고신대학교 의학부 학술지 제17권 제1호
Kosin Medical Journal
Vol. 17. No. 1, pp. 100~104, 2002

병리학적으로 확진된 해마경화로 인한 측두엽간질의 임상양상

김광수, Andrew J. Cole*

고신대학교 의학부 신경과학교실,
*MGH Epilepsy Service, Massachusetts General Hospital

Clinical Features of Temporal Lobe Epilepsy due to Pathologically Proven Hippocampal Sclerosis

Kwang soo Kim, Andrew J. Cole*

Department of Neurology, Kosin University College of Medicine, Busan, Korea
**MGH Epilepsy Service, Massachusetts General Hospital, Boston, Massachusetts, U.S.A.*

Abstract

Background The commonest pathology underlying temporal lobe epilepsy is hippocampal sclerosis which is associated with febrile convulsion in young children. The purpose of this study was to determine the clinical characteristics in patients with medically refractory temporal lobe epilepsy due to hippocampal sclerosis (HS) compared to patients with temporal lobe lesions (TLL). ***Methods*** Records of 122 consecutive patients who underwent surgery for epilepsy from January 1993 to April 2000 were retrieved from the MGH Epilepsy Surgery Database. Fifty-eight patients with temporal lobe epilepsy due to pathologically proven HS or TLL were identified and clinical data were reviewed. Patients were divided into two groups according to pathological findings, hippocampal sclerosis group and temporal lobe lesion group. Patients with dual or normal pathology were excluded. ***Results*** Pathologically proven HS was present in 32 patients, and 26 patients has temporal lobe lesions (cortical dysplasia, vascular malformation, gliomas, heterotopia). Mean age at onset was 12.6±9.8 years in HS group and 19.6±10.6 years in TLL group (p=0.012). Mean duration of epilepsy was 20.6±10.4 years in HS and 11.6±9.2 years in TLL (p=0.001). Febrile convulsion was present in 12 (28.1 %) of 32 patients with HS and 1 (3.8 %) of 26 TLL patients (p=0.002). Family history of seizure was more frequent in HS group but not statistically significant. Age at surgery, gender, monthly seizure frequency, presence of known etiology, and the existence of aura and secondarily generalized seizure were not significantly different between the two groups. ***Conclusions*** Epilepsy due to HS had a significantly earlier onset, and patients lived with the epilepsy for a significantly longer duration. Presence of febrile convulsions was significantly associated with HS.

Key words: Temporal lobe epilepsy, Hippocampal sclerosis, Clinical features

Introduction

Temporal lobe epilepsy (TLE) is the most common form of localization-related epilepsies and has been associated with various pathological lesions. Hippocampal sclerosis (HS) is the most frequent structural abnormality associated with TLE.[1,2] HS refers to neuronal loss and gliosis involving the hippocampus and often also the amygdala, uncus, and parahippocampal gyrus.[1,3] HS is found in 50% to 75% of surgical specimens from patients undergoing surgery for TLE.[1,3] In neuropathological series of surgically treated TLE,

교신저자 : 김 광 수
TEL: 051-990-6274 · FAX: 051-245-9364
E-mail: nekim@ns.kosinmed.or.kr

focal lesions other than HS have been reported. The lesions frequently associated with TLE include gliomas, hamartomas, vascular malformations and disorders of cortical development.[1,4-6]

O'Brien et al.[7] found no significant differences in the incidence of auras between patients with TLE due to mesial temporal sclerosis and those with TLE due to a discrete temporal neocortical lesion. Foldvary et al.[8] reported that mesial TLE patients were younger at onset of seizures and more likely to have a prior history of febrile seizures, CNS infection, perinatal complications, or head injury, compared with patients with lesional neocortical TLE. Few studies have reported clinical features on the basis of temporal lobe pathology

In this retrospective study, we compared the clinical features in patients with TLE due to HS with patients with TLE due to a discrete temporal lobe lesion. The aim of the study was to determine whether there are clinical difference between patients with mesial TLE and those with lesional TLE.

