Epileptic Disord 2009; 11 (2): 144-9

Epilepsy surgery in the elderly

An unusual case of a 75-year-old man with recurrent status epilepticus

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Received June 23, 2008; Accepted October 22, 2008

ABSTRACT – *Background*. Epilepsy surgery is increasingly well-supported as an effective treatment for patients with intractable epilepsy. It is most often performed on younger patients and the safety and efficacy of epilepsy surgery in elderly patients are not frequently described. *Case report*. We report a case of a 75-year-old right-handed man who underwent a left fronto-temporal craniotomy for resection of a suprasellar meningioma in 2002. Immediately following hospital discharge, he began to experience complex partial seizures. He continued to have frequent seizures despite treatment with multiple combinations of antiepileptic medications. He presented with status epilepticus every two or three months, and required long periods of hospitalization on each occasion for post-ictal confusion and aphasia. Scalp EEG showed continuous spikes and polyspikes and persistent slowing in the left temporal area, as well as spikes in the left frontal area. EEG telemetry recorded multiple seizures, all with a clear focus in the left temporal area. MRI scan showed an area of encephalomalacia in the left temporal lobe, as well as post-surgical changes in the left frontal area. Neuropsychological testing showed bilateral memory impairment with no significant cognitive decline expected after unilateral temporal lobe resection. A left anteromesial temporal lobectomy was performed with intraoperative electrocorticography. Since surgery, the patient was not seizure-free (Engel class II-b), but had no further episodes of status epilepticus in one year and two months of follow-up. *Conclusions*. This is one of the oldest patients reported in the literature with epilepsy surgery and supports the possibility of epilepsy surgery in elderly patients for particular cases. In addition, few cases with such a malignant evolution of temporal lobe epilepsy have been described in this age group.

Key words: epilepsy, epilepsy surgery, elderly, temporal lobe epilepsy

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doi: 10.1684/epd.2009.0240

Background

Epilepsy surgery is increasingly well-supported as an effective treatment for patients with intractable epilepsy. The short-term efficacy of epilepsy surgery for temporal lobe epilepsy has been established by one randomized clinical trial (RCT) (Wiebe *et al.* 2001). In this RCT, patients with temporal lobe

epilepsy were randomly assigned to medical or surgical treatment. After one year of follow-up, 58% of patients in the surgical group were free of disabling seizures, compared with only 8% in the medical group. This highly significant result ($p < 0.0001$) yielded a number needed to treat of two, which means that one of every two patients treated surgically will be rendered seizure-free (Wiebe *et al.* 2001). Other evidence, such as meta-analyses, have shown consistently that epilepsy surgery is efficient based on short and long term follow-up. Engel *et al.* (2003) published a meta-analysis to investigate epilepsy surgery including studies with an intermediate duration of follow-up (one to five years) involving 2 250 patients. The aggregate data showed that 65% of patients with anteromesial temporal resections were seizure-free, 21% patients had reduced seizures, and no improvement was observed for 14% patients. Tellez-Zenteno *et al.* (2005) recently investigated the outcome of epilepsy surgery after five years or longer and found that an improvement in temporal and extratemporal lobe epilepsy was sustained over time. Sixty percent of patients with temporal lobe epilepsy and 40% with extratemporal lobe epilepsy remained seizure-free. Furthermore, epilepsy surgery has shown clear improvement in many aspects of quality of life that include diverse aspects such as driving status, mortality and the use of antiepileptic drugs (Tellez-Zenteno *et al.* 2007).

The criteria used to define candidacy for epilepsy surgery vary between epilepsy centers, and usually include: the number of seizures, type of seizures, duration of disease and focal neurological findings, some centers also use age as an important criterion. Age is not a factor to exclude patients from surgery, although many centers do not operate on patients older than 60 years for certain reasons; some studies have published less favorable results following epilepsy surgery in elderly patients compared with younger patients (McLachlan *et al.* 1992). Also, a higher rate of complications has been reported in older patients (Grivas *et al.* 2006), such as strokes and aphasia in left temporal resections.

