi. Ima 4 godine mlađu sestru koja je zdrava. Majka je nezaposlena, u potpunosti je posvećena dječaku.

U dobi od 3 godine započele su promjene u ponašanju u obliku neposlušnosti, hiperaktivnosti i ljubomore prema mlađoj sestri koja povremeno prerasta u fizičku agresiju. U dobi od 4 godine i 5 mjeseci, iz govora razvijenog normalnog za dob (izražavanje u rečenicama), prestao je verbalno komunicirati. Obitelj je proživjela i tragediju, tada je od srčane bolesti naglo preminuo bratić po majci u dobi od 15 godina. Dječak od rane dobi izbjegava igru s drugom djecom, igra se većinom sam. Motorički je nespretan, čak i uz stalni nadzor ima česte padove i ozljede. U ožujku 2017. g. logoped i psiholog su utvrdili da ima niži kvocijent mentalnog razvoja, govorno-jezične teškoće i teškoće socijalne komunikacije.

Na tjelesnom planu boluje od astme (u terapiji montelukast, flutikazon, loratadin), često teško diše na nos, po noći hrče. U svibnju 2017. g. pregledao ga je otorinolaringolog: timpanogram as part of a specific speech and language developmental disorder.

In the family there is a positive psychiatric heredity to a schizoaffective disorder (father) and a depressive disorder (mother). The boy was born from mother's first pregnancy, held at rest due to cervical insufficiency. The mother was hospitalized for 2 weeks before the birth, which was naturally occurring, and the boy was kept for 5 days due to symptomatic treatment of newborn jaundice. The early psychomotor development was correct, he walked at the age of one year, controlled sphincters at the age of 2.5 years, had the first meaningful word at the age of one year, merged words into sentences at the age of 2 years. He did not go to kindergarten. He is growing up in a disrupted family, is exposed to parental disagreement. Parents divorced but because of unfavourable financial situation still live at the same address. He has a sister who is 4 years younger and healthy. The mother is unemployed, she is entirely devoted to the boy.

At age 3 changes in behaviour began in the form of disobedience, hyperactivity, and jealousy and physical aggression towards the younger sister. At the age of 4 years and 5 months, after fully developed speech for his age (expression in sentences), he stopped communicating. At that time the family experienced a tragedy, his 15-year-old cousin suddenly died of a heart disease. From an early age he avoided playing with other children, mostly plays alone. He is clumsy, prone to injury, even with constant monitoring. In March 2017 he was estimated by speech therapist and psychologist (lower quotient of mental development, speech-language difficulties, and difficulties of social communication).

He suffers from asthma (in the treatment with montelukast, fluticasone, loratadine), his nose is often clogged, snores during the night. In May 2017 he was examined by an otolaryngologist, the timpanogram was in order, a review of an audiologist was recommended. He is regularly vaccinated. No known allergy to medication.

gram je bio uredan, preporučen je pregled audiologa. Redovito je cijepljen prema kalendaru cijepljenja. Nema alergija na lijekove.

Prigodom prvog pregleda kod dječjeg psihijatra uspostavio se kontakt očima i komunikacija gestama. Govor je imitirao s nekoliko jednostavnih slogova (npr. ato-tu-ta; au-au) pri čemu se dobio dojam kako nešto pokušava objasniti. Kako je pregled tekao, postao je motorički nemiran, želio napustiti sobu, a na majčinu zabranu počeo bacati predmete iz blizine te udarati nogama u zid. Pokazale su mu se igračke na što se smirio, a igru je ostvarivao na razini nižoj od očekivane za dob (ubacivanje geometrijskih oblika). Preporučeno je ponavljanje logopedske procjene i pregled neuropedijatra.

