Journal of Advances in Biological and Basic Research 01[01] 2015
www.asdpub.com/index.php/jabbr e-ISSN-2454-6097

Review Article

The Landau Kleffner Syndrome

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Keywords:
Landau kleffner syndrome,
Aphasia,
Speech delay;

Abstract

The Landau Kleffner syndrome (LKS) or the syndrome of acquired epileptic aphasia was first described in 1957. LKS also called infantile acquired aphasia, acquired epileptic aphasia or aphasia with convulsive disorder. It is a rare childhood neurological syndrome. LKS is an epilepsy syndrome involving progressive neuropsychological impairment related to the appearance of paroxysmal electroencephalograph (EEG) activity. The disorder is characterized by gradual or rapid loss of language in a previously normal child. Affected children who have developed age-appropriate speech then experience language regression with verbal auditory agnosia, abnormal epileptiform activity, behavioural disturbances, and sometimes overt seizures. Behavioral disorders such as hyperactivity, aggressiveness and depression can also accompany this disorder.

1. Introduction

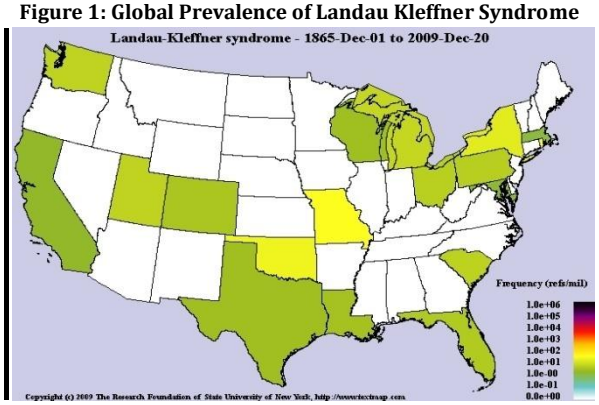
The correlation between paroxysmal EEG discharges and language deterioration was first suggested by Landau and Kleffner (1957), who reported five children with acquired aphasia associated with a convulsive disorder [1].

Landau Kleffner syndrome has three features:

- An acquired receptive aphasia.
- Temporoparietal spike-wave discharges in the awake state.
- Frequent generalised spike-wave discharges in sleep (electrical status epilepticus in sleep) (ESES) [2].

LKS occurs most frequently in normally developing children who are between 3 and 7 years of age, for no apparent reason, these children begin having trouble understanding what is said to them [3].The Landau Kleffner syndrome is a rare disorder characterized by an acquired receptive and expressive aphasia and epileptic seizures. It is also known as 'a syndrome of acquired aphasia with convulsive disorder,' or 'acquired aphasia of childhood with epilepsy'. It is defined on the basis of specific clinical and EEG criteria [4]. The aphasia may be primarily receptive or expressive, and auditory agnosia may be so severe that the child is oblivious to everyday sounds. Hearing is normal, but behavioral problems, including irritability and poor attention span, are particularly common .One-third of children diagnosed with autism spectrum disorders (ASDs) are reported to have had normal early development followed by an autistic regression between the ages of 2 and 3 years. This clinical profile partly parallels that seen in Landau-Kleffner syndrome (LKS), an acquired language disorder (aphasia) believed to be caused by epileptiform activity. Given the additional observation that one-third of autistic children experience one or more seizures by adolescence, epileptiform activity may play a causal role in some cases of autism [15].

Figure 1: Global Prevalence of Landau Kleffner Syndrome



(Source: The Research Foundation of State University of New York, http://www.textmap.com**)**

2. Clinical manifestation

Children, most often 3-7 years old, with no illness in the past develop LKS either acutely or subacutely. A history of perinatal insult, delay in acquisition of milestones and communication disorders in the family are generally absent.Family history of epilepsy has been reported in 12% of all patients, but only in 5% of nonepileptic cases. Inability to comprehend verbal sounds earliest speech deficit which may progress to involve non-verbal sounds as well. Eventually the child becomes totally unresponsive to all auditory stimuli. Verbal output is variably reduced and may consist of garbled, paraphasic, neologistic speech. Occasionally telegraphic speech with word finding difficulties may be prominent. Hearing is always normal. Symptomatic period of the language disorder may be as brief as a day to a protracted course over several months. Clinical seizures may antedate, accompany or follow aphasia. Seizures are absent in about 30% of the affected children inspite of the EEG always being abnormal [5]. The first manifestation of the language disturbance is an apparent "word deafness," or auditory verbal agnosia . Parents report a child no longer responds to their commands, even with raised voices. This auditory agnosia extends to familiar noises including bells, whistles, or a ringing phone. LKS represents selective loss of language in association with an abnormally paroxysmal EEG, eventually characterized by electrographic status epilepticus of slow-wave sleep (ESES).There is an intricate relationship between LKS, autism, ESES, and developmental dysphasias and the interaction between

epileptiform discharges and cognitive dysfunction remains enigmatic. The presence of fluctuation in language and behavioral deficits, however, should raise concern regarding an accompanying diagnosis of epilepsy.To compare and contrast patterns of epileptiform activity in children with autistic regressions versus classic LKS to determine if there is neurobiological overlap between these conditions. It was hypothesized that many children with regressive ASDs would show epileptiform activity in a multifocal pattern that includes the same brain regions implicated in LKS [15].