In this article we report a 75-year-old right-handed man with a very aggressive form of temporal lobe epilepsy manifested by recurrent events of status epilepticus, with two epileptogenic areas that underwent left temporal lobectomy guided by electrocorticography (ECoG). This is one of the oldest patients to have had epilepsy surgery reported in the literature. In addition, clustering of seizures and presence of status epilepticus observed in this patient has been only rarely reported for this age group.

Case study

We report the case of a 75-year-old right-handed man who had intractable complex partial seizures despite treatment with multiple combinations of anti-epileptic medications. In September 2002, he presented with gradual loss of vision in the left eye and was found to have a suprasellar meningioma. He underwent a left frontotemporal craniotomy using a trans-sylvian approach. The resection was classified as a Simpson grade III. Immediately following discharge, he began to have complex partial seizures. The semiology of seizures was characterized by lack of aura, followed by staring, unresponsiveness, lip-smacking and bimanual automatisms. He had approximately two to three seizures per week, as well as clusters of complex partial seizures followed by generalized tonic clonic seizures, culminating in status epilepticus every two or three months. He required long periods of hospitalization after each episode of status epilepticus due to prolonged post-ictal confusion and aphasia. He tried several anti-epileptic treatments including phenytoin, clobazam, levetiracetam, topiramate and lorazepam to prevent clusters without success. Scalp EEG showed continuous slowing in the left temporal and frontal area, abundant left mesial temporal spikes, as well as less frequent left frontal and left hemispheric spikes *(figure 1A, B)*. Due to the patient's frequent admission and prolonged stays in hospital a telemetry investigation was performed. Twenty-six complex partial seizures were recorded with onset over the left temporal area; electrode F7 *(figure 1C)*. MRI scan showed left hippocampal atrophy and an area of encephalomalacia in the left temporal lobe, as well as encephalomalacia in the area of the previous meningioma resection over the frontal area *(figure 2A, B)*. However the semiology of seizures, and ictal and interictal EEG were more consistent with a temporal onset. Neuropsychological testing was intended, but deferred, due to significant cognitive decline. No further loss of memory or cognition was expected after unilateral temporal lobe resection.

These results raised the possibility of performing intracranial recordings covering the left temporal and frontal regions. This option was considered due to the presence of two clear epileptogenic areas and the possibility of a frontal onset with rapid spread to the temporal region, or vice versa. This hypothesis was based on the seizure onset at one electrode (F7) which could show activity from the anterior temporal region or the inferior frontal region. Due to the age and comorbidity of the patient, a single procedure was preferred. The patient was deemed to be acceptable in terms of surgical risk by the anesthesiology team. A left anteromesial temporal lobectomy was carried out. Once the brain was exposed, intraoperative ECoG was performed *(figure 1D)*. In the frontal lobe, ECoG electrodes were placed in the surface of the brain over the inferior prefrontal gyrus, the pars opercularus and orbital part of the inferior frontal gyrus. In the temporal lobe, electrodes were placed in the superior temporal gyrus from posterior to anterior, with electrode 12 at Herschel's gyrus. In the middle and inferior temporal gyri, electrodes were