Methods

Patients

Records of 122 consecutive patients who underwent surgery for epilepsy from January 1993 to April 2000 were retrieved from the MGH Epilepsy Surgery Database. Fifty-eight consecutive patients with medically intractable temporal lobe epilepsy who had undergone epilepsy surgery were included in this study. All patients had pathologically proven hippocampal sclerosis, as defined as gliosis and neuronal loss over than 50% in CA1 subfield, or other lesion in temporal lobe. There were 24 men (41.4%) and 34 women (58.6%). Patients were divided into two groups according to pathological findings, hippocampal sclerosis (HS) group and temporal lobe lesion (TLL) group. Thirty-two (55.2%) of 58 patients had hippocampal sclerosis, and 26 patients (44.8%) had an isolated temporal lobe lesion. Patients with dual or normal pathology were excluded.

All patients had long-standing epilepsy inadequately controlled by antiepileptic medication, with mean 12.7 complex partial or generalized tonic-clonic seizures per month prior to epilepsy surgery.

Historical Evaluation

The medical records of patients were retrospectively reviewed. Clinical characteristics for each patient included age at onset, age at surgery, the duration of epilepsy, gender, monthly seizure frequency, the presence of known etiology, the presence of febrile convulsion, family history of seizure, and the existence of aura and secondarily generalized seizures. These historical features were compared between the two groups.

Statistical Analysis

Statistical analysis between HS and TLL groups were performed with Student's t-test, χ^2-test, Fisher's exact test. Differences in proportion of age at onset, age at surgery, duration of epilepsy, and monthly seizure frequency between the two groups were analyzed with Student's t-test. χ^2-test was used to analyze for differences of gender, presence of known etiology, presence of febrile convulsion, and existence of aura and secondarily generalized seizures between the two groups. Fisher's exact test was used to analyze for difference of family history of seizure. The level for statistical significance was set at $p<0.05$.

Results

Clinical Characteristics

Table shows the characteristics of patients with HS or TLL. The mean age at onset was 12.6±9.8 years in HS group and 19.6±10.6 years in TLL group. The mean age at onset of habitual seizures was significantly earlier in patients with HS($p=0.012$). The mean duration of epilepsy was 20.6±10.4

years in HS group, and 11.6±9.2 years in TLL group. The mean duration of epilepsy was significantly longer in patients with HS(p=0.001). The monthly seizure frequency was higher in TLL group, but there was no statistical significance. History of febrile convulsion was present in 12 (37.5%) of 32 patients with HS, and one (3.8%) of 26 patients with TLL(p=0.002). Age at surgery, gender, monthly seizure frequency, presence of known etiology, family history of seizure, the existence of aura, secondarily generalized seizure, and the side of operation were not significantly different between the two groups.

Table. Demography of atients

	Hippocampal Sclerosis (n=32)	Temporal Lobe Lesion (n=26)	p Value
Age at onset (mean±SD*, yr)	12.6±9.8	19.6±10.6	0.012†
Age at surgery (mean±SD*, yr)	33.±38.4	31.2±11.5	0.438†
Epilepsy duration (mean±SD*, yr)	20.6±10.4	11.6±9.2	0.001†
Gender (male/female)	11/21	13/13	0.230‡
Seizure frequency (mean±SD*, month)	9.1±6.5	16.6±20.6	0.087†
Presence of known etiology (%)	11 (34.4)	5 (19.2)	0.199‡
Presence of febrile convulsion (%)	12 (37.5)	1 (3.8)	0.002‡
Family history of seizure (%)	9 (28.1)	2 (7.7)	0.090§
Aura positive (%)	24 (75)	20 (76.9)	0.865‡
Secondarily generalized seizure (%)	23 (71.9)	20 (76.9)	0.662‡

*: standard deviation
†: student's t-test
‡: x^2-test
§: Fishers exact test

Pathological Findings

The pathology was available in all patients. Thirty-two (55.2%) of 58 patients who underwent temporal lobe surgery had hippocampal sclerosis. Of the 26 patients with temporal lobe lesion, nine patients had gliomas, six had cortical dysplasia, six had vascular malformation, one had heterotopia, and five had other pathologies including ischemia, inflammation and old infarct.

Discussion

This study shows that epilepsy due to HS had a significantly earlier onset, and patients lived with the epilepsy for a significantly longer duration. Presence of febrile convulsions was significantly associated with HS.

