Acta neurol. belg., 2006, **106**, 9-14

Surgery in temporal lobe epilepsy patients without cranial MRI lateralization

Y. B. GOMCELI[1], A. ERDEM[2], E. BILIR[3], G. KUTLU[1], S. KURT[4], E. ERDEN[5], A. KARATAS[2], C. ERBAS[2] and A. SERDAROGLU[6]

[1]Ministry of Health Ankara Training and Research Hospital, Department of Neurology, Ankara, Turkey ; [2]Ankara University Faculty of Medicine, Department of Neurosurgery, Ankara, Turkey ; [3]Gazi Universty Faculty of Medicine, Department of Neurology, Ankara, Turkey ; [4]Gazi Osman Pasa University Faculty of Medicine, Department of Neurology, Tokat, Turkey ; [5]Ankara University Faculty of Medicine, Department of Pathology,Ankara, Turkey ; [6]Gazi Universty Faculty of Medicine, Department of Pediatry, Ankara, Turkey

Abstract

High resolution MRI is very important in the evaluations of patients with intractable temporal lobe epilepsy in preoperative investigations. Morphologic abnormalities on cranial MRI usually indicate the epileptogenic focus. Intractable TLE patients who have normal cranial MRI or bilateral hippocampal atrophy may have a chance for surgery if a certain epileptogenic focus is determined. We evaluated the patients who were monitorized in Gazi University Medical Faculty Epilepsy Center from October 1997 to April 2004. Seventy three patients, who had a temporal epileptogenic focus, underwent anterior temporal lobectomy at Ankara University Medical Faculty Department of Neurosurgery. Twelve of them (16, 4%), did not have any localizing structural lesion on cranial MRI. Of the 12 patients examined 6 had normal findings and 6 had bilateral hippocampal atrophy. Of these 12 patients, 6 (50%) were women and 6 (50%) were men. The ages of patients ranged from 7 to 37 (mean : 24.5). Preoperatively long-term scalp video-EEG monitoring, cranial MRI, neuropsychological tests, and Wada test were applied in all patients. Five patients, whose investigations resulted in conflicting data, underwent invasive monitoring by the use of subdural strips. The seizure outcome of patients were classified according to Engel with postsurgical follow-up ranging from 11 to 52 (median : 35.7) months. Nine patients (75%) were classified into Engel's Class I and the other 3 patients (25%) were placed into Engel's Class II. One patient who was classified into Engel's Class II had additional psychiatric problems. The other patient had two different epileptogenic foci independent from each other in her ictal EEG. One of them localized in the right anterior temporal area, the other was in the right frontal lobe. She was classified in Engel's Class II and had no seizure originating from temporal epileptic focus, but few seizures originating from the frontal region continued after the surgery. In conclusion, surgery was successful in all 12 patients. We think that patients with no MRI lateralizing or localizing lesion should undergo epilepsy surgery after detailed presurgical evaluations, including invasive monitoring.

Key words : Temporal lobe epilepsy ; epilepsy surgery ; magnetic resonance imaging ; normal MRI ; bilateral hippocampal atrophy.

Introduction

In adult patients with epilepsy the majority has temporal lobe epilepsy (TLE). More than 70% of patients with TLE have hippocampal sclerosis (Janszky *et al.*, 2003). Intractable seizures usually depend on sclerosis. These patients are the candidates for surgery. The outcome of surgery in TLE particularly changes when clinical, electrophysiological, neuropsychological, and neuroimaging data are converging on a certain localization of epileptic focus (Kuzniecky *et al.*, 1993). Detailed medical history, physical and neurological examinations of patients and neuropsychological tests are very important for the evaluation of intractable TLE patients. Scalp long-term video-EEG monitoring is absolutely necessary in intractable TLE patients ; however, invasive recording is rarely required. The need for invasive recording depends on the type of the lesion that is seen on cranial magnetic resonance imaging (MRI) in cases with conflicting data (Diehl and Lüders, 2000). Another indication of the need for invasive recording to determine the epileptic focus is the recognition of dual pathology and normal cranial MRI (Diehl and Lüders, 2000).