Početkom lipnja 2017. g. učinjena je logopedska procjena prigodom koje je opservirano da se služi nezrelim komunikacijskim sredstvima, najčešće gestom pokazivanja uparenom s vokalizacijama (npr. pokazuje na kišu vani i na glavu kako će biti mokar). Jezično razumijevanje se nije uspjelo procijeniti zbog slabije pažnje, ostavio je dojam da ne razumije očekivanja i uputu ispitivača. Jednostavne naloge razumije u svakodnevnim situacijama. Zabranu razumije, ali ne poštuje uvijek. Teško je imitirao i najjednostavnije slogove. Ipak, povremeno se mogla čuti riječ sa značenjem (doma, mama). Odmah je uključen u logopedsku terapiju, s ciljem razvoja komunikacijskih sredstava i širenja broja funkcija kako bi se umanjila frustracija.

Sredinom lipnja učinjen je kontrolni pregled kod dječjeg psihijatra. Primijećen je napredak u ponašanju, počeo se uključivati u igru s drugom djecom, kada bi povrijedio majku ispričao bi se, u trgovini je bio spreman na kompromis, prema sestri je bio obazriviji, jedino što se komunikacija svela gotovo u potpunosti na geste. Pri pregledu je bio razigran, uspijevao je biti djelomično poslušan uz povremeno majčino fizičko sputavanje, što je doživljavao kao igru i nije prkosio.

During that first examination, the child psychiatrist established eye contact and gesture communication. He imitated speech with a few simple slogans (e.g. ato-tu-ta; au-au), leaving the impression that he was trying to explain something. As the examination went on he became motor-driven and wanted to leave the room. As his mother forbid it, he began to throw objects and kick his legs at a wall. The therapist showed him toys, he began to play and calmed down. The game was at a level lower than expected for his age (inserting geometric shapes). We recommended logopedic re-evaluation and examination by a neuropediatrist.

At the beginning of June 2017, he underwent a logopedic assessment that observed he used immature communication means, most often gestures paired with vocalizations (e.g. showing rain outside and pointing to the head as it would be wet). The linguistic understanding was not evaluated because of the lack of attention; he left the impression that he did not understand the examiners' expectations and guidance. Simple orders are understood in everyday situations. Lack of permission is understood, but he does not always respect it. It was hard for him to imitate the simplest slogans. However, occasionally a meaningful word could be heard (home, mom). He was immediately involved in logopedic therapy, with the aim of developing communication tools and expanding the number of functions to reduce frustration.

In mid-June a psychiatric examination was carried out. Progress in behaviour was noted, he began to be involved in playing with other children, when he would hurt his mother, he would apologize, towards his sister he was more cautious. But, he communicated almost entirely by using gestures. He was playful during the review, managed to be partially obedient with occasional interventions from his mother, which he experienced as a game and did not defy.

In early July 2017 he was reviewed by a neuropediatrist, EEG and MR brain imaging were rec-

Početkom srpnja 2017. g. pregledao ga je neuropedijatar, preporučeno je EEG i MR snimanje mozga. MR mozga učinjen 24. 7. 2017. g. bio je uredan („Nešto širi perivaskularni likvorski prostori sublentikularno obostrano. Diskretni hiperintenziteti bijele tvari peritrigonalno, prvenstveno odgovaraju nedovršenoj mijelinizaciji. Ostalo uredno."). Nalaz EEG-a bio je tehnički loš, nije ga se moglo analizirati, preporučeno je cjelonoćno snimanje u specijaliziranoj ustanovi. Sredinom srpnja 2017. g. pregledao ga je audiolog koji je preporučio detaljniju audiološku obradu upućivanjem u drugu ustanovu.

Krajem kolovoza 2017. g. kontrolnim pregledom kod dječjeg psihijatra opservirano je pogoršanje psihičkog stanja u obliku daljnjeg neposluha te fizičke agresije koju je počeo ispoljavati i prema drugoj djeci, koja se onda izbjegavaju s njim igrati. Noćni san postaje sve više narušen, isprekidan, budi se noću uz plač i strah. Tada smo, uz logopedski tretman, preporučili uključivanje u *neurofeedback* tretmane.

