

Landau-Kleffner syndrome: Relation of clinical, EEG and Tc-99m-HMPAO brain SPECT findings and improvement in EEG after treatment

Elvan SAYIT,* Eray DIRİK,** Hatice DURAK,*** Nevin UZUNER,**
Özden ANAL** and Necla T. ÇEVİK**

**Department of Nuclear Medicine, Celal Bayar University Faculty of Medicine, Manisa, Turkey
Departments of **Pediatrics and ***Nuclear Medicine, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey*

Landau-Kleffner syndrome (LKS) is a rare childhood disorder characterized by acquired aphasia with seizures and electroencephalogram (EEG) abnormalities. Tc-99m-HMPAO SPECT was performed in three right handed children with LKS. A relative decrease in perfusion was found in the left temporal cortex of all three patients and also in the left frontoparietal cortex of one patient with hyperkinetic behavior. Degree of regional cerebral perfusion impairment did not correlate with the severity of clinical and EEG abnormalities. Asymmetrical temporoparietal perfusion appears characteristic of LKS. SPECT findings in LKS were evaluated as useful in elucidating the pathogenic features of the disorder in the brain.

Key words: Landau-Kleffner syndrome, acquired aphasia, electroencephalography, single photon emission computed tomography

INTRODUCTION

LANDAU-KLEFFNER SYNDROME (LKS), first described by Landau and Kleffner in 1957, is an acquired aphasia associated with seizures and electroencephalographic (EEG) abnormalities.¹ It is a rare childhood epileptic syndrome, also known as acquired epileptic aphasia (AEA) of unknown etiology.² Psychomotor and behavioral problems are often observed.³ EEG abnormalities are frequently in the form of continuous spike-waves during slow-wave sleep (CSWS)⁴ but multifocal spike and spike-wave discharges are seen on EEG as well.⁴⁻⁶ Prognosis of this disorder is poor; though epileptic seizures can be controlled by antiepileptic medication, language disturbance persists.⁷⁻¹⁰ Cerebral perfusion changes have been reported in LKS patients on single photon emission computed tomography (SPECT), and asymmetrical temporoparietal perfusion appeared as a characteristic of LKS.¹¹ We have performed Tc-99m hexamethylene propyleneamine oxime (Tc-99m-HMPAO) brain SPECT to demonstrate cerebral perfusion abnormalities in three children with LKS.

Received June 7, 1999, revision accepted August 16, 1999.
For reprint contact: Elvan Sayit, M.D., Celal Bayar Üniversitesi
Tıp Fakültesi Nükleer Tıp A.B.D., 45030 Manisa, TURKEY.

MATERIALS AND METHODS

Brain SPECT was performed after administering 222 MBq Tc-99m-HMPAO (Ceretek, Amersham International, UK) intravenously when the child was in a quiet and dimmed room. Chloralhydrate was given for sedation 10 minutes after Tc-99m-HMPAO administration. Imaging was performed 30 minutes after injection, with a three headed gamma camera (GE/CGR Neurocam, Horsholm, Denmark) equipped with high resolution collimators. One hundred twenty-eight images of 35 second duration in a 64 × 64 matrix were obtained over 360 degrees. Two pixel thick slices in coronal and sagittal planes were obtained after reconstruction of two pixel slices in the transaxial plane parallel to the orbitomeatal line. Chang attenuation correction and Butterworth filter (Cutoff frequency: 0.4, power factor: 10) were used. Images were evaluated independently by two observers.

All of the three children were drug free (for at least three weeks) at the time of SPECT scanning. All patients with LKS had acquired aphasia without motor deficits and no sign of recent brain lesion. Primary hearing loss and mental retardation were excluded as the cause of the linguistic problems. No evidence of structural brain disorder was found by either computerized tomography (CT) or magnetic resonance imaging (MRI). All had a

follow up of at least 2 years.

CASE REPORTS

Case 1. A five-year-old right handed boy had a history of birth asphyxia but early development was normal. He walked and used single words by 16 months and started putting words together by 24 months. Speech gradually regressed at the age of 2.5 years, though he could follow a few oral commands. There was no history of seizures and systemic examination was normal. Spontaneous speech was limited to a few meaningless utterances. EEG showed CSWS.

