

Landau-Kleffner Syndrome Without Seizures – Would Speech Delay Justify the Treatment with Antiepileptic Drugs?

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ABSTRACT

Introduction: Landau-Kleffner Syndrome is a rare epileptic syndrome characterized by the association of receptive aphasia, epileptic seizures, behavioral disorders and electroencephalographic changes with discharges at the temporal lobe unilaterally or bilaterally. Seizures are not essential for diagnosis. **Case report:** J. V. S. S., 3 y/o male, with delay in acquirement of speech, psychomotor agitation and sleep disorder (sleeplessness). Attempt to communicate was established by gestures and pointing at things. His behavior characterized by agitation, restlessness, aggressiveness and difficulty to establish social contact with other children by the same age. MRI was normal and the EEG showed sharp-wave discharges in the left medial and posterior temporal regions. After three months of treatment with carbamazepine the child returned to an evaluation, presenting substantial improvement at speech, speaking simple words and with meaningful improvement on both behavioral and sleep patterns, as well as, social interaction. **Discussion:** Expression and reception speech disorders are relatively common in children with different epileptic syndromes, particularly in Landau-Kleffner syndrome. Epileptiform discharges can occur in people without epilepsy and use to be called subclinical discharges. What would be the impact of subclinical discharges on this population remains uncertain at the present time. We reviewed these interactions in the light of a representative case, showing favorable outcome following introduction of an antiepileptic drug.

Key words: Subclinical discharges, Landau-Kleffner Syndrome, speech delay.

RESUMO

Síndrome de Landau-Kleffner sem crises – atraso na aquisição da fala justifica o tratamento com drogas epilépticas?

Introdução: Síndrome de Landau-Kleffner é uma síndrome epiléptica rara caracterizada pela associação de afasia de recepção, crises epilépticas, distúrbios do comportamento e alterações eletrencefalográficas com descargas nos lobos temporais unilaterais ou bilaterais. Crises convulsivas não são essenciais para o diagnóstico. **Relato do caso:** J.V.S.S., masculino, três anos de idade, com atraso na aquisição da fala, agitação psicomotora e distúrbio do sono. Ele usava gestos e apontava para os objetos tentando se comunicar. Seu comportamento era muito agitado, impaciente, períodos de agressividade e muita dificuldade em estabelecer contato social com outras crianças da mesma idade. RNM foi normal e o EEG mostrou descargas de ondas agudas nas regiões temporais média e posterior esquerda. Após três meses de tratamento com carbamazepina a criança retornou para reavaliação, apresentando importante melhora da fala, falando palavras simples, melhora do comportamento e do padrão de sono e da interação social. **Discussão:** Alterações na linguagem de recepção e de expressão são relativamente comuns em crianças com diferentes síndromes epilépticas, particularmente na síndrome de Landau-Kleffner. Descargas epileptiformes podem ocorrer em pessoas sem epilepsia sendo denominadas descargas subclínicas. Qual o impacto das descargas subclínicas para estas pessoas é incerto até o momento. Relatamos o caso de um menino com descargas epileptiformes no EEG, sem história de crises convulsivas e excelente evolução clínica após tratamento com droga antiepiléptica.

Unitermos: Descargas subclínicas, Síndrome de Landau-Kleffner, atraso da fala.

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INTRODUCTION

Landau-Kleffner Syndrome (LKS) is a rare epileptic syndrome, reported by Landau and Kleffner in 1957,¹ characterized by the association of receptive aphasia, epileptic seizures in most cases, behavioral disorders and electroencephalographic changes with discharges at the temporal lobe unilaterally or bilaterally.²

The incidence of this syndrome is unknown in Brazil, although cases with behavioral and language disorders without epileptic seizures are supposed to be rare. This syndrome undertake neurologically healthy children, that were acquiring speech in an appropriate way. The accurated etiology remains uncertain. Astrocytoma, cranial trauma, neurocysticercosis, demyelinating diseases, brain vasculitis, perisylvian polymicrogyria, encephalitis were independently implicated in the nature of this condition. Although familial history of epilepsy is common in these cases, the precise genetic participation is not completely determined.^{2,3,4}

The goal of our study is to report the case a child presenting with LKS without epilepsy and with severe speech and behavior impairment that showed significant improvement following carbamazepine treatment, arguing the importance of the subclinical discharges as potential origin of the aphasia. This paper was approved by the Pequeno Príncipe Hospital Committee of Ethics. An informed consent was presented and signed by the patient's legal responsible allowing publication of the case report.

