Seizure 29 (2015) 63–68

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Surgical outcome in patients with MRI-negative, PET-positive temporal lobe epilepsy

Irem Yıldırım Capraz [a,*], Gökhan Kurt [b], Özgür Akdemir [c], Tugba Hirfanoglu [d], Yusuf Oner [e], Tugba Sengezer [f], Lütfiye Ozlem Atay Kapucu [c], Ayse Serdaroglu [d], Erhan Bilir [a]

[a] Gazi University, Faculty of Medicine, Department of Neurology, Ankara, Turkey
[b] Gazi University, Faculty of Medicine, Department of Neurosurgery, Ankara, Turkey
[c] Gazi University, Faculty of Medicine, Department of Nuclear Medicine, Ankara, Turkey
[d] Gazi University, Faculty of Medicine, Department of Pediatric Neurology, Ankara, Turkey
[e] Gazi University, Faculty of Medicine, Department of Radiology, Ankara, Turkey
[f] Guven Hospital, Department of Nuclear Medicine, Ankara, Turkey

ARTICLE INFO

Article history:
Received 8 October 2014
Received in revised form 11 March 2015
Accepted 25 March 2015

Keywords:
Medication-refractory epilepsy
Temporal lobe epilepsy
Epilepsy surgery
Electroencephalography
Magnetic resonance imaging
Fluorodeoxyglucose positron emission tomography

ABSTRACT

Purpose: The purpose of this study was to determine the long-term surgical outcomes of magnetic resonance imaging (MRI)-negative, fluorodeoxyglucose positron emission tomography (FDG-PET)-positive patients with temporal lobe epilepsy (TLE) and compare them with those of patients with mesial temporal sclerosis (MTS).

Methods: One hundred forty-one patients with TLE who underwent anterior temporal lobectomy were included in the study. The surgical outcomes of 24 patients with unilateral temporal hypometabolism on FDG-PET without an epileptogenic lesion on MRI were compared with that of patients with unilateral temporal hypometabolism on FDG-PET with MTS on MRI ($n = 117$). The outcomes were compared using Engel's classification at 2 years after surgery. Clinical characteristics, unilateral interictal epileptiform discharges (IEDs), histopathological data and operation side were considered as probable prognostic factors.

Results: Class I surgical outcomes were similar in MRI-negative patients and the patients with MTS on MRI (seizure-free rate at postoperative 2 years was 79.2% and 82% in the MRI-negative and MTS groups, respectively). In univariate analysis, history of febrile convulsions, presence of unilateral IEDs and left temporal localization were found to be significantly associated with seizure free outcome. Multivariate analysis revealed that independent predictors of a good outcome were history of febrile convulsions and presence of unilateral IEDs.

Conclusion: Our results suggest that epilepsy surgery outcomes of MRI-negative, PET positive patients are similar to those of patients with MTS. This finding may aid in the selection of best candidates for epilepsy surgery.

1. Introduction

Temporal lobe epilepsy (TLE) is one of the most medical treatment-resistant type of focal epilepsy in adults and surgical treatment may help approximately 70% of the patients become seizure free [1–3]. In the preoperative assessment of TLE cases, it is important that neuroradiological findings support the clinical and electrophysiological studies in identifying the epileptic focus.

The most frequent histopathological finding in TLE patients is mesial temporal sclerosis (MTS). The sensitivity and specificity of cranial magnetic resonance imaging (MRI) is quite high, about 80–97% [4,5]. Hippocampal sclerosis (HS) detected by MRI is among

Abbreviations: AED, antiepileptic drugs; ATL, anterior temporal lobectomy; AVM, arteriovenous malformation; CD, cortical dysplasia; CI, confidence interval; EEG, electroencephalography; FC, febrile convulsion; FDG-PET, fluorodeoxyglucose positron emission tomography; HM, hypometabolism; HS, hippocampal sclerosis; IED, interictal epileptiform discharge; MRI, magnetic resonance imaging; MTS, mesial temporal sclerosis; SGTCS, secondary generalized tonic-clonic seizures; TLE, temporal lobe epilepsy.

* Corresponding author at: Noroloji Bolumu, Gazi Universitesi Tip Fakultesi, Besevler, 06500 Ankara, Turkey. Tel.: +90 3122025329.
E-mail address: driremyildirim@yahoo.com.tr (I. Yıldırım Capraz).

http://dx.doi.org/10.1016/j.seizure.2015.03.015
1059-1311/

the most important positive predictive factors known to affect postoperative outcome [6–8]. While MTS is seen in 58–72% of TLE cases, it has been determined that MRI is normal in approximately 16% of the cases [5,9,10].

Although it has been reported in recent years that 3 T MRI provides 20–48% increase in providing new or additional information in comparison to 1–1.5 T MRI, other neuroimaging methods are required in the preoperative assessment of MRI-normal cases [11,12]. Therefore, fluorodeoxyglucose (FDG)-positron emission tomography (PET) is routinely used in many epilepsy centers for preoperative assessment to identify the epileptic focus. PET is a type of nuclear medicine imaging with multiple purposes, and gives information both on local and general brain metabolism. Glucose metabolism is the most frequently measured parameter and 18 F-FDG is the most commonly used molecule for this purpose. As a characteristic finding of epilepsy, there is a regional decrease in glucose uptake (hypometabolism) during interictal period. The definitive cause of hypometabolism is not known. The general opinion is that cerebral hypometabolism reflects neuronal cell loss; however, in fact, rather than the real structural area, cerebral dysfunction is caused by decreased synaptic input and electrical activity arising from the dysfunctional cortex. Therefore, hypometabolism extends far beyond the margins of the epileptic focus in the temporal lobe. In the light of this information, it can be concluded that hypometabolism on PET scan shows dysfunctional neural network [13].