Cranial MRI has an increasing impact in the evaluations of patients with intractable epilepsy because of its sensitivity in displaying lesions and histopathological substracts preoperatively (Mesial temporal sclerosis, tumoral processes, cortical dysplasia, anjioma- cavernoma, etc.) (Taillibert *et al.*, 1999). Although cranial MRI is one of the most important investigations before surgery, sometimes it may be normal or it may show bilateral hippocampal atrophy. Many patients with intractable epilepsy have normal MRI even when the epileptogenic area can be determined by clinical and long-term video-EEG monitoring evaluation.

In this study we have investigated the outcome of surgery in TLE patients without any structural abnormality and with bilateral hippocampal atrophy.

Patients and methods

In the research, which was conducted at the epilepsy monitoring unit of Gazi University Medical Faculty Department of Neurology from October 1997 to April 2004, 73 patients were evaluated and they underwent anterior temporal lobectomy as TLE. All of these patients were operated in Ankara University Medical Faculty Department of Neurosurgery. Detailed medical history was taken from all patients and each patient was given physical and neurological examinations, neuropsychological tests, long-term scalp video- EEG monitoring, and cranial MRI and Wada test. 61 (83.6%) of 73 patients had unilateral hippocampal atrophy. Twelve of them (16, 4%), who had medically intractable and a stereotyped seizure pattern, did not have any localizing or lateralizing lesion in cranial MRI. On visual inspection of the cranial MRI by two experienced radiologists 6 of 12 patients had normal cortical structures and 6 of them had bilateral hippocampal atrophy.

Of these 12 patients, 6 (50%) were women and 6 (50%) were men. The ages of patients ranged from 7-37 (mean : 24.5). They were evaluated from 96 hours to 264 hours (mean : 145, 8 hours).

Five patients, whose investigations resulted in conflicting data in their investigations, underwent invasive monitoring by the use of subdural strips. In five patients, additional sphenoidal electrodes were used instead of anterior temporal electrodes. Clinical seizure characteristics were evaluated throughout the monitoring to predict the region or regions of seizure origin.

All patients had MRI by a 1 T or a 1, 5 T magnetic resonance scanner (Siemens, Erlangen, Germany and GE Medical Systems, Milwaukee.WI, U.S.A.). By using the method of 3 dimensional monitoring on gradient echo sequence, contiguous 3 mm thick slices vision of the whole brain was captured. The sections of T1 (TR :400-500, TE :14-20, FOV : 24×24, thickness/slice gap : 3 mm/ 1 mm), T2 (TR :2000-2500, TE :70-80, FOV : 24×24, thickness/slice gap : 3 mm/1mm) and FLAIR (TR :9000, TE :118, IR : 2500, FOV : 24×24, thickness/slice gap : 3 mm/1 mm)were obtained as vertical to the long axis of hippocampus(oblique-coronal) and parallel to the long axis of hippocampus (oblique-axial). MRIs were analysed by two radiologists who were blind to all clinical details.

Video-EEG monitoring was performed by using the Telefactor system with up to 32 channels of EEG recorded continuously. International 10-20 system was used in electrode insertion.

Strip electrodes were made from a single row of 6 nicel electrode contacts approximately 2 mm and diameter of fixed interelectrode distance 10 mm. Strips could be inserted through a burr hole with different planned direction through the subdural spaces.

Results

Cranial MRI revealed bilateral hippocampal atrophy in six patients. The other six patients had no MRI abnormalites. Epileptic foci were determined by using ictal behavioral patterns and ictal EEG localization.

Sixty-one seizures, of which 11 were secondary generalized, were recorded. 5 patients had repeated monitoring because of conflicting data in their investigations. Invasive monitoring was performed because we could not determine the frontal/temporal origin in 3 of 5 patients and the central/temporal origin in one patient, by ictal EEG findings on scalp monitoring. Although ictal behavioral patterns of the last patient in this group supported the right temporal region, scalp monitoring showed the left temporal region. The second monitoring was done by using subdural strip electrodes.