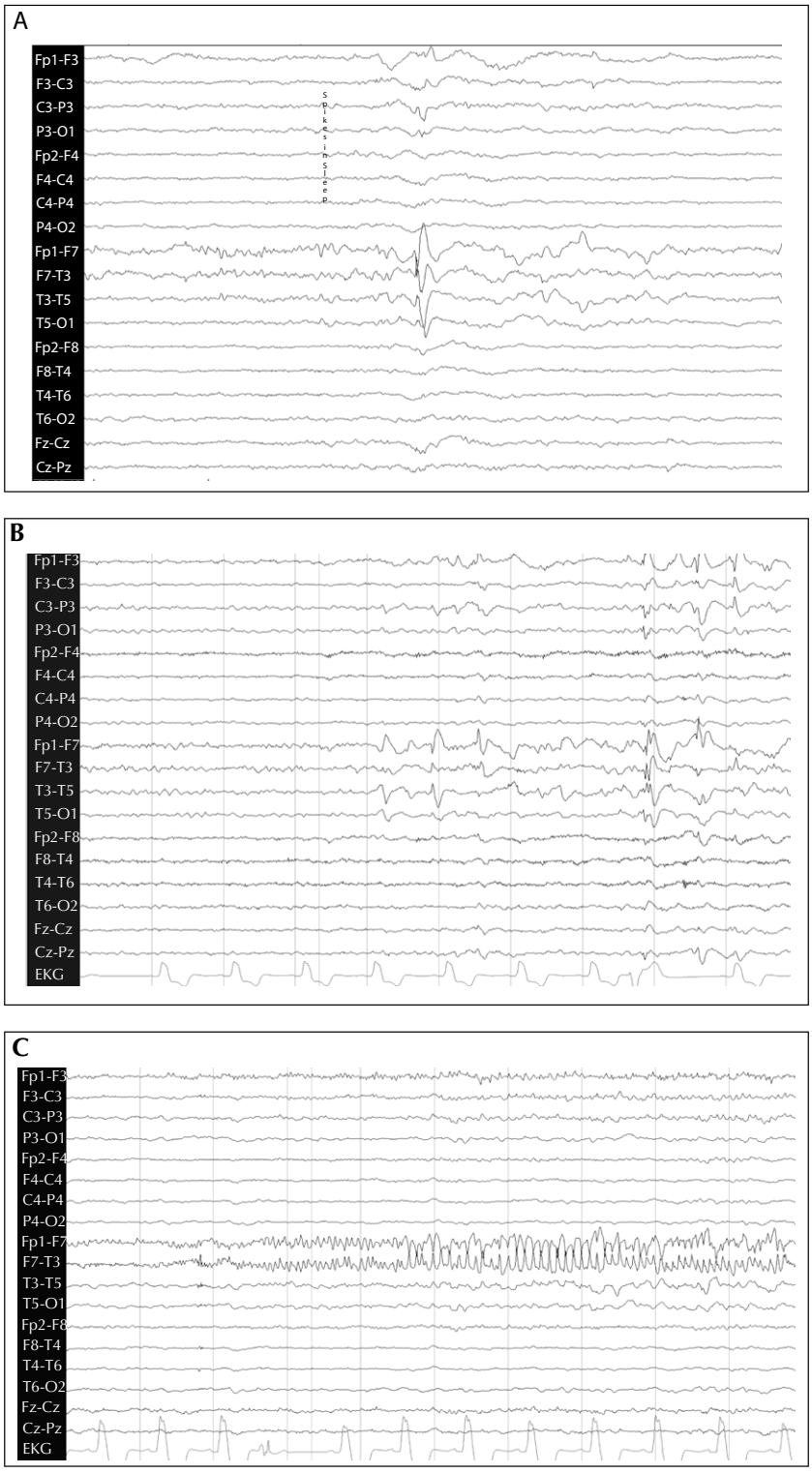

Figure 1. A) Shows high voltage left mesial temporal spikes (longitudinal bipolar montage). **B**) Shows left mesial temporal, left frontal spikes and left hemispheric spikes (longitudinal bipolar montage). In figure (**C**) one of the seizures recorded in the scalp is present with a clear onset at the electrode F7 (longitudinal bipolar montage).

