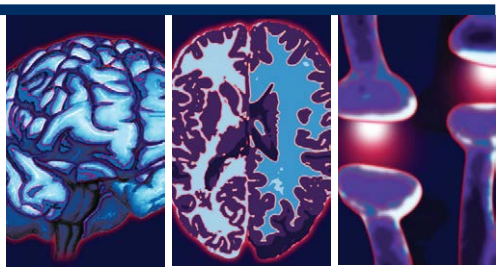
Case Report



Landau–Kleffner Syndrome: An Unusual Case With Progressive Ataxia Prior To Language Regression And Autistic-Like Behaviors

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ABSTRACT

Objective

To report a case with Landau-Kleffner syndrome (LKS) presenting with unusual clinical features.

Methods

The clinical features of the case including clinical manifestations, serial electroencephalography (EEG) outcomes, neuroimaging findings, neuropsychological outcomes, interventional approaches and long-term follow-up outcomes, were analyzed.

Results

This previously normal girl (3y10m), presented with progressive ataxia as an onset symptom, ensued with cognitive impairments and language regressions (characterized by verbal auditory agnosia and expressive aphasia), and autistic-like behaviors. She had no evidence of clinical seizures, with normal brain and spine MRI scans, intact auditory exams and normal brain auditory evoked potential, although the sleep- activated inter-ictal epileptiform discharges of EEG were revealed. The patient showed gradual resolution of symptoms with long-term high-dose steroids plus intravenous immunoglobulin (IVIG) regimens, in consistence with the gradual improvement of the outcomes of serial EEGs. She recovered and returned to normal kindergarten 1y1m after the onset of the disease, consistent with the normal EEG results. Her full-scale intelligence quotient (IQ) was 71 score, with verbal IQ 66 and performance IQ 81 respectively, tested at the time of 1y3m after the onset. The long-term prognosis of the case was good as she had good academic performance and was a monitor of the class at the time of her long-term follow-up of 5y8m after the onset.

Conclusion

LKS is heterogeneity entity, especially for those with the atypical onset such as ataxia, as well as absence of clinical seizures. The combination of long-term high-dose steroid plus IVIG regimens may be especially effective in LKS.

Key words

Landau-Kleffner syndrome (LKS), Ataxia, Language regressions, Autistic-like behaviors, Cognitive impairments, Steroid

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Introduction

Landau–Kleffner syndrome (LKS) or acquired epileptic aphasia, first described by Landau and kleffler in 1957 [1], is a rare childhood neurological disorder, being characterized by an acquired aphasia that emerges in relation to epileptiform electroencephalographic (EEG) abnormalities [1,2].

The most prominent defining feature of Landau-Kleffner syndrome is an acquired aphasia [2], whereas epileptic seizures are not a prerequisite for LKS. The typical type of aphasia is a verbal auditory agnosia, failure to provide a semantic significance to the different sounds. The loss of receptive language is followed or simultaneously occurred by expressive aphasia, a marked reduction in spontaneous speech. Other clinical manifestations include cognitive impairments and behavioral problems. These impairments may be global or focal, based on the location of the epileptic discharges, and progressive, presumably related to increasing epileptiform activity.

LKS is a heterogeneous entity, with rather significant variations in terms of age of onset, the aphasia's characteristics, EEG abnormalities, and comorbid cognitive and behavioral impairments [3], leading to the challenges of diagnosis. We reported an unusual LKS girl presenting with atypical onset prior to typical manifestations, and her long-term follow-up outcomes.

Case report

A previous healthy girl with LKS was reported, who was the 2nd child of the three children' family, a full-term baby (birth weight: 3.35 kg) via virginal sections following a normal 40 weeks pregnancy with unremarkable events and did not require support services after birth. The child's early developmental milestones achieved all the developmental domains including expressive and receptive language at the appropriate time with the babbling at 8 month, first word at 11 month, combining words available at the age of 2 years, when she generated sentences of 3 and 4 words with a good verbal comprehension. There was no other pertinent medical history before age 3 years and 10 months (3y10m). She had no known family history of epilepsy and other neurological disorders. Her older sister and younger brother did not have the same disorders as the girl had.

