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Cryptogenic West syndrome and subsequent mesial temporal lobe epilepsy

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ABSTRACT We report on a male patient who experienced a previously unreported sequence of cryptogenic West syndrome in infancy and subsequent mesial temporal lobe epilepsy. His complex partial seizures were consistently characterised by motionless staring with brief right eye blinking. Scalp electroencephalography (EEG) showed bilateral temporal spikes which were dominant on the right side. Magnetic resonance imaging (MRI) revealed no organic brain lesion. Invasive EEG recording captured seizures with right hippocampal onset. The patient became seizure-free following right temporal lobectomy at 27 years, 8 months of age. Pathological examination of the resected specimen revealed corpora amylacea and gliosis in the temporal cortex but no clear findings of hippocampal sclerosis. It is suggested that an epileptogenic lesion causing MRI-negative mesial temporal lobe epilepsy may give rise to apparent cryptogenic West syndrome in infancy.

Key words: cryptogenic West syndrome, mesial temporal lobe epilepsy, corpora amylacea, ictal intracranial EEG

Mesial temporal lobe epilepsy (MTLE) is an epileptic syndrome that is generally resistant to medical treatment but can often be successfully treated by surgical removable of the mesial temporal lobe (Wiebe *et al*., 2001; Téllez-Zenteno *et al*., 2005; Elsharkawy *et al*., 2009). Many patients with MTLE also have hippocampal sclerosis, which is believed to be attributable to some form of neuronal damage in icted on the immature mesial temporal structures in infancy or early childhood (Wieser, 2004).

Herein, we report a patient who had cryptogenic West syndrome in infancy and subsequent MTLE from childhood, who had complete remission of seizures following anterior temporal lobectomy; to the best of our knowledge, this sequence of epilepsy syndromes has not previously been reported.

Case report

This right-handed male patient was 27 years, 8 months old at the time

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of surgery. No abnormalities were discovered in his family history. The patient was born normally after an uneventful pregnancy and developed normally during early infancy.

Epileptic spasms in series began to occur with hypsarrhythmia on EEG at five months of age, and the patient was admitted to Okayama University Hospital. The patient s spasms showed no sign of lateralisation or temporal lobe semiology. A battery of examinations revealed no abnormalities regarding the underlying disorder. Neither interictal nor ictal EEGs showed asymmetry or dominance over the temporal region. He was therefore diagnosed with cryptogenic West syndrome. Treatment with antiepileptic medication failed, but synthetic adrenocorticotropic hormone (ACTH) therapy completely suppressed epileptic spasms with the disappearance of epileptic discharges on EEG at six months of age.

Complex partial seizures (CPSs) with motionless staring, facial pallor, and brief right eye blinking began to occur several times per week at 2 years, 11 months of age. CPSs continued to occur at a frequency of 4 to 10 times per month despite medical treatment and the patient gradually began to develop an ictal hand automatism and postictal vomiting and nausea. Epileptic discharges were observed over the right anterior temporal region starting at 4 years, 7 months of age. The ictal EEG of a CPS was recorded, with the origin in the same region. Thereafter, EEG showed temporal spikes that were consistently dominant on the right side, though left temporal spikes began to concurrently appear at 13 years of age. He graduated from a standard senior high school but had to withdraw from university due to an inability to concentrate.

The patient was re-admitted at 26 years of age as a candidate for surgical treatment. He was found to have simple partial seizures as well as CPSs. His simple partial seizures were associated with a sense of lightheadedness with occasional subsequent nausea but with no auditory or visual aura. His CPSs were characterised by initial blinking, dominant on the right side, and subsequent motionless staring and facial pallor, which were followed by automatisms in the mouth and the right upper extremity and a dystonic posturing in the left upper extremity. CPSs occurred daily with a duration of around 60 seconds. He was in a prolonged confusional state immediately after CPSs but with no postictal aphasia or paralysis. He never experienced secondary generalised seizures.