Intractable TLE due to HS often evolves in patients who experienced early childhood prolonged febrile convulsions,[9-11] though most children with febrile convulsions will not develop TLE.[19] Hamati-Haddad and Abou-Khalil[13] said that TLE was more likely to be proceeded by febrile convulsions than extratemporal epilepsy or generalized epilepsy. Barr et al.[14] examined the degree and frequency of reductions in hippocampal volume in 44 patients with TLE with and without a history of febrile seizures and reported that a history of febrile seizure is associated with the finding of a smaller hippocampus on the side ipsilateral to the subsequent temporal lobe focus. Several studies have reported an association of early childhood febrile convulsions with the presence of hippocampal sclerosis in intractable TLE.[2,7,9,15] We also found that a history of febrile convulsions in early childhood was more frequent in HS group than TLL group.

These findings showed significant differences in age at onset and duration of epilepsy between the groups. Patients with TLE due to hippocampal sclerosis had a earlier seizure onset and longer duration of epilepsy than patients with TLE due to temporal lobe lesion.

Burgerman et al.[16] compared the clinical characteristics between mesial temporal lobe seizure and neocortical onset temporal lobe seizure and found a non-significant tendency for a higher frequency of seizures in mesial TLE, and no difference in the duration of afebrile seizures and in the presence of a family history of epilepsy. Our study showed a tendency of a higher seizure frequency in HS group than TLL group, though this was not statistically significant.

O'Brien et al.[7] reported that there were no significant differences in the incidence of auras between patients with TLE due to mesial temporal

sclerosis and those with TLE due to a discrete temporal neocortical lesion. Foldvary et al.[8] reported that mesial TLE patients were younger at onset of seizures and more likely to have a prior history of febrile seizures, CNS infection, perinatal complications, or head injury, compared with patients with lesional neocortical TLE. In our study, there were no significant differences in age at surgery, gender, presence of known etiology, family history of epilepsy, presence of aura and of secondarily generalized seizure between the groups.

Conclusion

Epilepsy due to hippocampal sclerosis had a significantly earlier onset, and patients lived with the epilepsy for a significantly longer duration. Presence of febrile convulsions was significantly associated with hippocampal sclerosis.

References

1. Babb TL, Brown WJ: Pathological findings in epilepsy, In: Engel J Jr, ed. Surgical treatment of epilepsies, New York, Raven Press, 1987, 511-540
2. Falconer MA: Genetic and related aetiological factors in temporal lobe epilepsy: a review. Epilepsia 12:13-31, 1971
3. Meencke HJ, Veith G: Hippocampal sclerosis in epilepsy, In: Luders H, ed. Epilepsy surgery, New York, Raven Press, 1991, 705-715
4. Wolf HK, Campos MG, Zentner J, Hufnagel A, Schramm J, Elger CE, Wiestler OD: Surgical pathology of temporal lobe epilepsy: experience with 216 cases. J Neuropathol Exp Neurol 52:499-506, 1993
5. Boon PA, Williamson PD, Fried I, Spencer DD, Novelly RA, Spencer SS, Mattson RH: Intracranial, intraaxial, space-occupying lesions in patients with intractable partial seizures: an anatomoclinical, neuropsychological, and surgical correlation. Epilepsia 32:467-476, 1991
6. Cascino GD, Boon PAJM, Fish DR: Surgically remediable lesional syndromes, In: Engel J Jr, ed. Surgical treatment of the epilepsies, Vol 52, 2nd ed. New York, Raven Press, 1993, 77-86
7. O'Brien TJ, Kilpatrick C, Murrie V, Vogrin S, Morris K, Cook MJ: Temporal lobe epilepsy caused by mesial temporal sclerosis and temporal neocortical lesions: a clinical and electroencephalographic study of 46 pathologically proven cases. Brain 119:2133-2141, 1996
8. Foldvary N, Lee N, Thwaites G, Mascha E, Hammel J, Kim H, Friedman AH, Radtke RA: Clinical and electrographic manifestations of lesional neocortical temporal lobe epilepsy. Neurology 49:757-763, 1997
9. Sagar H, Oxbury J: Hippocampal neuronal loss in temporal lobe epilepsy: correlation with early childhood convulsions. Ann Neurol 22:334-340, 1987
10. Cendes F, Andermann F, Dubeau F, Gloor P, Evans A, Jones-Gotman M, Olivier A, Andermann E, Robitaille Y, Lopes-Cendes I: Early childhood prolonged febrile convulsions, atrophy and sclerosis of mesial structures, and temporal lobe epilepsy: an MRI volumetric study. Neurology 43:1083-1087, 1993
11. VanLandingham KE, Heinz ER, Cavazos JE, Lewis DV: Magnetic resonance imaging evidence of hippocampal injury after prolonged focal febrile convulsions Ann Neurol 43:413-426, 1998
12. Camfield P, Camfield C, Gordon K, Dooley J: What types of epilepsy are preceded by febrile seizures? A population-based study of children. Dev Med Child Neurol 36:887-892, 1994
13. Hamati-Haddad A, Abou-Khalil B: Epilepsy diagnosis and localization in patients with antecedent childhood febrile convulsions. Neurology 50:917-922, 1998
14. Barr WB, Ashtari M, Schaul N: Bilateral reductions in hippocampal volume in adults with epilepsy and a history of febrile seizures. J Neurol Neurosurg Psychiatry 63:461-467, 1997
15. Kuks JBM, Cook MJ, Fish DR, Stevens JM, Shorvon SD: Hippocampal sclerosis in epilepsy and childhood febrile seizures. Lancet 342:1391- 1394, 1993
16. Burgerman RS, Sperling MR, French JA, Saykin AJ, OConnor MJ: Comparison of mesial versus neocortical onset temporal lobe seizures: neurodiagnostic findings and surgical outcome. Epilepsia 36:662-670, 1995