The age of onset was 3y10m, presenting with progressive ataxia prior to cognitive impairments and language regressions, and autistic-like behaviors. The clinical features of the case including clinical manifestations, neurological examinations, clinical investigations and treatments were summarized in the **Table 1**. The research protocol was approved by the Institutional Review Board of the Guangzhou Women and Children's Medical Center. Written informed consent was obtained from the parents.

Discussion

Landau-Kleffner syndrome (LKS) is a rare childhood epileptic encephalopathy, along with a deterioration of cognitive, sensory, and/or motor functions results from epileptic activity [4]. One Japanese study has reported that the incidence of children with LKS aged 5～14 years was around 1 in a million in Japan [5].

■ LKS and onset

Age of onset: LKS commonly occurs between the ages of 3 and 7 years based on the ICD-10 guidelines, although onset as early as 18～22 months and as late as 13～14 years has also been stated. The mean age of onset of aphasia was 4.8 years with standard deviation 2.2 years was revealed, according to the analysis of 268 out of 337 LKS cases from the published English literatures [3]. Of which, the most cases (around 90%) presenting their onset was between the ages of 2 and 7 years old and approximately one third of these cases regressed before their 4 years old [3]. The age of onset of the case in our study was 3 years and 10 months, like most reported other cases before their fourth birthday, although she had an unusual neurological symptom's onset.

Symptom of onset: The onset of LKS may be insidious or sudden. One study reported that the language deterioration was the onset symptom found in the most cases [6], whereas other studies have stated that the epileptic seizures being the initial symptoms more often than the language disturbances [7]. In some rare cases, the parents claimed that they in fact gradually lost contact with their pediatric subjects, which might be attributed to the psychogenic regression [8].

In the current study, a previously normal girl with an onset of progressive ataxia without obvious precipitating factors at around 2-months prior to cognitive impairments and language regressions, and behavioral disturbances was reported. One Japanese study [9] had ever reported one case whose symptom of onset somewhat similar to our case, having ataxia before language regressions,

Table 1. The clinical process of the case

Phases/Date of visit /Visiting methods	Clinical manifestations	Neurological examinations	Main clinical investigations	Treatments
A/26-11-2012~12-12-20	1.Progressive ataxia without precipitating factors at the age of onset 3y10m; 2. The unusual posture when up and down stairs as the symptom of onset noted by parent; 3. Followed by the abnormal gait with wide-base, walking unsteadily and easily falling	NE at admission: Normal except cerebellar signs with wise-base gait and truncal ataxia.	1. CSF: Normal;	1. Progressive cerebellar ataxia was diagnosed.
	down.			2. Treated with 4~day (0.5
12/Hospitalization at local tertiary medical college affiliated hospital (after 2 days of onset).			2. Bilateral calcaneus, lumbar and pelvic x ray: Normal;	g/kg/d) IVIG + 3~day high dose (20 mg/ kg/d) MPN, followed by 4~day IV Dex (0.25 mg/kg/d).
			3.1~hour VEEG: Sleep-activity bilateral central-temporal IEDs without clinical events;	3. A slight improvement on sitting posture after treatment.
			4. Brain CT/MRI and Spine MRI	
			(Scan): Normal.	
B/12-12-2012~21-12-20	During hospitalization:	NE at admission: Normal except walking unsteadily with wide-base gait.	1. Repeated CSF: Normal;	Oral prednisone (1 mg/kg/d) was continued.
	1. Markedly improved in the walking posture after treatment with just left slightly unstable walking posture at discharge; 2. The status of restlessness or agitation noted sometimes.			
12/Hospitalization at GZWCMC.			2. 1~hour VEEG: Normal;	
			3. Repeated brain MRI (Scan + Contrast): Normal	
C/08-01-2013/Outpatien t at GZWCMC.	1. Ataxia was complete recovery;	NE at outpatient: Walking posture normal, but less communicated	Nil	Oral prednisone was tapered off after a total
	2. Somewhat less desires to communicate with others and less lively during daily life noted by parent.	with doctor.		1.75 months course of steroid.
D/08-01-2013~04-03-20	1. Verbal auditory agnosia: Did not understand what parents' or grandmother's said, e.g. asking her to call grandmother, she went to get a broom instead. 2. Expressive aphasia: Almost simultaneously, spontaneous speech gradually reduced with paraphasias and impairments in fluency and articulation, and even mutism sometimes. 3. Autistic-like behaviors: Including hyperactive, irritable, impulsivity, just did or played something she liked, stayed alone, no response to name call, although sometimes could take telephone up when ringing. 4. Others: Intelligence, memory and learning	Nil	Nil	Nil
	abilities backward noted by parent.			
13/ At home.				

