Importance of Early Drug Treatment in Prognosis of the Landau-Kleffner Syndrome

Šikić, Nada; Ivičević-Desnica, Jelena; Vrca, Anđelko; Škobić, Helena

Source / Izvornik: **Collegium antropologicum, 2001, 25, 529 - 534**

Journal article, Published version
Rad u časopisu, Objavljena verzija rada (izdavačev PDF)

Permanent link / Trajna poveznica: https://urn.nsk.hr/urn:nbn:hr:257:288587

Coll. Antropol. **25** (2001) 2: 529–534
UDC 616.853-036:612.821.5
Original scientific paper

Importance of Early Drug Treatment in Prognosis of the Landau-Kleffner Syndrome

N. Šikić[1], J. Ivičević-Desnica[1], A. Vrca[2] and H. Škobić[3]

[1] Hearing and Speech Rehabilitation Center, Polyclinic »SUVAG«, Zagreb, Croatia
[2] Department of Neurology, Clinical Hospital »Dubrava«, Zagreb, Croatia
[3] Department of Neurology, Clinical Hospital, Mostar, Bosnia and Herzegovina

A B S T R A C T

An expert team conducted a ten-year survey of eight children with Landau-Kleffner syndrome (LKS) identified among children referred to Polyclinic »SUVAG« in Zagreb because of hearing disturbances. Although LKS is a rare disorder it is extremely important to detect it because early diagnosis and prompt medicinal treatment may improve the prognosis, whereas neglect and late diagnosis result in language disability. Standard diagnostic criteria must be established to enable timely treatment.

Introduction

Symptomatology

Landau-Kleffner syndrome (LKS) is a rare childhood neurological disorder. It usually occurs in children between the ages of 3 and 9. It is manifested as a form of aphasia, with epileptiform activity shown up in EEG tests (multifocal spikes and spike wave complexes, which are not stable buts tending to progress). Other symptoms observed include epileptic seizures (in 67% of examinees) as well as disturbances in behavior and psychomotor development (in 71% of examinees, according to literature published internationally). From neuropathological point of view, verbal-auditory agnosia is observed with rapid reduction of spontaneous verbal expression. In affected individuals who have seizures, these seizures are typically infrequent, and occur either as generalized convulsions or partial seizures. The seizures disappear and epileptiform electroencephalogram usually settles down by the age of 15. However, the prognosis of receptive and expressive language ability varies and is much improved when treatment including medications and speech therapy is started early.

Since 1957, when original paper of Landau and Kleffner was published, about two hundred new cases have been

Received for publication March 7, 2001.

reported in literature. Pathogenesis of this syndrome has remained hypothetical. What is clinically observable is the disrupture in the chain: hearing – verbal integration – verbal expression. The exact location of pathological process has not been identified with certainty. Hypotheses included either a disruption of subcortical links responsible for activation of temporal lobe[1] or disturbed maturation of functional structures of interhemispheric paths, notably corpus callosum[2]. Some authors fined symmetrical thalamic nuclei despite significant cortical asymmetries, they suggest that corticothalamic neurons do not participate in the generation of spike-and-wave discharges or that they are inhibited by the pathological mechanisms. They have hypothesized that the acquired deterioration of cognitive function is caused by alteration of the maturation of one or several associative cortices, primarily involving local interneurons and corticocortical associative neurons[3]. Korkman (1998)[4] suggests that the primary deficit of the receptive aphasia is an impairment of auditory phonological discrimination rather than a generalized auditory agnosia. Paetau (1991, 1994)[5,6] find the epileptiform activity of LKS patients produced by sound-responsive neurons in the non -primary auditory cortex within the middle and posterior sylvian fissures. He suggests that unilateral discharges at or near the auditory cortex disrupt auditory discrimination in the affected hemisphere, and lead the suppression of auditory information from the opposite hemisphere is the two main criteria of LKS.

Because the disorder does not affect life expectancy, the reported cases have never included pathohistological analysis.

Objectives

An expert team at our institution, Polyclinic »SUVAG« in Zagreb, was involved in a ten-year survey of children with LKS. In our experience the prognosis of further speech development varied considerably. Out of eight children involved in treatment during that period, four children recovered, whereas four children developed severe language disability.