The interictal EEGs showed bilateral epileptic discharges (sporadic sharp waves) involving F7, F8, T1, and T2, with dominance over the right hemisphere. The ictal scalp EEGs revealed the onset of seizures as rhythmic 4 to 6 Hz theta activity in the right temporal region. Magnetoencephalography showed no consistent clusters of current dipoles. No organic brain lesion was detected by 1.5-Tesla MRI using T1- and T2-weighted images and uid-attenuated inversion recovery (FLAIR) (*gure 1; upper panel*). Positron emission tomography (PET) revealed a widespread area of hypometabolism involving the lower mesial part of the right temporal lobe (*gure 1; lower panel*).

His intelligence was categorised as mildly retarded according to the Wechsler Adult Intelligence Scale (WAIS)-R with a full-scale IQ of 67 at 26 years, 9 months of age. His verbal and performance IQ scores were 70 and 68, respectively, with no dissociation. His general memory score was 78, according to the Wechsler Memory Scale (WMS)-R at 27 years, 5 months of age: his verbal and visual memory scores were 81 and 82, respectively, with no dissociation.

Invasive seizure monitoring was undertaken by stereotaxic implantation of depth electrodes targeting the bilateral amygdalae and hippocampi, as well as by the placement of subdural electrodes over the right frontal and temporal lobes and the left temporal lobe under general anaesthesia during a right fronto-temporal and left temporal craniotomy. The intracranial EEG recording captured 23 clinical seizures with right hippocampal onset (*gure 2*) and one seizure with left hippocampal onset. In addition, 21 instances of an ictal EEG pattern with right hippocampal origin were recorded without clinical symptoms. The scalp and intracranial EEG recording showed no epileptic spasms. Therefore, the patient was diagnosed with right MTLE in spite of the negative MRI finding, and a resection of the right anterior temporal lobe (5 cm from the temporal tip) was performed (*gure 3*). Pathological examination of the resected specimen revealed diffuse intense gliosis with associated corpora amylacea in the temporal cortex but no clear findings of hippocampal sclerosis (*gure 4*).

The patient has been completely seizure-free for 2 years and 10 months since the surgery. Right temporal spikes completely disappeared from the EEG. Although rare spikes remained at T1 for one year after the operation, EEG showed no epileptic discharges during either wakefulness or sleep, 18 months after the surgery.

Discussion

The patient was diagnosed with cryptogenic West syndrome in infancy. His epileptic spasms were completely suppressed by synthetic ACTH therapy, which included the disappearance of epileptic discharges on EEG. However, the epilepsy returned as intractable localisation-related epilepsy. Both scalp and intracranial EEG findings consistently indicated that the seizure origin was in the right mesial temporal lobe. He became completely seizure-free following a right anterior temporal lobectomy. Therefore, his right mesial