On the ictal EEG recording of the 12 patients, it has been observed that ictal epileptiform discharges originated from the right temporal region in 6 patients, from the left temporal region in 5 patients. In one patient ictal epileptiform discharges originated from the right frontal and temporal region independent of each other. It was seen that in 6 patients interictal and ictal electroencephalographic (EEG) findings originated from the same temporal region. In 3 patients interictal abnormalities spread from the temporal region to the frontal or central area, the investigation of interictal EEG in 2 patients resulted in bitemporal findings. Only one patient who had right temporal epileptiform discharges on ictal EEG, had no abnormalities on interictal EEG.

Ictal behavioral patterns were retrospectively evaluated for each patient in detail. These patterns were aura, behavioral arrest, oral automatisms, ipsilateral\bilateral hand automatisms, contralateral\bilateral dystonic posturing, ipsilateral automatisms in the presence of contralateral dystonic posturing, ipsilateral\contralateral versive\ non-versive head and eye deviation, ictal vocalization, automatisms preserved responsiveness, and secondary generalization.

Table 1 displays the demographic data, MRI findings and surgery outcome.

Seven of these 12 patients underwent right anterior temporal lobectomy, whereas five of them had left anterior temporal lobectomy. The outcome of the patients were classified according to Engel with post surgical follow up ranging from 11 to 52 (median : 35.7) months. Six (50%) of the patients were seizure-free after anterior temporal lobectomy. Nine patients (75%) were classified into Engel's Class I and the other 3 patients (25%) were classified into Engel's Class II. In our series, 61 patients who had unilateral hippocampal atrophy underwent anterior temporal lobectomy. Postoperative follow-up time was ranging from 1 to

Table 1

Patient	Age	Sex	MRI Findings	Time (month)	Surgery outcome
1.	13	M	Normal	40	Rarely Nocturnal GTCS*
2.	22	F	Normal	26	Rarely Nocturnal GTCS + CPS
3.	30	F	Normal	33	Seizure-free
4.	30	M	Normal	52	Seizure-free
5.	22	F	Normal	24	Rarely rapidly generalized GTCS
6.	30	M	Bilateral	49	Seizure-free (36 months)**
7.	18	F	Bilateral	43	Seizure-free
8.	7	F	Bilateral	39	Seizure-free
9.	37	M	Bilateral	50	Seizure-free
10.	35	F	Normal	11	Seizure-free
11.	21	M	Bilateral	13	Seizure-free
12.	29	M	Bilateral	49	Rarely CPS***

* He had nocturnal GTCS during the cessation of antiepileptic drugs and followed seizure-free for 24 months.

** After surgery he had nocturnal GTCS for 9 months and he remained seizure-free for 36 months.

*** After surgery he was seizure-free for a period of 36 months and he rarely had CPS for 13 months.

(GTCS : Generalized Tonic-Clonic Seizure, CPS : Complex Partial Seizure).

53 (median : 20.6) months. Forty-four of them were followed up at least 11 months

(11 to 50, median : 26.1) just as our study group. In these 44 patients, 39 (88.6%) of them were classified into Engel's Class I, 1 patient (2.2%) into Engel's Class II, and 4 patients (9.0%) were placed into Engel's Class III.