Although LKS is a rare disorder, it is extremely important to suspect it because early diagnosis and prompt treatment may improve the prognosis, whereas neglect and late diagnosis leave permanent and irreparable consequences. Therefore standard diagnostic criteria must be established to enable that treatment is provided on time to all children affected with the disorder.

Materials and Methods

From 1989 to 1999 in Polyclinic »SUVAG« in Zagreb eight children with LKS were diagnosed and treated. The total number of children with speech disorder examined in that period is about 13,000 or 1,296 per year on the average. In 1,586 children with speech disorders there was one case diagnosed as LKS. The rate seems rather high compared to the low rate of cases reported in literature. However, one should bear in mind that our institution is specialized in hearing and speech disorders, therefore the children referred to it had already been detected as having auditory problems.

The age of children at the time of LKS diagnosis was between 4 and 7 years. There were four boys and four girls (Table 1).

At the first examination carried out by a speech pathologist at Polyclinic SUVAG, children were suspected of having aphasia. Because the disorder was acquired (the children affected had already acquired language abilities before the onset of the disorder), the speech pathologist referred the children to other specialists in the team.

TABLE 1
TIME FROM THE FIRST EPILEPTIC SEIZURE TO THE IMPLEMENTATION OF AET (T_{ES-AET}), IQ MEASURED BY VERBAL AND NON-VERBAL SCALE AT THE TIME OF ARRIVAL (T_0) AND AFTER 10 YEARS PERIOD (T_{10})

Patients	Sex	TES-AET (months)	IQ by verbal scale at T_0*	IQ by non-verbal scale at T_0	IQ by verbal scale at T_{10}*	IQ by non-verbal scale at T_{10}
Case 1	M	0	76	140	–	85
Case 2	M	24	67	94	75	80
Case 3	M	12	–	95	95	105
Case 4	M	3	83	118	100	120
Case 5	F	6	62	95	100	100
Case 6	F	0	60	110	–	110
Case 7	F	18	–	80	85	90
Case 8	F	6	65	92	90	95

* In cases denoted by »–« verbal IQ-test was not applicable

First of all, hearing tests were conducted, including objective audiometry. For all examinees tone audiogram indicated either a normal hearing status, or a light hearing disorder of conductive type that could not have affected the development of speech because it enabled normal social contacts. In brainstem auditory evoked potentials tests, conducted with all examinees, absence of upper cortical responses (auditory evoked potentials of slow latencies) either bilaterally or only on the left was detected. In literature, these findings are related to dysphasic disorders in speech development[7].

In psychological assessment all examinees demonstrated normal nonverbal intelligence. Verbal diagnostic methods, if applicable, indicated deviation (by more than two standard deviations) of receptive language development in comparison to expressive language development. Other tests included Reynell Developmental Language Scales, Leiter Nonverbal Performance Scale R, and Developmental Test Čutirić (psychomotor development scales), BL, BS and WISC.

Psychiatric assessment was needed because behavioral disturbances were apparent in all examinees. Psychiatrist observation, continuous monitoring and family history did not give any indication of a primary psychotic disorder in development of the children. The presence of behavioral disturbances was associated with inability to understand speech or even gestures.

Neurological examination did not confirm existence of any neurological defects in the are of enervation of cranial nerves, lateralization, dynamostatics or sensibility. Primary problem was emotional disturbance.

EEG test performed with all children in wakefulness detected one or more foci, manifested as spikes or spike wave complexes 3–4 Hz, multiple spike elements and slow waves. Because of clearly identified signs of EEG abnormality, abnormalities in behavior, detected epileptic seizures of the GM type or complex psychomotor crises in wakefulness and in sleep, further neuro-radiological examination was requested[8].

Computerized Axial Tomography was performed with all eight cases and the findings were normal. The findings of Magnetic Resonance Imaging scan of the brain (with contract dye) were also normal.

Polysomnogram was conducted in the Sleep Disorders Center at Clinical Hospital »Vrapče«. In the test, carried out during the night, EEG epileptic status was detected, having duration of 3–5 hours. The findings were considered pathognomonic.

Routine biochemical blood tests were performed (CBC, ESR, liver enzymes, blood sugar levels, amino-acids, alkaline phosphatase, ammonium in blood, ceruloplasmin, urea, creatinine, urine) and all values were normal. An ophthalmologic exam (fundus) was requested. All eight examinees had normal findings.