Početkom rujna 2017. g. pristigao je nalaz cjelonoćnog EEG snimanja: uvjerljivo epileptigeno promijenjen, na osnovi čega je postavljena dijagnoza Landau Kleffnerovog sindroma. Poslan je uzorak za analizu panel gena za epilepsiju. Krajem rujna uveden je u terapiju antiepileptik etosuksimid. Uključen i u tretman radnog terapeuta.

Na kontrolnom pregledu kod neuropedijatra u prosincu 2017. g., nakon početnog pozitivnog učinka i pomaka na uvođenje antiepileptika, opservira se ponovno pogoršanje u obliku javljanja afektivnih kriza prigodom kojih prestane disati i poplavi, preporučuje se uvođenje anksiolitika diazepama po potrebi.

U siječnju 2018. g. prigodom kontrolnog pregleda kod dječjeg psihijatra također je preporučeno uzimanje nižih doza anksiolitika diazepama, povremeno i po potrebi. Zamijećena je nastavna regresija ponašanja, dječak nije u potpunosti svjestan posljedica svojih djela i

ommended. MR imaging was done on 24 July, 2017 and it was in order ("discrete hyperintensities of white matter peritrigonally, primarily corresponding to unfinished myelination."). The EEG finding was technically bad, could not be analysed. It was recommended to redo the EEG examination at a specialized institution. In mid-July 2017 he was examined by an audiologist that recommended more detailed audiological examination in another institution.

At the end of August 2017, he was re-examined by a child psychiatrist. The following was observed: a deterioration of the mental state in the form of further disobedience and physical aggression that he began to show towards other children who then avoided playing with him. Night sleep became more and more disturbed, intermittent, he was waking up at night while weeping and fearful. At that time, with logopedic treatment, we recommended starting with neurofeedback treatments.

At the beginning of September 2017 arrived the result of EEG recording during a whole night of sleep, which showed convincingly epileptogenically altered EEG, and the diagnosis of Landau Kleffner syndrome was established. A sample for analysis of epileptic genes was submitted. At the end of September, he was introduced to the therapy of an antiepileptic drug ethosuksimide. Also, he was included in the treatment by an occupational therapist.

In December 2017, after the initial positive effect on the introduction of antiepileptic drugs, affective crises started to appear, in which he would stop breathing and "turn blue". A neuropediatrist recommended the introduction of anxiolytic drug diazepam.

In January 2018 a child psychiatrist also recommended to occasionally take lower doses of anxiolytic diazepam. Further regression of the behaviour was noted, the boy was not fully aware of the consequences of his actions and the possible danger to himself and others that

moguće opasnosti za sebe i druge koja slijedi. Ponašanje regredira, predmete iz neposredne blizine stavlja u usta, igra postaje nesvrsishodnija. U obitelji se događaju velike promjene, s majkom i sestrom preselio je u Sigurnu kuću, majka je formirala novu bračnu zajednicu, očuh je na radu u inozemstvu. Planiraju preseljenje koje je otežano jer otac ne daje privolu. Majci je pružen suport te je preporučeno ustrajanje na strukturiranim odgojnim mjerama te nastavak radno-terapijske i logopedske terapije.

U vrijeme pisanja ovog članka dječak je i dalje u liječenju. S povećavanjem doze antiepileptika više se ne javljaju noćni napadaji, posljedično je smanjen dnevni umor. Kontinuirano je uključen u logopedsku terapiju u kojoj se radi na uvođenju potpomognute komunikacije manualnim znakovima i sličicama, što pozitivno utječe na njega te se smanjuje frustracija i agresija u ponašanju. Izražavanje je i dalje na razini nehotičnih vokalizacija i nekoliko slogova i vokala koje dječak na poticaj ponavlja. Jezično razumijevanje zasad je ovisno o vizualnim podražajima s obzirom da je kod dječaka prisutna verbalno-auditivna agnozija koja mu onemogućava razumijevanje slušnih podražaja iz okoline. Očekuju se nastavni pozitivni pomaci jer se planira daljnja titracija terapije antiepileptikom, a i jer se primjećuju usvojene adekvatnije odgojne vještine majke.