E/04-03-2013~21-03-20	During hospitalization:	NE at admission: Normal except less spontaneous	1.Repeated brain MRI (Scan + Contrast) and MRA: Normal; 2. Auditory exam and BAEP:	1. The suspected LKS was made;
	1. Some abnormal behaviors: occupied the bench, stereotyped behaviors (e.g. repeatedly touched her	speech with	Normal;	2. Repeated 5~day course
13/Hospitalization at GZWCMC.				(0.4 g /kg/d) IVIG.
				3.Parent hesitated to
	toes), and weird behaviors (e.g. went to other wards to get the high-heeled shoes). 2. A little bit improved in communication, and a slightly more vocalizations and more frequencies of	Dysarthria and non-meaningful vocalizations; reluctant to communicate	3. Two 1~hour VEEGs tested at the interval of 7 days, with the nearly similar outcomes: Sleep-activity bilateral frontal-temporal IEDs without	accept the long-term high-dose steroid regimen or AEDs for her daughter, instead choosing to discharge for further observation the changes of her daughter at home.
	laughs after IVIG treatment.	with others.	clinical events.	
F/21-03-2103~10-04-20	1. Some abnormal behaviors:Hyperactivity, irritability,easily temper tantrum, compulsive behaviors (insisting on grandmother should company with her every night when sleep),stereotype behaviors	Nil	Nil	Nil
13/At home.	(repeatedly play her own toes, liked to sit on the ground and repeatedly moved back and fro), picking something on the ground into mouth.			
	2. Unlike to actively communicate with others and less spontaneous speech with dysarthria sometimes. 3.Liked to rummage through others'			
	belongings.			
G/10-04-2013~25-04-20	During hospitalization:	NE at admission:	1~hour VEEG: Sleep-activity left	1. The long-term
13/Hospitalization at	1. After initial 3~day course MPN	Spontaneous	side frontal-temporal IEDs	high-dose steroid treatment regimen given.
GZWCMC.	given, eye-contact showed a little bit	language less	without clinical events.	
	better. 2. The frequencies of	with dysarthria;		2. The dose of MPN was gradually tapered from 10-5-2.5-1.25 mg/kg/d at the 3 days interval, and changed into the oral prednisone (1.5mg/kg/d) at discharge.
	eye-contact better and temper tantrum	unwilling to		
	less, after 8~day course MPN	answer.		
	treatment. 3. At discharge, she could			
	even erect her thumb as a "praise			
	symbol"; more vocalizations, although			
	only with "Yo, Yo" sounds; more			
	positive attitudes about circumstances.			
H/08-05-2013~14-05-20	1. At home (25-04-2017~08-05-2017):	NE at admission:	1~hour VEEG: Sleep-activity left	1. Repeated 5~day course of IVIG (400 mg/kg/d).
				2. Oral prednisone (1.5mg/kg/d) continued.