Results

One boy and one girl in the group were included only in speech therapy because the parents had not consented to any medication. Both children developed the syndrome of verbal agnosia. Seizures were not observed in the ten-year period (the period in which the older girl was included in speech therapy). Behavioral disturbances were reduced. EEG patterns settled into normal values. Today the two children attend the regular elementary or secondary school with special program. They communicate by gestures and lip-reading although they both have normal tone audiogram values.

One boy was referred to our institution for diagnosis and therapy only three years after the onset of the disorder. In that period he had been diagnosed as and treated with monovalent antiepileptics. When he was admitted at our institution the seizures settled down, and EEG patterns did not indicate the need for a change in medications. Today, at the age of 18, the patient has verbal agnosia. The most recent audiograms indicated the progressive loss of hearing (isolated tones) and progressive development of central auditory dysfunction. The boy completed the special vocational education for an assistant cook, but since the last year the loss of intellectual abilities has been observed. Epileptic manifestations have not been observed. In spite of normal hearing functions identified in audiograms, the sounds he utters are as if he was a deaf child. He is not able to lip-read and he uses gestures to communicate.

One boy was prescribed cortico-steroids two years after the onset of first symptoms. In that period he had been taking AED carbamazepine because his parents rejected any additional therapy. At present he attends elementary school with special program at our institution. His behavior is normal but he still has significant difficulties in communication because of reduced ability to comprehend speech (dysphasic disturbances). He is able to hear and speak at a lower developmental level.

Four children took combined anti-epileptic therapy (mainly valproic acid, carbamazepine and clonazepame) and corticosteroids (dexamethason). Three years after discontinuation of drug therapy, the three children attend the regular elementary school with normal program. They have normal behavior, normal hearing and speech, normal EEG patterns and normal sleep cycles.

Discussion

Pathophysiology of the syndrome is still unknown. Some suggested causes included a very slow viral infection as in slowly progressive local encephalitis, but this was not confirmed in neuropathological studies. Other authors suggested the existence of vascular anomaly or sequel of cysticercosis[9,10].

Authors from USA report a treatment with subpial intracortical transection in some patients with LKS, success depends on selection of cases having severe epileptogenic abnormality than can be demonstrated to be unilateral in origin de-

spite a bilateral electrographic manifestation[11].

Aphasia is a consequence of verbal agnosia caused by cortical or subcortical dysfunction of auditory system. Loss of speech with paroxysmal EEG patterns indicates that the two features are correlated. It has been observed that symptoms improve when EEG patterns settle[12–14].

Many authors agree that the period from the onset of the first LKS symptoms to the time when anti-epileptic therapy is introduced is critical[15,16]. The corticosteroids should be given in high doses as soon as the diagnosis is firmly established and should be continued in maintenance dose for several months or years to avoid escape.

It is considered that LKS is not an uniform but a complex syndrome in which three forms can be distinguished: 1) aphasia of transitory character; 2) aphasia of persistent character; 3) aphasia of atypical character.

Prognosis is difficult to make. In a paper that included a series of 45 cases, the appearance of first symptoms was assessed as critical because at the age of 5–6 there exists a plasticity of language representation in cortex and a damage in the dominant hemisphere results in creating language structures in other hemisphere. All authors agree that behavioral disturbances develop because of the syndrome and the frustrating inability to communicate typical for aphasia[17,18].

In the series of eight cases diagnosed with LKS, treated and included in speech therapy at Polyclinic SUVAG, the prognosis was directly related to the time elapsed from the onset of the disorder to the beginning of treatment. The four children that were diagnosed in less than a year after the first appearance of symptoms (seizures) and promptly treated (anti-epileptics for one-two years, corticosteroids two months) had a good recovery. Today they have normal EEG patterns and no clinical symptoms.

Conclusion

The following guidelines must be followed to identify LKS syndrome:

- *speech pathologist* examination to detect aphasia
- detailed *audiological tests* (including auditory evoked potentials) to exclude peripheral hearing impairment
- *psychological tests*, non verbal methods, to assess intellectual ability
- *psychiatric* observation to exclude primary psychotic developmental disturbances and psychotherapy to treat behavioral disturbances
- *neurological* examination including EEG tests (in wakefulness and in sleep), and neuro-radiological examination (CAT and MRI scan) to exclude existence of any other neurological disorders

Multidisciplinary approach must be used to arrive at diagnosis. Because of complexity of symptoms, medicinal treatment and speech therapy must be continually followed up by a team of specialists at an institution specialized in diagnosis and therapy of language disorders.