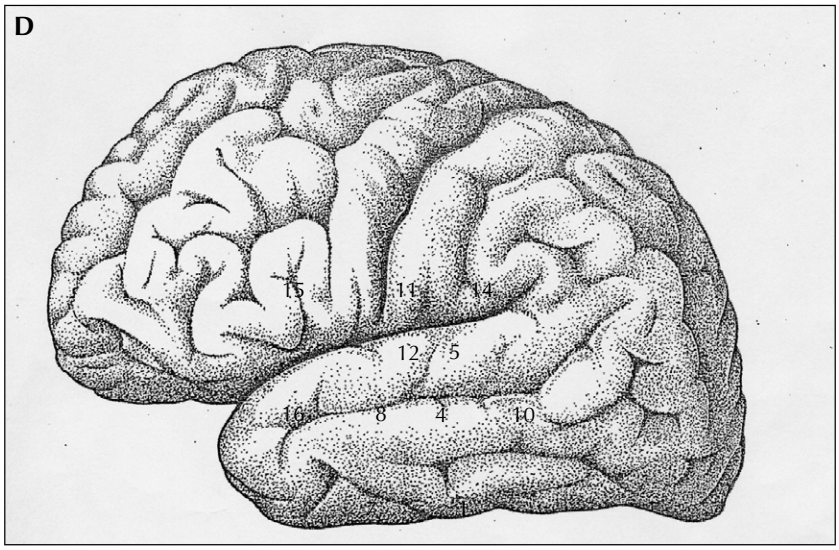

Figure 1. D) Shows the map of the ECoG. Electrodes were placed in the inferior prefrontal gyrus (11), the pars opercularis (14) and orbital part (15) of the inferior frontal gyrus. In the temporal lobe, electrodes were placed in the superior temporal gyrus (5, 12, 16), with electrode 12 at Herschel's gyrus, in the middle temporal gyrus (10, 4, 8), and the inferior temporal lobe (7, 1). Electrodes were also placed in the mesial temporal lobe in the amygdala and anterior hippocampus: multiple spikes were observed at electrodes 12, 4, 1, and 10, and less frequently at electrodes 7, 8, 11, and 14. Also frequent spikes were observed in the electrodes placed in the hippocampus. After resection spikes remained at electrode 10.

placed posteriorly and anteriorly. Electrodes were also placed in the mesial temporal lobe in the amygdala and anterior hypocampus. The ECoG showed spikes over both the left temporal (mesial and neocortical areas) and frontal areas, but much more frequent over the left temporal area. A resection of 4.5cm extending back from the tip of the temporal lobe was carried out. Frequent spikes were also seen by the electrodes placed in the hippocampus. The temporal horn was exposed and entered, identifying the hippocampus. The anterior hippocampus was then resected. The ECoG was then repeated revealing extinction of the majority of spikes, but a few posterior spikes persisted near the edge of the resection, which included the speech areas. In order to reduce the risk of speech deficits, no further resection was done. Histological examination of tissue samples were sent to pathology for evaluation. These included samples from the superior, middle and inferior temporal gyri, subiculum, the anterior hypocampus, amygdale, and uncus. The posterior left middle and inferior temporal gyri showed patchy mild to moderate cortical astrocytic gliosis, as well as mild white matter rarifaction and myelin pallor. There was no appreciable neuronal loss. The tissue pathology was not diagnostic of mesial temporal sclerosis.

After surgery the patient had mild expressive aphasia for a few days, which then resolved. The patient stayed in hospital for 20 days before being discharged to go home. He did not have any seizures in hospital. In one year and two months of follow-up, the patient has had two complex partial seizures but the tendency to cluster has been controlled successfully and he has had no episodes of status epilepticus. The patient and his family report that their quality of life has improved. The patient became more interactive and participative with the family and after surgery he was able to live independently with his wife.

Discussion

This case reports the second oldest patient described in the literature who has had epilepsy surgery as a treatment for intractable epilepsy. The oldest patient was reported by Acosta *et al.* (2008) and was 76 years old. The favorable outcome of this patient supports the efficacy and safety of epilepsy surgery in elderly patients for particular cases. Furthermore, few cases with such a malignant evolution of temporal lobe epilepsy have been described in this age group.