13/Hospitalization at	Behavior disturbances getting better,	Could actively	side frontal IEDs without clinical	
GZWCMC.	e.g. controlling emotions better; no	laugh at doctor	events.	
	longer taking others' things; could	with "Yo, Yo"		
	even happily say "grandmother" when	sounds, and even		
	returned home after discharge last	could response		
	time, although no more spontaneous	and give her toy		
	words thereafter; a couple of times,	to doctor when		
	could even eat rice by herself. 2.	asked, although		
	During hospitalization: Behaviors	clapping her		
	getting more organized; more	palms purposelessly sometimes.		
	utterance of "Yo, Yo" sounds; could eat between-meal nibbles by herself, although still need to be fed by mother three meals a day; sometimes still liked to clap her palms purposelessly.			
I/29-05-2013~01-06-201	1. At home (14-05-2013~29-05-2013):	NE at admission:	1~hour VEEG: Sleep-activity	1. Oral prednisone (1.0mg/kg/d) continued.
3/Hospitalization at	Better controlling her emotions; could	Could answer	left side frontal IEDs without	
GZWCMC.	follow some instructions. 2. During	simple questions;	clinical events.	
	hospitalization: Said simple words;	even could recite		
	could understand instructions sometimes; unwilling to answer	whole Chinese		
	sometimes.	poem "goose"		
		when asked.		
J/29-07-2013~01-08-20	1. At home (01-06-2013~29-07-2013):	NE at admission:	1~hour VEEG: Normal.	1. The diagnosis made. Of confirmative LKS was
				2. Oral prednisone (0.5mg/kg/d) continued.
13/Hospitalization at	Language ability and behavior	Could take and		
GZWCMC	disturbances markedly improved with	show a toy to doctor and say		
(after 8 months of onset).	almost returned to normal level; could	"garden baby";		
	eat by self; played with other children;	Corporation during NE.		
	picked someone she liked. 2. During			
	hospitalization: Spoke freely, and			
	acted according to instructions.			
K/28-08-2013/Outpatien t at GZWCMC.	At home (01-08-2013~28-08-2013):	NE at outpatient: Saw doctor with	Nil	Oral prednisone (0.5mg/kg/d) continued.
		smile.		
	Uneventful with eager to go to school.			
L/25-09-2013/Outpatien t at GZWCMC.	At home (28-08-2013~25-09-2013):	Saw doctor with	Nil	Oral prednisone (0.25mg/kg/d) continued.
	Uneventful with eager to go to school; liked to played with other children	smile; answered accordingly.		
M/23-10-2013/Outpatie	At home (25-09-2013~23-10-2013):	Happily laughed	1~hour VEEG: Normal	Oral prednisone 0.125 mg/kg/d) continued.
	Returned to normal child's situation with eager to go to school, and loved to play with other children.			
nt at GZWCMC.		when knew she		
		could return to		
		kindergarten.		

N/27-12-2013/Outpatien t at GZWCMC (1y1m	At home (23-10-2013~27-12-2013):	At outpatient:	Nil	Prednisone tapered off
after onset).	Returned to normal kindergarten as a student; having a desire to excel.	In response to the point when asked.		
O/03-03-2014/outpatient at GZWCMC (1y3m	Uneventful at home and school.	At outpatient:	WSIC-IV：FIQ：71 ；PIQ: 81 ； VIQ：66.	Nil
after onset).		In response to the point when asked.		
P/26-07-2017/Telephone	PG 1 student and served as a class	Nil	Nil	Nil
follow-up (after 4y8m of	Monitor (Teacher's comment: enthusiastic, kind and responsible)			
onset)	with good academic performance such			
	as Chinese 98.5 and Math 100 at final			
	exam of the semester.			
Q/26-08-2018/Telephon e follow-up (5y8m after	PG 2 student and served as a class monitor with good academic	Nil	Nil	Nil
onset)	performances.			
ABB: LKS: Landau–Kleffner syndrome; y: year; m: month; NE: Neurological Examinations; CSF: Cerebral Spinal Fluid; MRI: Magnetic Resonance Imaging; CT: Computed Tomography; VEEG: Video Electroencephalography; IEDs: Interictal Epileptiform Discharges; GZWCMC: Guangzhou Women and Children's Medical Center; IV: Intravenous; Dex: Dexamethasone; MPN: Methylprednisolone; IVIG: Intravenous Immunoglobulin; MRA: Magnetic Resonance Angiography; BAEP: Brainstem Auditory Evoked Potential; AEDs: Antiepileptic Drugs; WSIC-IV: Wechsler Intelligence Scale for Children 4th Version; FSIQ: Full Scale Intelligence Quotient; VIQ: Verbal Intelligence Quotient; PIQ: Performance Intelligence Quotient. PG: Primary Grade.				