Audiometry, brain stem auditory evoked responses (BAER) and brain CT were normal. He was treated first with Na-valproate and clonazepam but there was no improvement. Dexamethasone (4 mg/day) was added to the treatment regimen, and 2 months later EEG findings were improved but language disorder persisted. At follow up, monosyllabic speech was resumed but response to oral commands was inadequate. Tc-99m-HMPAO SPECT was performed and mildly decreased perfusion in the left temporal cortex was seen (Fig. 1).

Case 2. A nine-year-old right handed boy, product of a full term normal delivery achieved developmental milestones at appropriate ages. Single word speech began at 18 months and by 24 months he used sentences containing two to three words. At the age of 5 years, his speech became disturbed and a behavior change occurred. He had an episode of generalized tonic clonic seizures followed by irritability and hyperkinetic behavior at 6 years. At the time of examination, he was hyperkinetic but could carry out simple but not complex commands. There were no other neurological deficits. EEG showed continuous frontoparietal spike and wave discharges. Cranial CT, cranial MRI, BAER and audiometry were normal. Carbamazepine followed by Na-valproate was started for treatment. Repeated EEG was within normal limits.

There was no recurrence of seizures and his language and behavior improved greatly. Noticeable decreased perfusion in the left temporoparietal cortex and mildly decreased perfusion in the left orbitofrontal cortex were found on brain SPECT (Fig. 2).

Case 3. A seven-year-old right handed boy was the product of a full term normal delivery and had normal developmental milestones. Monosyllabic speech began at the age of 16 months and sentences appeared by 2 years. Right partial motor seizures with secondary generalization began at the age of 3. Seizure frequency was 1–2 per month and decreased to once a year afterwards. He became less responsive to verbal instructions and expressive language decreased noticeably. There was no spontaneous speech, only occasional single word responses to questions. Neurological examination was normal except for language disorder. EEG showed CSWS. Seizures were controlled with carbamazepine and Na-valproate.

At follow up, EEG was in normal limits and improvement in language and no recurrence of seizures were observed. Greatly decreased perfusion was found in the left temporal cortex in brain SPECT (Fig. 3).

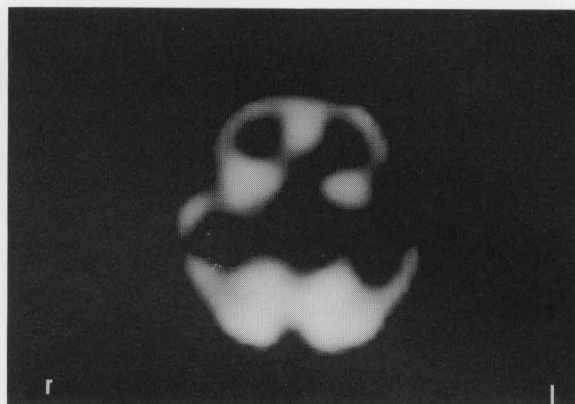
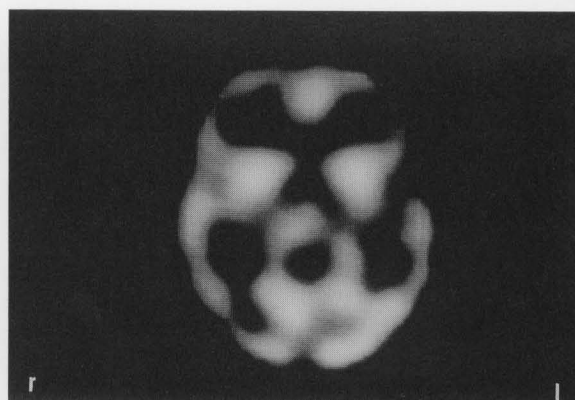
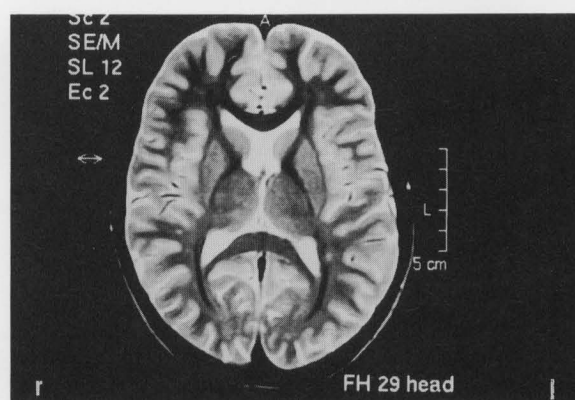


