



Case Report

Landau-Kleffner Syndrome in a Ten-Year-old Nigerian Child

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ABSTRACT

Background: Landau-Kleffner Syndrome (LKS) is a rare childhood epileptic encephalopathy that presents as acquired epileptic aphasia. Lost speech is often difficult to retrieve. Early diagnosis and treatment improve the chances of recovery of lost speech capacity. We report its presentation, management and outcome in a ten-year old Nigerian child.

Method: The clinic record of the child was retrieved from Medical Records unit of Lagos State University Teaching Hospital (LASUTH), Ikeja, Lagos, Nigeria. His detailed clinical history, examination findings, investigation results, treatments given, clinic follow-up, as well as disease progression were reviewed and summarised.

Results: Illness started at age of three years with difficult to control refractory seizures and he was put on multiple anti-epileptic drugs. At age five, he developed progressive aphasia, behavioural and cognitive deficits, with self-injurious behaviour. Risperidone alleviated behaviour deficits for a while. Seizures however got worse. A full evaluation was carried out by the Paediatric Neurologist, and an electroencephalographic test report showed 1-2Hz spike-wave activity in the temporo-parietal leads, with generalised spread. A diagnosis of LKS was made, and treatment adjusted accordingly with improvement in clinical state.

Conclusion: Though rare, LKS can occur in Nigerian children. A high index of suspicion is advised in a child with onset of acquired aphasia.

INTRODUCTION

Epileptic encephalopathies are a group of age-related severe epileptic disorders in which ongoing seizure activity progressively impact the disease negatively.[1] They often go unrecognised in Nigerian children and sometimes get passed off as generalised epileptiform disorders. Infantile spasms are the commonest of these rarely occurring disorders. Other epileptic encephalopathies include Ohtahara syndrome, Dravet Syndrome, Lennox-Gastaut Syndrome, Landau-Kleffner Syndrome [1] etcetera.

Landau-Kleffner Syndrome (LKS) is a rare childhood epileptic encephalopathy characterised by progressive deterioration of speech, cognitive impairment, behaviour changes, abnormal electroencephalographic findings and clinical seizure activity.[2] It commonly manifests in children between 3 – 8 years of age with previous normal development and is commoner in males. The site of epileptiform activity relates to the speech areas in the brain (temporal and parieto-occipital regions), and the electrical abnormalities are often activated by sleep.[2] Favourable response to therapy is possible with early identification and treatment,[3] and delay may result in permanent loss of speech.[3] Its aetiology remains unclear with likely heterogenous factors.[4-6] A high index of suspicion for LKS is important, particularly in children with presumed autistic spectrum disorder noticed to

be having a fluctuating clinical course or regression.[6]

A few hundred cases of LKS have been reported in the literature since its first description over seventy years ago.[2] An epidemiologic study of incidence reported about 1 in a million cases in Japan.[7] This is the only reported estimation of incidence and prevalence of LKS in literature. No report of incidence has been made in the Nigerian childhood population. This report outlines the clinical characteristics, management, and outcome noticed in a ten-year old Nigerian child who presented and was managed with this disorder.

CASE REPORT

The child is a ten-year old boy first seen at the Paediatric Neurology Clinic in LASUTH at the age of seven years. His illness started at the age of three years when he developed episodes of recurrent generalised tonic-clonic seizures during sleep, each lasting a few minutes. Seizure events progressively worsened from weekly to daily episodes. There were no other medical complaints. He was attended to by a General Practitioner in a private hospital. Electroencephalography (EEG) done showed focal sharp wave epileptiform activity with secondary generalisation against a background diffuse encephalopathy. He was commenced on Carbamazepine and Phenobarbitone. No improvement was observed with the seizures.

Two years later (at age 5 years), his speech slowed progressively and communication reduced. He developed difficulty understanding spoken words and subsequently lost acquired speech. He also became hyperactive with associated aggression, injurious behaviour, cognitive impairment and regression of milestones. He was placed on Risperidone and Levetiracetam. His symptoms improved for a while but his seizures later worsened, and he was brought to LASUTH for worsening of refractory seizures, cognitive impairment, behavioural difficulties and injurious behaviour at age 7 years.

He is the only child of a single mother, and a product of normal pregnancy, labour and puerperium. The neonatal period and developmental milestones were normal until the onset of symptoms at age three years. Nutrition and vaccination were satisfactory. No significant family history of chronic ill health was reported, and there was no history of symptomatic risk factors for seizures.