In Engel's Class II, a 22-year-old female, Case 2, had additional psychiatric problems and she had used antiepileptic drugs irregularly. She had nocturnal generalized seizure and rarely complex partial seizures. The other patient, who was also a 22-year-old female, Case 5, rarely had rapidly generalized tonic-clonic seizures whereas complex partial seizures were lost. Cranial MRI revealed no MRI abnormality in this case. In the scalp video-EEG monitoring of this patient we lateralized seizures to the right hemisphere but the epileptic area could not be determined for certain. After that, invasive monitoring was done by using strip electrodes. This patient had two different ictal EEG onsets independent of each other. One of them was seen on the right anterior temporal area, the other was on the right frontal lobe. The seizures which generated from the right anterior temporal lobe were complex partial semiology whereas the others were rapidly generalized seizures originating from the right frontal lobe. Deciding on surgery for this patient was very difficult. However, she had to undergo anterior temporal lobectomy in order to increase her quality of life because she had 3 complex partial seizures in a week and almost only 1 rapidly generalized seizure in every three or four months. Her complex partial seizures were lost after the operation, but rapidly generalized seizures continued. Interestingly, oligodendroglioma was diagnosed in pathological investigation (Fig. 1). When this pathology was seen, MRI was examined again and no abnormality was seen to make a new interpretation (Fig. 2). The remaining patient, Case 12, who was classified into Engel's Class II, rarely had complex partial seizures although he regularly continued to take antiepileptic drugs.

Pathological examination revealed hippocampal sclerosis in 8 (66.6%) patients, neocortical gliosis in 2 (16.6%) patients, ganglioglioma in 1 (8.3%) patient, and oligodendroglioma (8.3%) in the other.

Discussion

In intractable epilepsy, long term video- EEG monitoring, especially ictal EEG is very helpful for presurgical evaluation. Recently, cranial MRI has been the most important technique in displaying structural abnormalities that might be epileptic foci.

We have found out that in patients with normal cranial MRI or bilateral hippocampal atrophy, long-term video-EEG monitoring can localize the seizure focus and can lead to successful epilepsy surgery.

In recent studies, it has been found out the success rate of epilepsy surgery in patients with cranial MRI abnormality has been higher than the rate in patients with normal cranial MRI (Berkovic *et al.*, 1995, Zentner *et al.*, 1996).

Garcia *et al.* reported that 24 of 25 (96%) patients with lateralized MTS in cranial MRI were seizure-free after anterior temporal lobectomy (Garcia *et al.*, 1994). However, Berkovic *et al.* found out that only 62% of the patients with unilateral MTS in cranial MRI were seizure-free during a period of 2 years (Berkovic *et al.*, 1995).

Scott *et al.* investigated 40 patients without definite MRI abnormalities. Five of them were also monitorized by using intracranial electrodes. Only 3 (7, 5%) of them proceeded to surgery. They also evaluated 182 patients with abnormal MRI and 93 (51%) patients had undergone surgery after scalp video-EEG monitoring. Eight (4.3%) patients were also remonitored by using intracranial electrodes and 7 of them underwent surgery. They suggested that patients with MRI abnormality had a higher chance of surgery than patients with normal MRI (Scott *et al.*, 1999).

Quigg *et al.* investigated absolute volumes and volume differences of hippocampus in patients with mesial TLE by using MRI in order to determine bilateral atrophy and the effect of hippocampus volume on the outcome of temporal lobectomy. They concluded that asymetry and bilateral atrophy had no clear relation to surgical outcome (Quigg *et al.*, 1997).

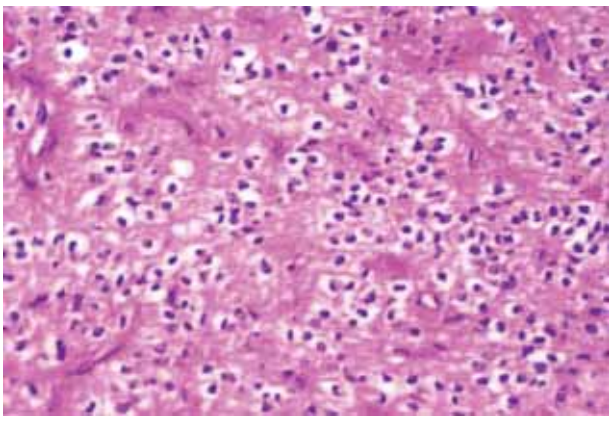

FIG. 1. — Tumour cells with round, homogeneous nuclei, clear cytoplasm and well defined plasma membrane, H-EX400.