Fig. 1 Two pixel thick transaxial slice from Tc-99m-HMPAO brain SPECT of case 1. There is a relative decrease in cerebral perfusion involving the left temporal cortex.



a



b

Fig. 2 a) Two pixel thick transaxial slices of case 2. Decreased perfusion in left temporoparietal cortex and mildly decreased perfusion in left orbitofrontal cortex are observed. b) Corresponding MR image shows no abnormality.

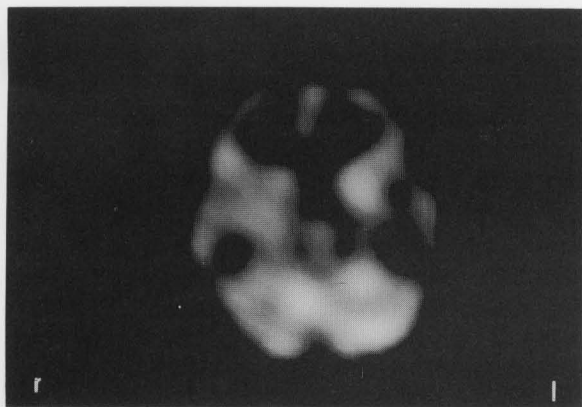


Fig. 3 Two pixel thick transaxial slice of case 3 reveal markedly decreased cortical perfusion involving the left temporal cortex.

DISCUSSION

Two pediatric epileptic syndromes, LKS and epilepsy with continuous spike-waves during slow-wave sleep, have much in common and cannot be clearly differentiated, so they are likely to represent different aspects of a single syndrome.¹² Landau and Kleffner¹ reported that persistent convulsive discharge in brain tissue results in functional ablation of areas responsible for normal linguistic behavior. Several other authors agree that the continuous spike-waves during slow-wave sleep are responsible for the appearance of complex and severe neurologic impairment and psychiatric disturbances.⁵⁻⁷

In LKS, the seizures may be partial, generalized, tonic clonic and myoclonic. Cases 2 and 3 had generalized tonic clonic seizures but case 1 had no clinical seizures, even though CSWS was present. Similar cases of acquired aphasia have been reported with EEG seizure activity but no clinical seizures.⁷ Behavior problems, particularly hyperkinetic behavior, are seen frequently, as in case 2. In cases 1 and 3, neurological examination was normal except for the language disturbance. Case 2 had hyperactivity and language disturbance.

The relationship between EEG abnormalities and neuropsychological disorders is as yet unclear. Landau and Kleffner¹ observed that the diurnal EEG and speech abnormalities developed in parallel to each other and concluded that EEG abnormalities were directly related to functional disorganization of the speech centers. In our study, case 1 with the most abnormal EEG had the most disturbed speech. All three patients had a basically similar pattern of perfusion abnormality in Tc-99m-HMPAO SPECT. Though it seems not possible to draw a conclusion from only these three cases, we could not observe any correlation between the degree of perfusion impairment and the severity of the clinical and EEG abnormalities. This issue needs further study to clarify the relationship. Case 1 had mildly decreased and case 3 had markedly

decreased Tc-99m-HMPAO uptake in the left temporal cortex. Case 2 had greatly decreased Tc-99m-HMPAO uptake in the left temporoparietal cortex; as well as mildly decreased uptake in the left orbitofrontal cortex. This case had hyperkinetic behavior and the perfusion abnormality involved the frontal cortex. The presence of perfusion defects most often involving the central frontal lobes in hyperactivity disorders has also been suggested by Lou et al.¹³ The frontal lobe hypoperfusion may therefore be due to the behavioral abnormality in this patient.