along with hemiparesis, urinary incontinence and convulsions at the age of 4 years and 10 months, followed by acquired aphasia a year later.

■ LKS and EEG findings/seizures

Despite the severe electroencephalographic abnormalities, seizures never occur in the 20–30% of LKS patients [10]. The types of the seizures reported in the LKS can be different, including partial complex, partial clonic, generalized tonic-clonic, and atonic seizures [3,11], although absence of clinical seizures was found in our case through the course.

No single epileptiform abnormality could consist of all cases of LKS [12]. The electroencephalographic manifestations of the epileptiform disorder included generalized, bilateral, focal or multifocal, spike or spike-wave discharges (1～3 Hz), usually with a central or temporal lobe predominance [13]. The abnormalities were frequently activated by sleep, particularly at sleep onset [13] and during slow wave sleep. The pattern of continuous spikes and

waves during slow sleep (CSWS) or electrical status epilepticus in sleep (ESES) in patients with LKS tends to be unilateral or clearly lateralized. The presence of CSWS/ESES in LKS appears to relate to the continuation of language impairments, and if lasting more than 3 years may be associated with the long-term language deficits [14].

The presence of CSWS/ESES is not a prerequisite for a diagnosis of LKS. In one case series of 25 LKS patients, the CSWS pattern was found in only 9 patients [15]. Another study [16] reported three children whose sleep EEG with normal outcomes after several months of the onset of language regression, although a final diagnosis of LKS was confirmed when subsequent sleep EEG showed interictal epileptiform discharges (IEDs). Similarly, our case did not demonstrate the CSWS/ESES, instead consistent with sleep-activated IEDs.

The symptoms of the case in our study were related to the severity of the epileptiform activity. For instance, the consistent changes of sleep-activated bilateral frontal, central and temporal IEDs (1-3 Hz) were found before steroid plus IVIG treatment **(Table 1: A)**. Subsequently, the improvements of ataxia associated with the normal EEG after the 1st steroid plus treatment **(Table 1: B)**; the gradual ameliorations of autistic-like behaviors as well as language ability either on auditory or on expressive after the 2nd long-term high dose steroid plus treatment, in accordance with the gradual improvements of serial EEG outcomes e.g. from bilateral IEDs **(Table 1: E)** to unilateral IEDs **(Table 1: G, H, I)**, and final normal EEG **(Table 1: J, M)**.

■ LKS and language regressions

The language loss is characterized by a severe disturbance of auditory language comprehension and combined with a substantial disruption of expressive language [3]. Children may fail to orient to their name being called or comprehend orally presented information that they could previously attend to and understand without difficulty. Similarly, current case who did not understand what parents or grandmother's said, e.g. asking her to call grandmother, she went to get a broom instead **(Table 1: D)**, although the outcomes of auditory exams and brainstem auditory evoked potentials were normal . Similarly, one study included 29 LKS patients reported all had moderate to severe auditory verbal agnosia [10].

Basically, the receptive language difficulties were accompanied or closely followed by reductions and distortions of verbal output. Speech became "garbled" and dysfluent, marked by articulatory errors, word-finding difficulties, and declines in the frequency, length, and complexity of verbal utterances [3]. Likewise, our case occurred both in the verbal auditory agnosia and expressive aphasia simultaneously, gradually developed just only with "Yo Yo" jargon, although being mutism at times **(Table 1: D)**.