On examination, he was not dysmorphic, and his head circumference was normal for age. He was alert, aware of his environment, but hyperactive and restless. He said only a few words after much prompting and his speech was slurred. The cranial nerves were intact and there were no upper motor neuron signs. Other organ systems were intact. He however had old and active bruises and wounds on his forehead and arms on account of falls resulting from his seizures and injurious behaviour.

A diagnosis of refractory generalised epilepsy was made. It was presumed that his anti-epileptic drugs (AEDs) were inappropriate and dosages were suboptimal. His mother stated that drug administration was regular. The Carbamazepine and Phenobarbitone were discontinued, while Diazepam (Clobazam was unavailable) and Topiramate were commenced. His seizures reduced, and he achieved periods of seizure freedom. He however reacted to Topiramate with mood swings, irritability, urinary difficulty and continuous sneezing. Topiramate was discontinued and replaced with Lamotrigine, resulting in a reduction in seizure frequency and severity.

Five months later, his seizures got worse, and a repeat EEG done showed 1-2Hz spike and wave activity mostly in the temporo-parietal regions bilaterally with generalised spread, suggestive of LKS (Figure 1). Renal and liver function test results were normal. An MRI of the brain was not done. Prednisolone was subsequently added to his therapy. Hyperactivity and seizures reduced, made two-word phrases, no longer injured himself, had no new wounds, and his slurred speech improved. His current antiepileptic medications are Lamotrigine, Clobazam (replaced Diazepam), and Prednisolone. He has been stable in the last six months, commenced school, attends social events, and the mother resumed regular economic and social activities. His most recent EEG - a sleep EEG - also showed 1-2Hz spike and wave activity prominently in the bilateral temporo-parietal leads with generalised spread (Figure 2). He is being followed up in the Paediatric Neurology Clinic. Parental consent for this report was obtained.

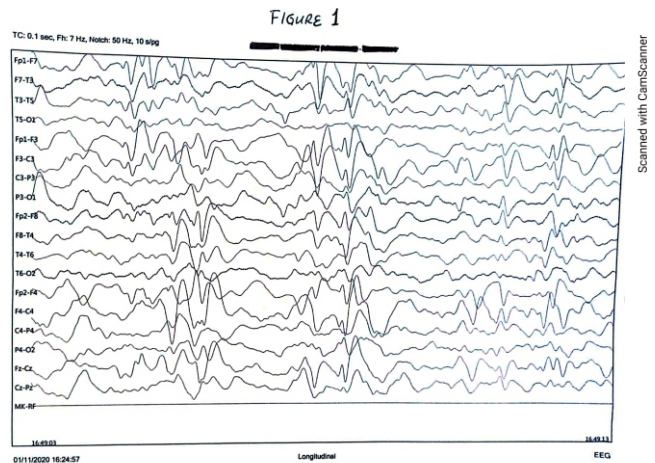


Figure 1: Awake EEG with 1-2Hz spike-wave epileptiform activity at age 8 years

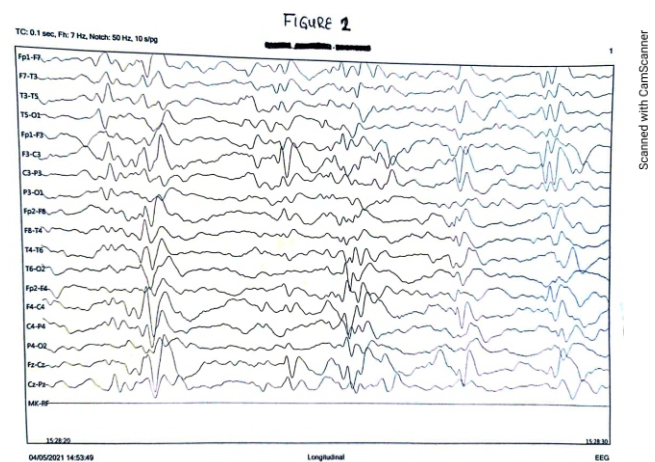


Figure 2: Sleep EEG with 1-2Hz spike wave epileptiform activity at age 10 years

DISCUSSION

Landau-Kleffner Syndrome - an epileptic aphasia – is a rarely occurring epileptic encephalopathy seen in children who had normal development until the onset of the disease.[1,2] Progressive or sudden loss of receptive and expressive speech are the main characteristics of this condition [2,3] and may be the sole presentation in some cases. Associated features are seizures, cognitive and behavioural impairment. Children aged 3-8 years are most often affected though the condition can present in children aged up to 20 years.[2] Landau-Kleffner Syndrome (LKS) was diagnosed in the index case, a male, at the age of 7 years. His symptoms started at age of three with brief, refractory generalised, tonic-clonic seizures during sleep, with postictal confusion, cognitive regression and hyperactivity. Two years later, he developed progressive loss of speech, with cognitive and behavioural deficits. This presentation aligns with what is commonly reported in literature.[1-3]