Few reports exploring the surgical outcome after epilepsy surgery in elderly patients have been published. Boling *et al.* (2001) reported the seizure outcome in 18 patients older than 50 years old following temporal lobe resections. Sixty-one percent of patients reached Engel class I outcome, 22% Engel class II, and 17% Engel class IV. Their study did not have a control group of a younger population. McLachlan *et al.* (1992) reported the seizure outcome after temporal lobe surgery in 20 patients older than 45 years old compared with 68 younger patients. After a follow-up of five years, 30% of older patients were seizure-free *vs* 40% in the younger group. The

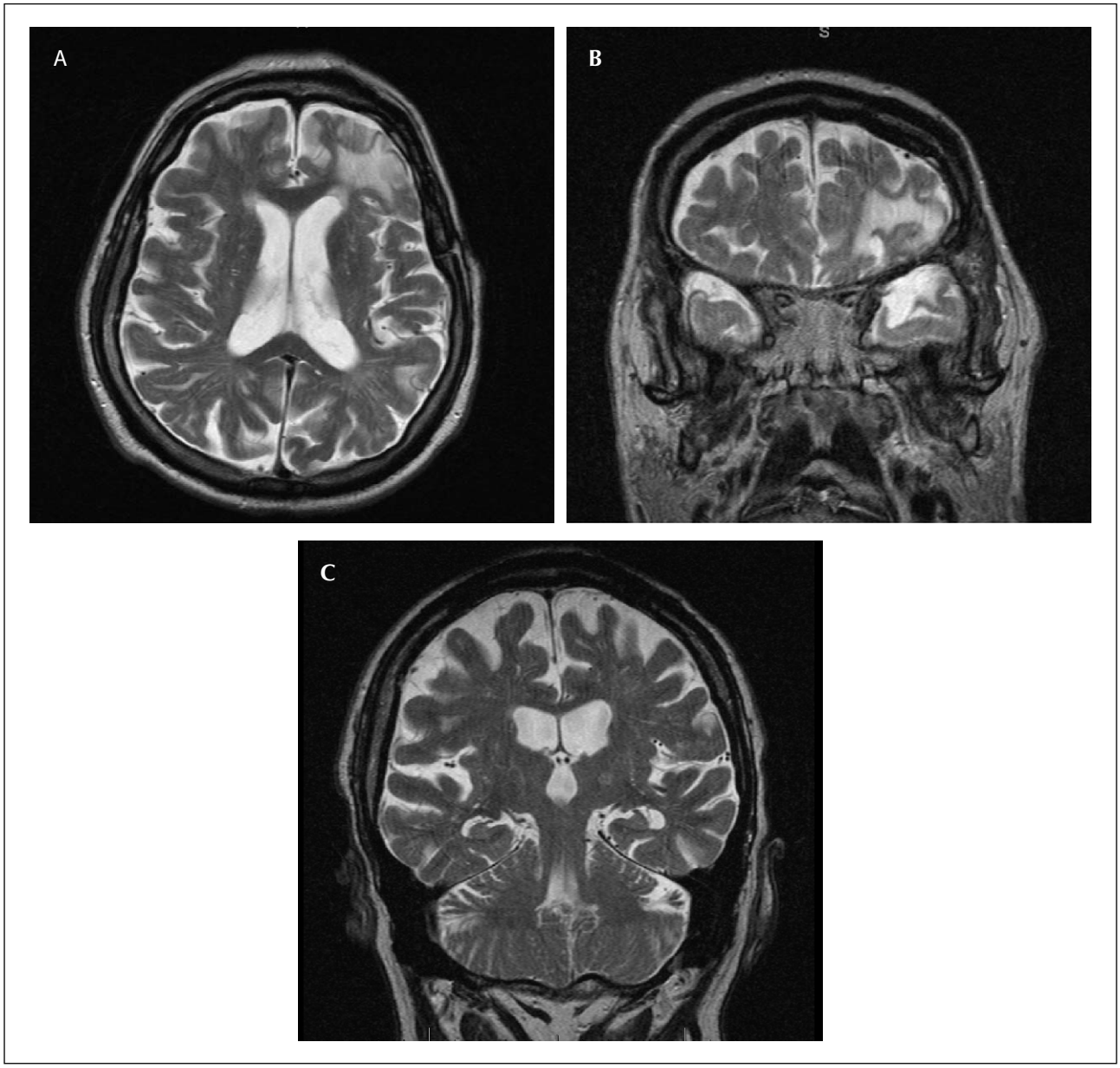

Figure 2. A) Is an axial T2 image showing an area of encephalomalacia over the left frontal area. **B**) Shows the previous area of encephalomalacia over the left frontal area and a second area over the anterior temporal region. **C**) Shows atrophy of the left hippocampus, along with more generalized brain atrophy.