RASPRAVA

Ponajprije bismo se osvrnuli na pravodobnost uspostavljanja dijagnoze. Dječaku je u svibnju 2017. godine preporučen pregled kod neuropedijatra, a u rujnu iste godine je uključen u terapiju antiepileptikom, koja je presudna u sprječavanju daljnjih oštećenja mozga. Sa stručne strane u konkretnom prikazanom slučaju zamjetna je iznimno dobra diferencijalna dijagnostika i upućivanje djeteta na sve neophodne potrebne dijagnostičke preglede. Postoji prostor za poboljšanje skraćenjem liste čekanja za pojedine pretra-

could follow. He placed objects from close proximity in his mouth, played differently. His family underwent major changes, with them moving to a safe house, the mother entering into a new marriage with a stepfather that worked abroad. They planned relocation, but the father did not give his consent. We provided support to the mother and recommended structured educational measures and continuation of the occupational and speech therapies.

At the time of writing this article, the boy is still in treatment. With increasing doses of antiepileptics, no night-time seizures occur, resulting in reduced daily fatigue. He is continuously involved in speech therapy with introducing assisted communication (in the form of sign language and pictures), which has a positive influence and reduces frustration and aggression. Expression is still on the level of vocalization and several vocals that the child repeats when encouraged to do so. Language comprehension is now dependent on visual stimuli, as there is a presence of verbal-auditory agnosia that prevents him from understanding any auditory stimuli. Positive outcomes are expected as further titration of antiepileptic therapy is planned, and also due to the fact that the mother is adopting more appropriate education skills.

DISCUSSION

It's important to set the diagnosis in time. In May 2017, the boy was referred to a neuropediatrician, and in September of the same year antiepileptic pharmacotherapy was initiated, crucial in preventing further brain damage. From a professional point of view in the present case, a very good differential diagnosis and referral of the child to all the necessary diagnostic examinations are noticeable. Further improvements could be made, such as shortening of the waiting list for certain examinations, which is a general problem, and not only for this diagnostic category. Introduced pharmacotherapy with antiepileptics proved to

ge, što nije problem isključivo ove dijagnostičke kategorije. Uvedena farmakoterapija antiepilepticima pokazala se uspješnom, noćni napadaji se više ne pojavljuju. Iako su općenito kod LKS epileptički napadaji rijetki, zbog uvijek prisutnih epileptogenih promjena preporuka je da se terapija antiepilepticima uvodi. Za razliku od epilepsije, regresiju govora je mnogo zahtjevnije liječiti i potreban je multidisciplinski pristup. Često se događa da unatoč aktivnom pristupu ne vidimo značajnije terapijske pomake. Dijete nije u mogućnosti u potpunosti sudjelovati u intervencijama, jer ih dobrim dijelom nije sposobno shvatiti. Prigodom pretraživanja literature za prostor Hrvatske naišli smo na prikaz djeteta s LKS sindromom čija je prva klinička manifestacija bila konvulzivni napadaj a tek zatim regresija govora. Naglašen je također problem razvoja govora i izazova koje on predstavlja (11). Iako je bolest progresivna, česta su spontana poboljšanja i pogoršanja, što smo jasno mogli zamijetiti kod dječaka. Faze pogoršanja su uobičajeno trajale nekoliko mjeseci, a jednako dugo su trajale i faze poboljšanja. Dječak je ispoljavao glavninu smetnji ponašanja opisanih u literaturi, kao što su deficit pažnje, impulzivnost, hiperaktivnost, izljevi bijesa i agresije (5,8). Majka prikazanog djeteta prigodom cijelog procesa obrade, praćenja i liječenja bila je vrlo suradljiva, savjesno je dovodila dijete na tjedne terapije i pokušavala primijeniti sve preporuke. Unatoč našim naporima i savjetovanjima ima nerealna očekivanja od liječenja i nije sposobna shvatiti ograničenja djeteta, što je razumljivo s obzirom da je do 3. godine života dijete imalo uredan razvoj govora. U sklopu LKS-a razvoj dječaka bit će određen i ograničen spoznajnim teškoćama zbog čega je istovremeno potrebno raditi i na pružanju suporta majci.