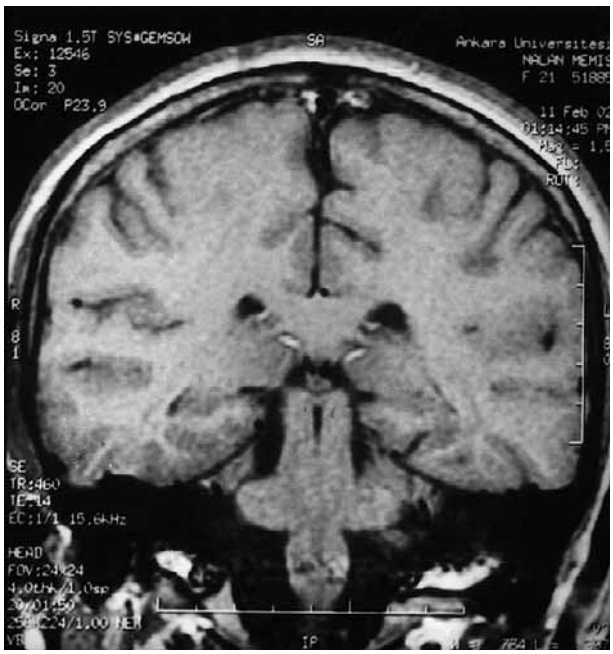

FIG. 2. — Normal MRI findings, case 5

Cukiert *et al.* investigated the results of surgery in patients who had bilateral independent temporal lobe spiking with normal MRI or bilateral mesial temporal sclerosis. Sixteen patients were studied and all of them were evaluated by using bilateral subdural grid electrodes (Cukiert *et al.*, 2000). Eleven patients had normal MRI (Group I) and five patients had bilateral mesial temporal sclerosis (Group II). In their postsurgical follow up, 72% of Group I and 80% of Group II were seizure-free. They concluded that patients with normal MRI seemed to have a worse prognosis than patients with unilateral or even bilateral mesial temporal sclerosis. In our study, 77.3% of patients with normal MRI were classified into Engel's Class I. However, in bilateral hippocampal atrophy group, 84.4% of patients were placed into Engel's Class I. We think that our results support this study.

There is insufficient information regarding the role of ATL, optimal presurgical evaluation strategy, and post-ATL seizure outcome among medically refractory TLE patients because of the small number of MRI negative patients in recent ATL series (McIntosh AM *et al.*, 2001).

In a recent study, 115 patients with partial epilepsy, who had received intracranial electrode evaluation, were analyzed by Siegel *et al.* Fourty-three patients (37%) had normal cranial MRI. Among these 43 patients, 25 (58%) of them had focal seizure onset, 12 (28%) patients had multifocal origin and 6 (14%) patients had no focal seizure origin during invasive monitoring. 24 of 25 patients who had focal seizure origin underwent cortical resection. 20 (83%) patients had a good surgical outcome, 15 of these patients were seizure-free (Engel's Class I) and 5 had rare seizures (Engel's Class II). Six of the 12 patients with multifocal seizure origin and 1 of 6 patients who had no focal seizure origin underwent other forms of epilepsy surgery. Two patients with multifocal seizure origin and one patient, who had no focal seizure origin with nonlateralized frontal lobe epilepsy, underwent anterior corpus callosotomy. All three of these patients had a > 80% reduction in the frequency of their disabling seizure types. Four patients with multifocal origin, 2 of whom had palliative resections, had vagal nerve stimulators implanted ; however, although early results have been promising, there has been insufficient follow-up. They concluded that successful epilepsy surgery was possible in patients with normal MRI and that careful presurgical evaluations were necessary (Siegel *et al.*, 2001).