3. Etiology

The etiology of LKS remains unknown, and may be due to diverse causes. Encephalitis has been postulated, but not verified. There was no evidence of inflammation, demyelination, hippocampal sclerosis or dysgenesis [1]. Low-grade brain tumors, closed-head injury, neurocysticercosis, and demyelinating disease have been associated with the clinical picture of acquired epileptic aphasia [6]. However their case was atypical with elevated CSF protein and focal imaging abnormalities [1]. Bilateral perisylvian polymicrogyria may also present with new onset of speech disturbance after a 2-year period of normal language and EEG findings typical of acquired epileptic aphasia [6].

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 [7].

All of the children with LKS appear to be perfectly normal until their first seizure or the start of language problems. There have been no reports of children who have a family history of LKS. Therefore, LKS is not likely to be an inherited disorder [3]. Some suggested causes are demyelinating or encephalopathic processes, infectious or inflammatory illnesses, unilateral brain lesions, and autoimmune diseases [8].

4. Diagnosis

Landau-Kleffner syndrome is commonly diagnosed using an EEG, a scan that shows the brain's electrical waves, as well as other diagnostic tests [8]. computed tomography (CT) and magnetic resonance imaging (MRI) findings are normal. There are uncommonly mild elevations of CSF protein white matter changes on CT/MRI, or a structural lesion [1]. Functional imaging by single-photon emission computed tomography (SPECT) and positron emission tomography with ^{18}F-flurodeoxyglucose (FDG-PET) have consistently revealed a predictable pattern of abnormalities in LKS. Several SPECT studies in patients with LKS are available and reported abnormalities conform to asymmetric increased or decreased temporo-parietal perfusion depending on the timing of the study [5].Typically, abnormalities are seen in the temporal or parietal areas and can be either bilateral or lateralized to either hemisphere [9].

To diagnose Landau-Kleffner syndrome, it is important for the child's doctor to understand his development particularly in terms of language to perform a variety of tests, such as:

- Neuropsychological testing to evaluate how his brain processes language and performs other functions, and to find out the specific type of language problem that is affecting him
- EEG while the child is awake and asleep
- Neuroimaging (CT or MRI) [10].

The age of onset was from 2 to 10.5 years of age. All patients had acquired aphasia, characterized by verbal auditory agnosia. All patients had epileptic seizures. Partial motor seizures during sleep occurred in 8 patients, and other seizure type including atypical absence seizure and generalized tonic-clonic seizure were also observed. Psychological and behavioral abnormalities occurred in 9 patients. There were no abnormalities of hearing and neuro-imaging tests in all patients, and family histories were negative. All the patients had EEG abnormalities. Focal spike and waves of temporal lobe were recorded in 9 patients. Electrical status epilepticus during sleep (ESES) was observed on Video-EEG (VEEG) monitoring in 4 patients [16].

5. Treatment

The pharmacologic treatment of LKS is problematic due to several confounding observations. The benign course of the epilepsy versus devastating language impairment, fluctuating course of aphasia, lag of improvement in relation to the EEG, possibility of spontaneous remission, and rarity of the disorder render multiple barriers to controlled clinical trials. The determination of treatment efficacy is difficult [1]. Most anti-epileptic drugs are effective in preventing the seizures, but have little effect or behaviour or language problems. For the language difficulties, high-dose corticosteroids seem to give the best results. Benzodiazepines may also be tried. Intravenous immune globulin (IVIG) also appears to have good results in some cases [10]. Corticosteroids have been an efficacious treatment for both clinical and EEG abnormalities. This was reported by McKinney and McGread leading to the speculation of chronic encephalitis as the etiology of LKS [1]. Some children who have not responded to medication have shown reduction in seizures and improved language through a surgical procedure called multiple subpialtransection [9].

Commonly used medicines include sodium valproate (Epilim), ethosuximide (Zarontin) and clobazam (Frisium). A steroid called prednisolone and a medicine called sulthiame (Ospolot) may also be helpful [11]. Benzodiazepines have demonstrated efficacy in reducing epileptiform activity in the short term. Transitory resolution of the ESES pattern was observed after the administration of clonazepam. Diazepam has a shorter half-life than clonazepam, which can be advantageous in a condition such as CSWS where more severe epileptiform activity occurs during the night [12].

6. Prognosis

Although the outlook for seizures in children with LKS is good, many children will be left with significant language, learning and behavioural difficulties. The seizures usually stop by the age of 15, although a small number (about one in 10) continue to have infrequent seizures [11]. Several variables may influence prognosis, including age of onset, pattern of language deficit, frequency and topography of EEG discharges, duration of epilepsy, and efficacy, and adverse effects of anticonvulsants [1].

7. Conclusion

LKS is an epilepsy syndrome characterized by acquired aphasia and epileptiform EEG abnormalities eventually characterized by ESES. The language disorder could be the result of a paroxysmal disruption of language function during the time of its greatest development [1]. LKS evolution, language networks involved in the spread of abundant idiopathic interictal abnormalities (and mainly slow waves) may be progressively inhibited and become unable to carry out their normal physiological role [13]. Landau Kleffner syndrome is an epileptic encephalopathy characterized by acquired verbal auditory aphasia and seizures in most of the patients associated with continuous or almost continuous spike-and-wave discharges during slow wave sleep. The most commonly used treatments were clobazam, ethosuximide, sulthiame, High-dose

steroids were also administered. Adequate and early management may avoid language and cognitive deterioration [14].

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