국문초록

배경 측두엽간질의 가장 흔한 병리소견은 해마경화이며, 이러한 병리소견은 어릴 때 열성경련과 관계가 있다. 본 연구는 병리학적으로 확진된 해마경화로 인한 측두엽간질 환자의 임상양상을 알아보고 해마경화 외 다른 측두엽병변으로 인한 측두엽간질 환자의 임상양상과 서로 비교하여 차이가 있는지 알아보고자 한다.

방법 1993년 1월부터 2000년 4월까지 Massachusetts General Hospital에서 간질수술을 실시하였던 122명 중 병리학적으로 해마경화 혹은 다른 측두엽병변이 확진된 측두엽간질 환자 58명을 대상으로 진료기록을 토대로 후향성 연구를 하였다. 연구대상 환자는 병리조직소견에 따라 해마경화가 있는 해마경화군과 다른 측두엽병변을 보였던 측두엽병변군으로 나누어 서로 비교하였다. 병리조직검사에서 해마경화와 다른 측두엽병변을 같이 가지고 있는 경우와 조직검사에서 정상소견을 보였던 환자들은 제외하였다.

결과 병리학적으로 해마경화가 확진된 환자는 32명이었고, 나머지 26명은 피질이형성증, 혈관기형, 신경교종, 헤테로토피아 등 측두엽병변을 보였다. 평균 발작시작연령은 해마경화군이 12.6±9.8세, 측두엽병변군이 19.6±10.6세였다(p=0.012). 간질의 평균기간은 해마경화군이 20.6±10.4년, 측두엽병변군이 11.6±9.2년이었다(p=0.001). 열성경련은 해마경화군 환자 32명 중 12명 (28.1%)과 측두엽병변군 26명 중 1명 (3.8%)에서 있었다(p=0.002). 발작의 가족력은 해마경화군에서 더 많았으나 통계학적으로 유의하지 않았다. 간질수술연령, 남녀비, 발작빈도, 알려진 원인유무, 전조유무, 이차성 전신성 발작유무 등은 두군 간에 차이가 없었다.

결론 해마경화로 인한 측두엽간질 환자는 측두엽병변으로 인한 측두엽간질 환자에 비하여 발작 시작연령이 더 어렸으며, 간질수술하기 전까지 더 오랜 기간동안 간질병력을 가지고 있었다. 열성경련의 병력빈도는 해마경화군에서 유의하게 높았다.

중심단어: 측두엽간질, 해마경화, 임상소견