■ LKS and behavioral disturbances/ cognitive impairments

About two thirds of children with LKS emerge behavioral disturbances. The most frequently observed behavioral problems are attentional deficits, impulsivity, distractibility, and hyperactivity; others consisted of aggression, anger with tantrums, withdrawal, social deficits, and sometimes autistic-like behaviors such as avoidance and withdrawal, resistance to change in daily activity, gestural stereotypes, echolalia and echopraxia, hyperlexia, or psychotic-like presentations [3,17].

Nonlinguistic cognitive functions were affected in approximately half of the patients [18]. A subtle behavioral or cognitive manifestation of epilepsy can be defined as follows with the two ways [19]. First, epileptiform discharges not presenting as obvious seizures may nevertheless affect cognition and/or behavior. Second, the actual seizures may be obvious but the way they affect cognition or behavior may not be. These impairments may be global or focal, depending on the location of the epileptic discharges, and progressive, presumably related to increasing epileptiform activity. Studies demonstrated that interictal epileptiform activity could disrupt cognition. Similarly, our case existed cognitive dysfunction, such as memory decline and learning disorder, as well as behavioral disturbances such as autistic like behaviors **(Table 1)**, which was related to sleep-activity IEDs of EEG. In LKS, the autistic features can be the results of the epilepsy itself [20].

A retrospective study of 14 LKS children [21] has revealed that the 57% cases evidenced attentional or other behavioral problems, 50~57% having deficits in auditory working memory and verbal memory. Academically, the majority had poor reading fluency and comprehension, and 50% exhibited difficulty with mathematics. The global intellectual functioning ranged from 59 to 101. As a contrast, the full scale IQ of our

case was 71 tested at the time after her returning to kindergarten, although the verbal IQ was still lower than that of performance IQ (Table 1: O).

■ LKS and etiology

The etiology of LKS is still unknown [22], but involvement of the frontal and/or temporal lobes is frequently stated [23]. It is unclear whether LKS represents the late manifestation of pre-existing anomalies in neurodevelopment or the result of acquired pathogenetic influences such as an abnormal autoimmune response or both. Like our case (Table 1), the most effective treatment has been used with long-term cortico-therapy in high doses, which supporting possibilities the presumption that the participation of autoimmune factors in the origin of LKS. Recently, the striking finding of mutations in the N-methyl-D-aspartate (NMDA) receptor subunit gene GRIN2A as the first monogenic cause in up to 20% of patients with epilepsy-aphasia spectrum including LKS suggests that excitatory glutamate receptors play a key role in these disorders [24, 25], although our case didn't carry out genetic research.

MRI scans are normal in most LKS cases, but PET and SPECT studies have showed focal or multifocal changes or perfusion asymmetries predominantly affecting, but not restricted to the temporal regions [26]. Functional MRI study [27] suggested intact temporal lobe processing but an altered temporal to frontal connectivity.

■ LKS and diagnosis

The symptoms of LKS are heterogeneous, and these symptoms can lead to misdiagnosis, which makes the EEG examination as an important determinant in the differential diagnosis. One national study found that the parents of children with LKS often struggled with the local health authorities to obtain the correct diagnosis and adequate help [6].

A delay between initial symptoms and definitive diagnosis is not unusual in rare diseases. Sometimes, rarely also the mild neurological symptomatology can be seen as accompanying signs of the disease. Likewise, our case not only developed atypical initial neurological symptoms of ataxia, but also did not experience epileptic seizures; secondly the EEG pattern did not demonstrate CSWS/ESES, instead with IEDs; thirdly, the initial symptoms of behavioral problems and language regression developed insidiously. For instance, the status of restlessness or agitation occurred only sometimes during hospitalization (Table 1: B) or somewhat less desire to communicate with others at outpatient clinic (Table 1: C) at that time when the symptom of ataxia was recovery; Furthermore, there were no family history of seizures of this case. Taken the above evidences together, causing the challenges to diagnose of LKS for the case. Specifically, initial diagnosis of progressive cerebellar ataxia (Table 1: A), ensued the suspected LKS (behavioral problems and language regressions and cognitive impairments, plus sleep-activated IEDs), followed confirmative LKS diagnosis (constellation of clinical findings plus the severity of symptoms in accordance with the changes of serial EEGs outcomes) (Table 1).