According to the research conducted by Holmes *et al.*, while trying to find out effective predictors about the results of surgery with 23 TLE patients who had normal MRI, the best results (78% of patients were seizure-free) were observed in patients in whom the interictal and ictal findings showed the same temporal area. Overall, 48% (11/23) patients were seizure free, 39% (9/23) had > 75% reduction in seizures, while 13 % (3/23) had < 75% reduction in seizures. They claimed that surgery results were unfavorable for the patients (29% of patients were seizure-free) who had ictal EEG findings initiated by bitemporal or multifocal interictal discharges and mid-posterior temporal areas (Holmes *et al.*, 2000). In our study 6 patients had normal cranial MRI. Four of these patients, who had normal MRI, underwent surgery according to the scalp monitoring results ; yet, 2 patients were remonitored by using subdural strip electrodes. Three patients underwent right anterior temporal lobectomy and the others underwent left. In their 11 to 52 months follow-up, 3 of them remained seizure-free. Contrary to Holmes *et al.*'s research, in our study it was seen that the interictal and ictal findings showed the same temporal area

Table 2

Comparison of the recent studies in patients without MRI lateralization

Group	Patients	MRI	Invasive monitoring	Follow up	Good surgical outcome*
Cuikert *et al.*	11	Normal	11	mean 14 months	72%
	5	BHA**	5		80%
Siegel *et al.*	24***	Normal	24	≥ 2 years	83%
Holmes *et al.*	23	Normal	6	≥ 2 years	87%
Sylaja *et al.*	17	Normal	None	≥ 1 year	70%
Chapman *et al.*	24	Normal	15	mean 29 months	75%

* Explained in relevant paragraphs.
** Bilateral hippocampal atrophy.
*** Patients who had only focal seizure onset.

only in one patient who was classified into Engel's Class I. The other 3 patients who were classified into Engel's Class II had ictal and interictal origins in the same area.

The seizure outcome after ATL of 17 patients who had refractory TLE with normal MRI (without PET or SPECT) was reported by Sylaja *et al.* In their series, 7 (41%) patients achieved an excellent seizure outcome and 5 of them remained seizure-free. In addition, 5 (29%) patients had > 75% reduction in their seizure frequency. They concluded that the antecedent history of febrile seizures, strictly unilateral anterior ictal epileptiform discharges, and concordant type I ictal EEG pattern (regular, well-modulated, 5 to 9 Hz, unilateral temporal and/or subtemporal rhythm) might be predictors of an excellent post-ATL outcome of MRI negative patients (Sylaja *et al.*, 2005).

In another recent study reported by Chapman *et al.*, 24 adult and pediatric patients with normal preoperative MRI underwent epilepsy surgery. Nine of them had frontal, 13 of them had temporal, one of them had central and the last one had multilobar resections. During the follow-up, 37% of patients were seizure-free and 75% of patients had 90% reduction in their seizure frequency with weekly or monthly seizures. Seizure outcome did not differ on the basis of the location of resection or histopathology. And they thought that there was no single test or a combination of tests (EEG ; PET or ictal SPECT) that further predicted postoperative seizure outcome (Chapman *et al.*, 2005).

The results of previous studies are shown in Table 2.

In our study the surgery was successful in all 12 patients : 9 of them were classified into Engel's Class I, and 3 of them into Engel's Class II. One patient who was classified into Engel's Class II had additional psychiatric problems and showed discordance for antiepileptic drugs. The other had no seizure originating from temporal epileptic focus, but few seizures that originated from frontal region continued. The last patient rarely had complex partial seizures although he regularly continued to take antiepileptic drugs. In our series, patients with unilateral hippocampal atrophy (Engel's Class I, 88.6%) had a better prognosis than the patients without MRI lateralization (Engel's Class I, 75%).

We conclude that patients with no MRI lateralizing or localizing lesion should undergo epilepsy surgery after detailed presurgical evaluations, including invasive monitoring. We believe that TLE patients who have medical intractable seizures with normal cranial MRI or bilateral hippocampal sclerosis should have the opportunity of presurgical evaluation and epilepsy surgery.