No drug seems effective in abolishing CSWS in the treatment regimen started after SPECT imaging. Combined treatments with antiepileptic drugs such as valproate, ethosuximide or clonazepam, sleep-modifying drugs such as amitriptyline or amphetamine and corticosteroids resulted in transient improvement in speech, seizures and EEG abnormalities.^{4,7-10} Prognosis of this disorder is poor; although epileptic seizures may be controlled by antiepileptic drugs or corticosteroids, noticeable language difficulties frequently persist.¹⁰ In cases 2 and 3, seizures were controlled with Na-valproate and carbamazepine and their EEG and language disorders were notably improved, but in case 1, Na-valproate and clonazepam were unable to cause any improvement. Two months after the addition of dexamethasone to the treatment regimen, EEG findings were improved but language disorder persisted.

Asymmetrical temporoparietal perfusion appears to be characteristic of LKS, and may be helpful in differentiating from findings in other childhood linguistic and behavioral disturbances.¹¹

It is not clear yet whether Tc-99m-HMPAO SPECT may be used as a prognostic indicator in LKS. But it may allow further definition of pathogenic mechanisms of LKS and related disorders.

REFERENCES

1. Landau W, Kleffner F. Syndrome of acquired aphasia with convulsive disorder in children. *Neurology* 7: 523-530, 1957.
2. Commission on classification and terminology of the International League Against Epilepsy. Proposal for revised classification of epilepsies and epileptic syndromes. *Epilepsia* 30: 389-399, 1989.
3. Roulet Perez E, Davidoff U, Despland P, Deonna T. Mental and behavioral deterioration of children with epilepsy and CSWS; Acquired epileptic frontal syndrome. *Dev Med Child Neurol* 35: 661-674, 1993.
4. Deonna T, Peter C, Ziegler A. Adult follow up of the acquired aphasia-epilepsy syndrome in childhood. Report of 7 cases. *Neuropediatrics* 20: 32-138, 1989.
5. Tasinani C, Berreau M, Dravet C, Dalla Bernardina B, Roger J. Epilepsy with continuous spikes and waves during slow sleep. In: Bureau M, Dravet C, Dreifuss FE, Perret A, Wolf P, eds., *Epileptic Syndromes in Infancy Childhood and Adolescence*. London: John Libbey Company, pp. 194-204, 1992.

6. Rinthana PJ, Chugani HT, Sankar R. Landau-Kleffner syndrome with continuous spikes and waves during slow wave sleep. *J Child Neur* 10: 127–133, 1995.
7. Hirsch E, Marescaux C, Maquet P, Metz Lutz MN, Kiesman M, Salmon E, et al. Landau-Kleffner syndrome: a clinical and EEG study of five cases. *Epilepsia* 31: 756–767, 1990.
8. Caraballo R, Grillo E, Sprano A, Fejerman N. Long term steroid treatment in two patient with acquired epileptic aphasia. *Pediatr Neurol* 8: 364, 1992.
9. De Negri M. Developmental dysphasias, epilepsy and Landau-Kleffner syndrome. *Brain Dev* 15 (4): 319, 1993.
10. Soprano AM, Garcia EF, Caraballo R, Fejerman N. Acquired epileptic aphasia: neuropsychologic follow-up of 12 patients. *Pediatr Neurol* 11: 230–235, 1994.
11. O'Tuama LA, Urion DK, Janicek MJ, Treves ST, Bjornson B, Moriarty JM. Regional cerebral perfusion in Landau-Kleffner syndrome and related childhood aphasias. *J Nucl Med* 33: 1758–1765, 1992.
12. Park Y, Hoffman JM, Radtke AR, Delong R. Focal cerebral metabolic abnormality in a patient with continuous spike waves during slow wave sleep. *J Child Neur* 9: 139–143, 1994.
13. Lou HC, Henriksen L, Bruhn P, Barner H, Nielsen JB. Dysfunction in attention deficit and hyperkinetic disorder. *Arch Neurol* 46: 48–52, 1989.