Seizures are common in children with LKS and can

present as focal motor, generalised tonic-clonic, head drops or as atypical absences.[2,3,6] They can be refractory with attendant socio-cognitive effects. The index case had difficulties with seizure control from onset and used six different AEDs. He also developed adverse reactions to Topiramate which had earlier controlled his seizures. Carbamazepine and Phenobarbitone are not recommended for treating seizures in LKS.[8,9] Seizure control was achieved after a change in AED following diagnosis of LKS. Literature reports a progressive decline in the incidence of seizures by middle adolescence.[8] The index patient is in his late childhood.

Language impairment in LKS often starts with receptive impairment and progression to expressive deficits.[2,6] The index case developed progressive non-responsiveness to calls or communication at home, leading to loss of speech. He also had associated behavioural deficits which worsened his illness, leading to the presentation at the psychiatric hospital and the use of Risperidone. Regression of speech in an otherwise normally growing child should raise suspicion of the occurrence of LKS. Autism Spectrum Disorder (ASD) is a possible differential, particularly in the presence of behavioural deficits. Regression of speech occurs earlier in children with ASD, often before age of 3 years. Single words are affected as compared to the loss of established vocabulary and language in children with LKS.[6,10,11] Also, children with ASD often have abnormal development of spoken language and impaired ability to initiate or sustain conversation.[10,11] Seizures and EEG abnormalities are also known to occur in children with ASD.[11,12]

The aetiology of LKS is unknown and debated. Finding structural deficits in the brain in cases of LKS is rare while genetic associations have been highlighted.[4,5] Structural, immunologic, infectious and traumatic factors have been linked with the incidence of LKS.[2,6] No aetiological factors were identifiable in the index case. The child's prenatal, perinatal, postnatal and developmental histories were uneventful up until the first presentation with seizures at the age of three years. Consanguinity was not reported in the parents and the family history was negative for seizure disorders, behavioural or cognitive deficits, and stigmata of genetic neurologic conditions. No history of preceding head trauma was elicited. However, a brain MRI was not done.

Clinical features and electroencephalography (EEG) are key in the diagnosis of LKS. Bilateral independent 1-3Hz spike-wave activity in the temporo-parietal leads, particularly in sleep with associated clinical features, are characteristic of LKS.[2,3,6,12] General spread is also reported as well as multifocal or unilateral spikes.[8,13,14] The clinical features of LKS and the characteristic EEG records in the index case are similar to what is reported in literature.[2,3,6,12]

Valproate, Clobazam, Lamotrigine, Topiramate, and Levetiracetam are recommended for use as AEDs in children with LKS while Phenobarbitone, Carbamazepine and Phenytoin are discouraged for use.[8,9] Phenytoin and Carbamazepine are thought to increase the duration of spike-wave activity in sleep and phenobarbitone intensifies behaviour problems while having no effect on language.[8,9] Clobazam is believed to significantly reduce continuous

spike-wave discharges and is associated with language improvement.[9] McKinney et al. reported that corticosteroids are efficacious in treating clinical and EEG abnormalities in LKS.[10] Phenobarbitone, Carbamazepine, Levetiracetam, Topiramate and Valproate were used at different stages of the disease in this patient. AED choice was influenced by the physician's expertise. Topiramate withdrawal was due to adverse drug reactions. Comorbid conditions sometimes are a greater burden on children with LKS and their families than the aphasia and seizures seen in the disease. Speech, cognition, behaviour and hyperactivity improved with appropriate therapy, and the child was able to resume school.

Late diagnosis is common in LKS[3,4] and occurred in this report due to the absence of an experienced Physician – often a Neurologist – to evaluate the child. The disease is a rare clinical condition that is often missed. Delay in diagnosis can result in loss of previously acquired speech. The index case had lost speech for four years before diagnosis was made. Despite subsequent use of appropriate medication and speech therapy, little speech was recovered and was limited to occasional 2-word phrases uttered in response to prompting from the mother.

This report highlights the consequence of the general lack of knowledge of LKS. A high index of suspicion is important, and children with sudden onset loss, or regression of speech - even in the absence of associated seizures - should be evaluated for possible LKS. A detailed history and conduct of a sleep EEG are advised. Early identification and institution of appropriate therapy greatly improve the chances of full or significant recovery of speech in diagnosed cases.

We conclude that though LKS is a rare condition, it does occur and can result in loss of speech and other significant comorbid effects in the Nigerian child.

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