corresponding outcomes for the older *vs* the younger group were Engel II 35% *vs* 44%, Engel III 25% *vs* 12%, and Engel IV 10% *vs* 4%, respectively. There was a trend in this study to show better prognosis in the younger group, although this did not reach statistical significance. In the study by Sirven *et al.* (2000), patients were divided into two groups of older and younger than 50 years old. This study reported a significant difference in patients with temporal resections, and 53% became seizure-free in the older group compared with 75% in the younger group. Grivas *et al.* (2006) reported the surgical outcome of 52 patients without controls; 71% of patients reached Engel class I, < 19% Engel class II, 8% Engel class III and 2% Engel class IV. Finally, Acosta *et al.* (2008) reported a series with the oldest patients ever reported. Out of seven patients, four achieved an Engel class I outcome (seizure-free), two were Engel class II, and one was Engel class IV. The patient we report here attained Engel class II, an excellent outcome considering his longstanding pattern of recurrent status epilepticus.

Age is an important criterion for epilepsy surgery and surgery is usually performed in patients younger than 60 years old, however, there is variation among different centres and on a few occasions, epilepsy surgery is performed in patients older than 65 years old. Age constitutes a determinant in the decision for epilepsy surgery and the risk of higher frequency of peri-operatory complications, more comorbidities, possible cognitive decline post-operatively, and less favorable seizure outcome should be considered. McLachlan *et al*. (1992) reported the outcome in 20 patients where the mean age was 51 years old (range: 45 to 60 years), Boling *et al*. (2001) reported 18 patients with a mean age of 54 years old, with the oldest being 64 years old. Sirven *et al*. (2000) reported a study with 30 patients ranging from 50 to 66 years old, and Grivas *et al*. (2006) with 52 patients with a mean age of 55.9 years old (range: 50 to 71 years). Acosta *et al*. (2008) reported seven patients that ranged between 60 and 76 years old. Only the oldest patient in that series was older than this reported case.

The occurrence of complications is a major concern when considering epilepsy surgery in the elderly population. Boling *et al*. (2001) found a similar rate of complications in 18 patients older than 50 years old than in 200 patients younger than 50 years old. Complications reported in patients in the older group were epidural hematoma requiring evacuation, pulmonary embolism, mild dysphasia and a wound infection. Grivas *et al*. (2006) reported a study with 52 patients older than 50 years old with complications in 7.7% of patients, including deep venous thrombosis, intracerebral hemorrhage, pneumonia and a small ischemic stroke. In this study there was no comparison with a younger group. Finally, McLachlan *et al*. (1992) reported no complications in a group of patients older than 45 years old, but surprisingly, did find complications in the younger age group. The patient we report here had transient aphasia after surgical resection, presumably due to edema and local irritation of peri-sylvian language centers.

Another interesting aspect in this case was the development of two epileptogenic areas after the resection of the meningioma. It is possible that the initial seizure in this patient may have been related to the meningioma localized in the left frontal area. Epileptogenic discharges from this area may have propagated through association fibers such as the uncinate fasciculus to the temporal lobe. During the tumor resection a second epileptogenic area may have been triggered in the temporal area. Studies in animal models have shown that rats can develop temporal lobe epilepsy after a head injury due to mossy fiber sprouting in the hippocampus, as well as loss of dentate hilar neurons (Kharatishvili *et al*. 2006). The epileptogenic area in the left temporal lobe might also have been triggered by retraction of the temporal lobe during the transsylvian approach. □

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