be successful, night-time seizures no longer appear. Although epileptic seizures are rare in LKS due to continuously present epileptogenic alterations, it is recommended that an antiepileptic therapy is introduced. Unlike epilepsy, speech regression is much more difficult to treat and requires a multidisciplinary approach. It is often the case that despite the active approach, we do not see any significant therapeutic changes. The child is not able to fully participate in the interventions as is largely unable to understand them. When searching for Croatian literature, we came across a child with LKS syndrome whose first clinical manifestation was a convulsive attack and then speech regression. The emphasis was also placed on the problem of speech development and the challenges it poses (11). Although the disease is progressive, spontaneous improvements and deteriorations are common, which we can clearly see in this case. The deterioration phenomena usually lasted for several months, and the improvement phases for the same length of time. The boy showed most of the behavioural disturbances described in the literature, such as attention deficit, impulsiveness, hyperactivity, outbreaks of anger, and aggression (5,8). During the entire process of monitoring and treatment the mother was very cooperative, conscientiously brought the child into weekly therapy and tried to apply all the recommendations. Despite our efforts and counselling, she still has unrealistic treatment expectations and is incapable of understanding the limitations of the child. This is understandable since the child had first 3 years of normal speech development. Within LKS, the development of the boy will be determined and limited by cognitive difficulties, which is why it is also necessary to work on supporting the mother.

ZAKLJUČAK

U radu smo nastojali ukazati prije svega na multidisciplinsku obradu i jaku povezanost između dječjih psihijatara, pedijatara i surad-

CONCLUSION

In this paper, we have tried to point out to the multidisciplinary approach and the strong connection between psychiatrists, paediatricians,

nih struka u sustavu sa ciljem što brže dijagnostike i upućivanja djeteta u tretman. Često se upravo ovaj poremećaj okarakterizira kao mutizam, autizam ili neki drugi pervazivni razvojni poremećaj čime izostaje pravodobna obrada i intervencija. Specifičnost Landau Kleffnerovog sindroma je akutni gubitak govora i jezika u djeteta koje se do tada govorno normalno razvijalo te globalna regresija ponašanja, no rijetkost susretanja s ovim sindromom čini ga iznimno zahtjevnim za dijagnosticiranje. Dijagnoza se postavlja specifično epileptogeno promijenjenim nalazom EEG-a uz uredan nalaz MR-a mozga, zajedno s kliničkim manifestacijama sindroma. Nadamo se kako ćemo ovim prikazom povećati svijest stručnjaka i prepoznavanje ovog sindroma, s ciljem što ranije intervencije i rehabilitacije. Važno je naglasiti da se govorna rehabilitacija može započeti i prije postavljanja dijagnoze, na osnovi kliničke slike, kako bi ishod liječenja bio što bolji.

and other health care professionals with the aim of speeding up the diagnosis and referral of the child to treatment. This disorder is often characterized as mutism, autism, or some other pervasive developmental disorder, which results in delays of medical treatment. The specificity of Landau Kleffner syndrome is an acute loss of speech and language in a child who developed normal language and global regression of behaviour, but the rarity of encountering this syndrome makes it extremely demanding to diagnose. The final diagnosis is based on an epileptogenically altered EEG finding during sleep with an orderly brain MRI finding, along with clinical manifestations of the syndrome. We hope that this presentation will increase the awareness of the experts and the recognition of this syndrome, with the aim of early intervention and rehabilitation. It is important to emphasize that speech rehabilitation can be started even before the diagnosis is made, based on the clinical signs, making the outcome of the treatment as good as possible.

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