■ LKS and Treatment

In view of the relationship between the occurrence of CSWS/ESES and the language deterioration, early and aggressive therapy is mandatory [10]. Early effective treatment may reverse some of these features [28]. Clinical practice suggests that amelioration in neuropsychological functioning may be related to control of ongoing epileptiform activity in LKS. Several antiepileptic drugs (AEDs), such as valproate, ethosuximide, clonazepam, or clobazam have been demonstrated to be effective.

However, standard antiepileptic drugs often control the clinical seizure activity but may not improve the neuropsychologic dysfunction in LKS. Steroids seem to have more long-lasting effects. Early diagnosis, before mutism or global deterioration develops, appears to be esential for effective therapy with minimal neuropsychological sequelae [29]. The series including 44 patients treated with hydrocortisone starting at 5 mg/kg/day with a maintenance dose of 2 mg/kg/day until the end of a full year of treatment [30]. More than 75% of the patients responded to this regimen within the first 3 months, with normalization of the EEG in about half of them. Although relapse occurred in 14 patients, 20 patients (45.4%) were long-term responders. As a contrast, our steroids long-term high-dose regimen treated with methylprednisolone beginning at 10 mg/kg/days with a maintenance dose of 1mg / kg/day of prednisone until the end of a 7.5 months of treatment plus the intermittent infusions of intravenous immunoglobulin (IVIG) (Table 1: G~M). In terms of novel treatments, adrenocorticotropic hormone is currently preferred due to its clinical and electroencephalographic efficacy.

Amongst the other therapeutic approaches, the benefits of IVIG were not confirmed in a recent series [31], although the promising result in some cases has also been reported. Data on the use of vagus nerve stimulation and ketogenic diet were too scarce to draw conclusions [32, 33]. In addition, surgery using multiple subpial transections can be considered in the refractory cases, although negative outcomes were also argued [34].

■ LKS and prognosis

The long-term outcome of LKS is not completely clear. The outcome of the disease is variable, and serious disturbances of language remain sometimes until adulthood [35]. In addition, the course of recovery in LKS is also comparatively slow or limited. Likewise, our case returned to normal school 1y1m after onset **(Table 1: N)**.

Some studies indicated that whether the aphasia onset occurred before or after 5 years of age had an important impact on long-term outcome [36], but other studies did not confirm this prospective [7]. Our case had relatively good long-term outcomes, although whose onset age was before age 5 **(Table 1: A)**. Nevertheless, long-term language and language-related difficulties may also occur with later onset [7]. One study [6] found that children who had experienced a short initial aphasic period and marked fluctuations in speech ability had the best prognosis with respect to future language outcome.

Patients with LKS had an overall poor quality of life [7], the prognosis of LKS is known to be difficult to predict and uncertain since speech deficiencies typically persist [36]. Fortunately, the long-term prognosis of the case in our study was good as she had a good academic performances, as well as served as monitor of the class 5y8m after the onset **(Table 1: P & Q)**, although she did not repeat IQ test.

Conclusion

LKS is heterogeneity entity, especially for those with the atypical onset such as ataxia, as well as absence of clinical seizures. The combination of long-term high-dose steroid plus IVIG regimens may be especially effective in LKS.

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Conflict of Interest

There are no conflicts of interest for all authors in this study.

Author Contributions

CWX conceptualized and drafted the study. CWX, YSD, GYY, ZYN and ZKL clinically treated and long-term assessed the subject. NSY, ZYY, PBW and OSP performed serial neuroelectrophysiological assessments. All authors have agreed on the final version.

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