CASE REPORT

J. V. S. S., a 3 y/o male, referred to neurological evaluation due to delay in acquirement of speech, psychomotor agitation and a sleep disorder. He was the only child of healthy unrelated parents. No familial history of epilepsy or any other severe neurological affection was given. Pregnancy and delivery were uneventful. Birth was at term (39 weeks of gestational age), Apgar score 9 (first minute) and 10 (fifth minute), birth weight was 3,500 grams, height was 50 cm, head circumference of 37 cm, maternity hospital discharge was at the second day of life. He had a normal motor development, with head control at three months, sat unsupported at six months, crawled at eight months, walked supported at eleven months and unsupported at 13 months. Anal sphincter control occurred at the age of two and urinary sphincter control at the age of two and a half.

At the age of two years and two months, the child was referred (by the pediatrician) to speech therapy due to speech acquirement delay. At the time of the first neurological exam, with three years and two months of age, the child presented monosyllabic speech and shouts. His speech was unmeaning even to his relatives. He used gestures and pointed to objects trying to communicate.

His behavior was very agitated, impatient, regardless, there were moments of aggressiveness and presented much difficulty to establish social contact with other children with the same age.

Landau-Kleffner Syndrome with no seizures was clinically suspected and a week later endorsed by neurophysiologic (i.e., EEG test) examination. The electroencephalographic video-monitoring was performed with the 10-20 system of electrode placement, with a total duration of eight hours, during short periods of wake and phase I sleep and long periods on phase II sleep. Sharp-wave discharges stood out from the baseline activity, with a maximum electronegativity at the left medial temporal and posterior regions, and less frequently at the left frontal region, with bilateral secondary synchrony. Several sudden awakenings during sleep, with no electrographic correlation were documented. The brain magnetic resonance imaging and auditory brainstem evoked potentials were normal.

Carbamazepine was then initiated at 10 mg/kg/day dose BID. After three months of treatment, the child was back for evaluation, presenting substantial improvement at speech, speaking simple words like "mamãe" ("mommy"), "papai" ("daddy"), "vovó" ("grandma"), "vovô" ("grandpa"), "sim" ("yes"), "não" ("no"), "água" ("water"), "aleluia" ("halleluiah") and with meaningful improvement of behavior. In addition, his mother reported improvement on both the sleeping pattern and social interaction after beginning the antiepileptic drug therapy.

DISCUSSION

In 1836, Marc Dax, French neurologist, published his studies outcome relating structural lesions on the left brain hemisphere, right hemiparesis and loss of speech ability. Years later, French anatomist Pierre Paul Broca would confirm Dax's pioneer studies. In 1861, when Broca performed the necropsy of a patient that would become known worldwide as "Tan", he defined that lesions placed on the third circumvolution of the frontal lobe would be responsible to the loss of speech ability. Carl Wernicke, German anatomist, psychiatrist and neuropathologist, contemporaneous with Broca, was the responsible for the creation of the neurological model of language known as "Wernicke-Geschwind model" and by the discovery that the speech and perception area would be placed on the posterior portion in the superior temporal gyrus. Anatomically, Wernicke's area is related to the Broca's area through the arcuate fasciculus that belongs to the superior longitudinal fasciculus.^{5,6}