FDG-PET scans localize the seizure focus correctly in 85–90% of TLE patients. Regional hypometabolism is also identified in FDG-PET scans of 60–82% of MRI-negative patients [14–16]. At the same time, FDG-PET is useful in predicting surgical outcome. In a large meta-analysis, it was found that while ipsilateral hypometabolism showed a predictive value of 86% for good surgical outcome, the corresponding value was between 71% and 80% in patients with normal MRI findings [13]. Although the underlying physiopathology in these cases is not completely enlightened, it has been put forward that it is a different syndrome from MTS that can be surgically treated [5,17].

Although it is considered that the surgical outcomes of MRI-normal cases are worse than that of patients with MTS, the studies performed in recent years support the fact that if PET, electroencephalography (EEG) and the results of other preoperative assessments are consistent and identify a single focus, this group has similar results to MTS group. It has also been reported in many series that MRI-normal cases have better surgical outcomes in comparison to patients with MTS [13–18].

The purpose of this study was to determine the long-term surgical outcomes of MRI-negative, FDG-PET-positive TLE patients and compare them with those of patients with MTS.

2. Material and methods

Patients who were diagnosed with medically refractory TLE and underwent standard anterior temporal lobectomy (ATL) between 2006 and 2013 at Gazi University Medical Faculty Epilepsy Center were retrospectively evaluated. Among 167 patients aged more than 17 years, 141 cases with a postoperative follow-up period of at least 2 years and unilateral temporal hypometabolism on FDG-PET scan were included in the study. The same preoperative assessment protocol was used in all patients. The present study was approved by the Institutional Ethical Board of Gazi University Faculty of Medicine and performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

As the first step of preoperative assessment, a detailed clinical and medical history of the patients was obtained, and all the patients underwent physical and neurological examination. Afterwards, all cases were monitored with scalp electrodes and additional anterior temporal electrodes using international 10–20 electrode system on 32-channel EEG until a sufficient number of typical seizures were recorded. If the rate of interictal epileptiform discharges (IEDs) were $\geq$80% in EEG recordings in one temporal lobe, the IEDs were considered unilateral. Temporal lobe localization and right/left lateralization of the patients were determined by correlating with ictal clinical signs and ictal and interictal EEG.

In all cases, cranial MRI was performed with temporal lobe epilepsy protocol using superconducting magnets with multichannel head coils in the supine position. While 1.5 T MRI (GE SIGNA EXCITE, Milwaukee, USA) was used in imaging in the first years of the study, assessments were performed by 3 T MRI (Siemens MagnetomVerio, Erlangen, Germany) in the last 4 years. Temporal lobe epilepsy protocol included axial and sagittal T1 weighted, axial T2 weighted, oblique coronal FLAIR perpendicular to the long axis of both hippocampi, and 3D inversion recovery (IR). The whole brain volumetric series were acquired using a 3D IR technique with a slice of 1 mm thickness, zero interslicegap, 256×222 matrix size, and a single signal average. T2 weighted oblique axial images through the long axis of both hippocampi consisting of 20 slices werealso obtained with 3 mm slice thickness and 0.75 mm interslice gap. All images were evaluated by experienced neuroradiologists.

Standard brain FDG-PET imaging protocol was used in all cases. The reconstruction of PET images was performed using FORE-OSEM iterative reconstruction method. Imaging was performed using Discovery ST (GE Medical Systems, Milwaukee, WI, USA) PET/CT camera system. Trans-axial and coronal PET images were prepared considering the AC/PC (anterior commissure/posterior commissure) line, and additional transverse sections were obtained according to temporal lobe plane. PET images were evaluated visually by 2 experienced nuclear medicine specialists independently without any knowledge on patients, surgery and follow-up results. Statistical parametric mapping (SPM) analysis was performed, if necessary. Consequently, FDG-PET images were classified into groups having right or left temporal hypometabolism. Cases with normal, bilateral or extratemporal PET findings were excluded. Patients with discordance regarding hypometabolism between ictal EEG and PET were also excluded.

All cases underwent psychiatric and neuropsychological assessment before surgery. None of the patients had a psychiatric disorder that was a definite contraindication for surgery, such as acute psychosis. Patients who were diagnosed with depression and anxiety disorder were followed-up with antidepressant therapy. All patients were administered a battery of neuropsychological tests by a neuropsychologist. Patients who were scheduled for surgery underwent WADA test or fMRI. Recently, fMRI rather than WADA was used reliably in most of the patients in our routine clinical practice, as is used in many epilepsy centers.

The results of preoperative assessment protocols were discussed in a multidisciplinary council, and if clinical and semiological findings, interictal and ictal EEG activities, and neuroimaging and neuropsychological assessments were consistent with each other and localize a single focus, surgery decision was made and the surgical technique was determined. ATL was performed for all patients by the same surgeon at the Department of Neurosurgery in our hospital. Standard anterior temporal resection was performed in all patients.

In the postoperative period, the patients were evaluated in terms of seizure state and antiepileptic drug (AED) use at 2 and 6 months, and thereafter once a year by the same epileptologist. In accordance with the AED withdrawal protocol of our clinic, the same drug treatment was continued for 6 months postoperatively in all patients. One of the AEDs was discontinued in patients who were seizure-free at the end of 6 months, by gradually decreasing the dose of the drug. Thereafter, the dose of the second drug was