REFERENCES

1. KELERMAN, K., Eur. J. Pediatr., 128 (1978) 207. — 2. NJIOKIKTJEN, CH., Neuropediatrics, 14 (1983) 123. — 3. MAQUET, P., E. HIRSCH, M. N. METZ-LUTZ, J. MOTTE, D. DIVE, C. MARESCAUX, G. FRANCK, Brain, 118 (1995) 1497. — 4. KORKMAN, M., M. L. GRANSTROM, K. APPELQUIST, E. LIUKKONEN, J. Int. Neuropsychol. Soc., 4 (1998) 566. — 5. PAETAU, R., M. KAJOLA, M.

KORKMAN, M. HAMALAINEN, M. L. GRANSTROM, R. HARI, Neuroreport, 2 (1991) 201. — 6. PAETAU, R., J. Clin. Neurophysiol., 11 (1994) 231. — 7. MARN, B.: Ocjena funkcionalne sposobnosti aferentnih slušnih puteva u djece s dislalijom. In Croat. M.Sc. Thesis. (University of Zagreb, Zagreb, 1992). — 8. ŠIKIĆ, N., Arhiv ZMD, 30 (1988) 69. — 9. NAKANO, S., T. OKUNO, H. MIKAWA, Brain Dev., 11 (1989) 43. — 10. HOLMES, G. L., M. MCKEEVER, Z. SAUNDERS, Epilepsia, 22 (1981) 631. — 11. MORRELL, F., W. W. WHISLER, M. C. SMITH, T. J. HOEPPNER, L. DE TOLEDO-MORRELL, S. J. PIERRE-LUIS, A. M. KANNER, J. M. BUELOW, R. RISTANOVIĆ, D. BERGEN, Brain, 118 (1995) 1529. — 12. THARPE, A. M., G. D. JOHNSON, M. E. GLASSCOCK, Am. J. Oto., 12 (1991) 3. — 13. LANDAU, W. M., Arch. Neurol., 49 (1992) 353. — 14. LANDAU, W. M., F. R. KLEFFNER, Neurology, 7 (1957) 523. — 15. LERMAN, P., T. LERMAN-SAGIE, S. KIVITY, Dev. Med. Child Neurol., 3 (1991) 257. — 16. MARESCAUX, C., E. HIRSCH, S. FINCK, P. MAQUET, E. SCHLUMBERGER, F. SELLAL, M. N. METZ-LUTZ, Y. ALEMBIK, E. SALMON, G. FRANCK, Epilepsia, 31 (1990) 768. — 17. RAPIN, I., S. MATHIS, A. J. ROWAN, G. G. GOLDEN, Dev. Med. Child Neurol., 19 (1977) 192. — 18. METZ-LUIS, M. N., P. MAQUET, A. DE SAINT MARTIN, G. RUDOLF, N. WIOLAND, E. HIRSCH, C. MARESCAUX, Int. Rev. Neurobiol., 45 (2001) 505.

N. Šikić

Hearing and Speech Rehabilitation Centre, Polyclinic »SUVAG«, Lj. Posavskog 10, 10000 Zagreb, Croatia

ZNAČAJ RANOG MEDIKAMENTOZNOG LIJEČENJA U PROGNOZI LANDAU-KLEFFNEROVOG SINDROMA

S A Ž E T A K

Ekspertni tim proveo je 10-godišnje praćenje osmero djece s Landau-Kleffnerovim sindromom. Ova djeca identificirana su među djecom koja su primljena u Polikliniku »SUVAG« u Zagrebu, zbog poremećaja u slušanju. Premda je LKS rijedak poremećaj, iznimno je važno da se on prepozna jer rana dijagnoze i pravovremeno medicinsko liječenje mogu poboljšati njegovu prognozu, dok zapušteni i kasno dijagnosticirani slučajevi rezultiraju s teškoćama govora. Autori zaključuju kako se standardni dijagnostički kriteriji moraju ustanoviti kako bi se omogućilo pravovremeno liječenje.