Several theories try to explain the speech acquisition process in infancy. As Skinner suggests in his behavioral theory that speech would be acquired through teaching, being then a conditioned behavior, Chomsky suggests that

oral language would be genetically determined.⁷ Although verbal and non-verbal language acquisition relies on the social contact since the first months of life, it is undeniable the role of the structural and functional integrity of countless neuronal circuits in the brain cortex.⁶ The term “afasia”, introduced in medical literature by Trosseau, means the partial or total loss of speech ability, and it can be classified as reception afasia, expression afasia or mixed type.⁵

Expression and reception speech disorders are relatively common in children with different epileptic syndromes, particularly on those who have an epileptogenic focus involving temporal posterior and/or frontal regions on the dominant brain hemisphere.⁸ The real impact of the interictal epileptiform discharges on the brain function remains in discussion yet. The moment of onset and the topography of the discharges certainly influence the brain cortex physiology. In LKS the onset of the discharges coincide with the time in which the development of speech is extremely active, occurring the settlement of new neuronal connections, fortification of preexistent ones and extinction of unnecessary synapses. The accurate neurophysiologic mechanism of stagnation and involution of acquired speech in patients with LKS is not completely clear yet. Some authors believe that there is a functional disconnection of brain cortex areas responsible by reception language (temporal medial-posterior cortex) and cortical areas responsible by spoken language, in the junction of frontal, temporal and parietal lobes in the left brain hemisphere.⁹ How much speech commitment is resulting from morphologic changes in brain cortex microstructure and how much is related exclusively to functional changes is not totally cleared either. Although brain magnetic resonance is normal in most patients with LKS, the existence of cortical microstructural alterations cannot be ruled out.^{3,4,9}

In LKS “classic presentation”, with epileptic seizures, the treatment ideally aims to simultaneous seizure control, behavioral disorders control and language rehabilitation. It must be highlighted that carbamazepine is not a first choice drug in the treatment of LKS, and there are reports of increase in frequency and intensity of the seizures. Despite the fact that there are no clinically controlled studies comparing antiepileptic drugs effectiveness in LKS treatment until this moment, valproic acid, ethosuximide, diazepam, clobazam, clonazepam, in addition to intravenous immunoglobulin and corticosteroid therapy are the drugs of choice. Probably lamotrigine, sulthiame, vigabatrin and levetiracetam may also be effective.¹⁰ In clinically refractory cases, surgical procedures (multiple subpial transections perpendicularly to the brain cortex surface – Morrell’s surgical technique) can be indicated.¹¹ In our patient, we chose carbamazepine due to the familial and

personal history of allergic reactions and atopy, besides overweight and unavailability of ethosuximide in our country.

Epileptiform discharges can occur in people without epilepsy and use to be called subclinical discharges. A substantial part of these subjects present signs of cognitive dysfunction during these discharges when they are evaluated by psychometric tests, and this phenomenon is known as transitory cognitive impairment. In children and adolescents the transitory cognitive impairment can be associated to behavioral disorders and commitment of psychosocial functions.¹² Laporte et al.¹³ analyzed the influence of subclinical discharges on the cognition in subjects with attention deficit hyperactivity disorder that never had epileptic seizures, and concluded that the use of antiepileptic drugs improved significantly the cognitive aspects in this population. The authors suggest that the principle of treatment with antiepileptic drugs limited to patients with epileptic seizures must be reviewed. Similarly, behavioral disorders, school difficulties and speech acquisition delay can be present in children with specific benign epileptic syndromes, such as the benign childhood epilepsy with centrotemporal spikes, laying a probable relation with the presence of subclinical discharges (interictal discharges mainly during sleep).¹⁴

FINAL REMARKS

In our patient, the development of speech occurred normally until about eighteen months of age, when his family observed speech stagnation and regression. Even after a long phonoaudiological treatment the child did not present any improvement. Three months after the carbamazepine treatment started, the child presented marked improvement on speech, behavior and sleep pattern. This case observation suggests that there is an intimate relationship between functional changes in the brain cortex affected by interictal discharges and the verbal language disorder. In this way, we suggest that children with epileptiform discharges in the speech area, even without epileptic seizures, can be favored with antiepileptic drug treatment.

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