REFERENCES

Berkovic S. F., McIntosh A. M., Kalnins R. M. *et al.* Preoperative MRI predicts outcome of temporal lobectomy : an actuarial analysis. *Neurology*, 1995, **45** : 1358-63.

Chapman K., Wyllie E., Najm I. *et al.* Seizure outcome after epilepsy surgery in patients with normal preoperative MRI. *J. Neurol. Neurosurg. Psychiatry*, 2005, **76** : 710-713.

Cukiert A., Sousa A., Machado E., Buratini J. A., Forster C., Argentoni M. Results of surgery in patients with bilateral independent temporal lobe spiking (BLITS) with normal MRI or bilateral mesial temporal sclerosis(MTS) investigated with subdural grids. *Arq. Neuropsiquiatr.*, 2000, **58** (4) : 1009-13.

Diehl B., Lüders H. O. Temporal lobe epilepsy : when are invasive recordings needed ? *Epilepsia*, 2000, **41** (Suppl 3) : 61-74.

Garcia P., Laxer K., Barbara N., Dillan W. Prognostic value of qualitative magnetic resonance imaging hippocampal abnormalities in patients undergoing temporal lobectomy for medically refractory seizures. *Epilepsia*, 1994, **35** : 520-4.

Holmes M. D., Born D. E., Kutsy R. L., Wilensky A. J., Ojemann G. A., Ojemann L. M. Outcome after surgery in patients with refractory temporal lobe epilepsy and normal MRI. *Seizure*, 2000 Sep, **9** (6) : 407-11.

JANSZKY J., SCHULZ R., EBNER A. Clinical features and surgical outcome of medial temporal lobe epilepsy with a history of complex febrile convulsions. *Epilepsy Research*, 2003, **55** : 1-8.

KUZNIECKY R. I., BURGARD S., FAUGHT E. *et al.* Predictive value of magnetic resonans imaging in temporal lobe epilepsy surgery. *Arch. Neurol.*, 1993, **50** : 65-9.

MCINTOSH A. M., WILSON S. J., BERKOVIC S. F. Seizure outcome after temporal temporal lobectomy : current research practice findings. *Epilepsia*, 2001, **42** : 1288-307.

SCOTT C. A., FISH D. R., SMITH S. J. M. *et al.* Presurgical evaluation of patients with epilepsy and normal MRI : role of scalp video-EEG telemetry. *J. Neurol. Neurosurg. Psychiatry*, 1999, **66** : 69-71.

SIEGEL A. M., JOBST B. C., THADANI V. M. *et al.* Medically intractable, localization-related epilepsy with normal MRI : presurgical evaluation and surgical outcome in 43 patients. *Epilepsia*, 2001, **42** (7) : 883-888.

SYLAJA P. N., RADHAKRISHNAN K., KESAVADAS C., SARMA P. S. Seizure outcome after anterior temporal lobectomy and its predictors in patients with apparent temporal lobe epilepsy and normal MRI. *Epilepsia*, 2004, **45** (7) : 803-9.

TAILLIBERT S., OPPENHEIM C., BAULAC M., DORMONT D., MARSAULT C., CABANIS E. A., TOURBAH A. Yield of fluid - Attenuated inversion recovery drug-resistant focal epilepsy with noninformative convantional magnetic resonance imaging. *Eur. Neurol.*, 1999, 41-64-72.

QUIGG M., BERTRAM E. H., JACKSON T., LAWS E. Volumetric magnetic resonance imaging evidence of bilateral hippocampal atrophy in mesial temporal lobe epilepsy. *Epilepsia*, 1997, **38** (5) : 588-94.

ZENTNER J., HUFNAGEL A., OSTERTUN B. *et al.* Surgical treatment of extratemporal epilepsy : clinical, radiologic and histopatologic findings in 60 patients. *Epilepsia*, 1996, **37** : 1072-80.

Y. B. GOMCELI,
Isci blokları mah.381.sok Idareciler sitesi,
C blok No : 17 Karakusunlar 06520,
Ankara/Turkiye
E-mail: yasemingomceli@hotmail.com.