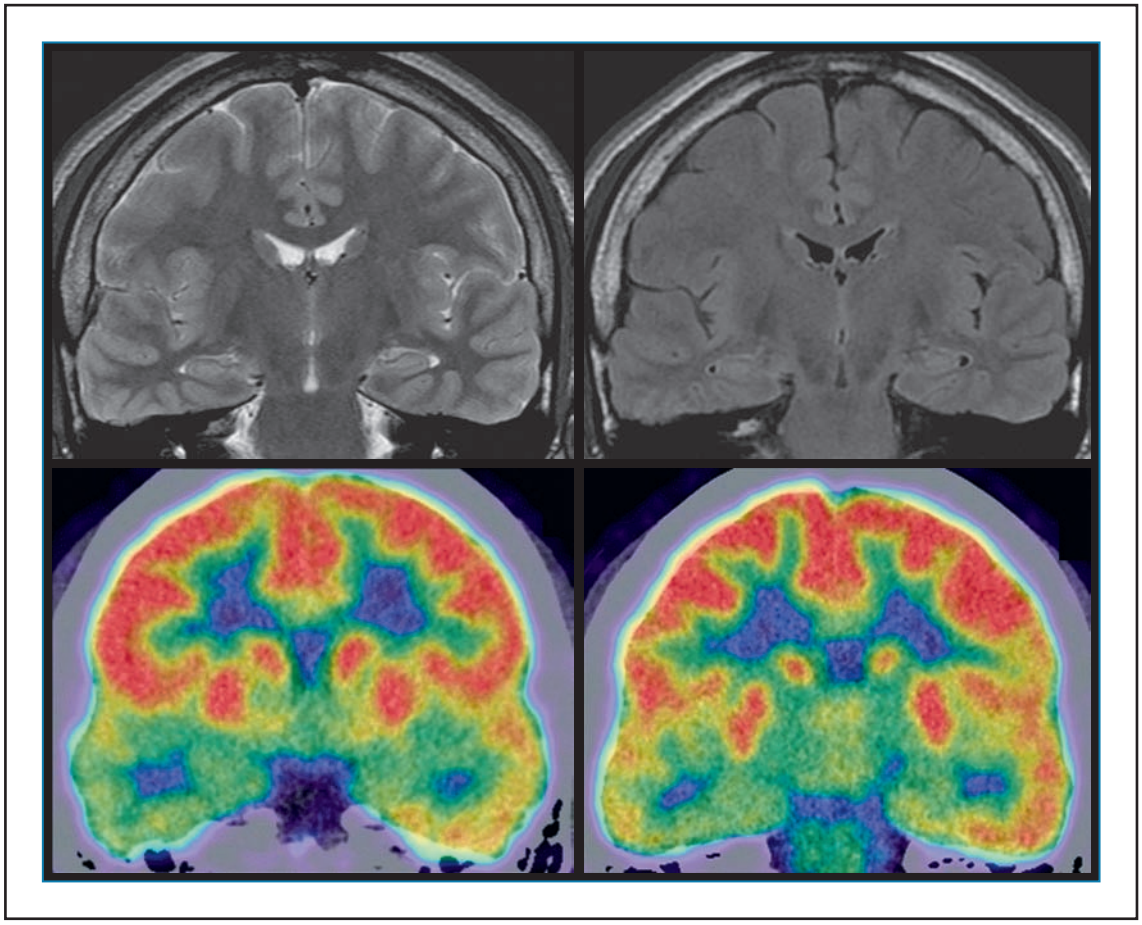

Figure 1. Neuroimaging studies.
Coronal T2-weighed (upper left panel) and uid-attenuated inversion recovery (FLAIR) (upper right panel) images from MRI demonstrate no signal abnormality or atrophy. Positron emission tomography/computed tomography (PET/CT) (lower panel) shows a widespread area of hypometabolism involving the lower mesial part of the right temporal lobe.

temporal lobe must have been the source of the epileptogenicity prior to the surgery.

MTLE is typically associated with hippocampal sclerosis, but approximately 15% of all patients with MTLE lack hippocampal sclerosis based on neuroimaging (Jackson *et al*., 1994). In the current patient, hippocampal sclerosis was not found during either neuroimaging or histopathology. Corpora amylacea, which was detected from the specimen, is observed in patients with MTLE with predominance in the CA1 region, and it is believed to be a consequence of the neurodegeneration that is correlated with the duration of epilepsy (Radhakrishnan *et al*., 2007). This is a non-specific finding that can be observed not only in patients with epilepsy, but also in patients with other disorders (Keller, 2006). Therefore, corpora amylacea in the current patient must be a secondary phenomenon due to seizures.

Surgical prognosis in patients with MTLE without hippocampal sclerosis is generally poorer than in patients with hippocampal sclerosis, probably due to the presence of a dual pathology or erroneous estimation of the epileptogenic region by presurgical evaluation (Berkovic *et al*., 1995; Bell *et al*., 2009; Immonen *et al*., 2010). In the current patient, we used subdural electrodes, which covered a considerably large cortical area, in addition to depth electrodes targeting the hippocampi and amygdalae. Such careful investigation was necessary due to the possibility that his seizures might have originated from outside of the mesial temporal structures since his epilepsy was initially diagnosed as non-lesional West syndrome in infancy. Consequently, we were able to confirm that the origin for a majority of his seizures was in the right hippocampus, leading to seizure freedom following right anterior temporal lobectomy.

Although patients who have partial seizures following West syndrome are not exceptional (Ohtsuka *et al*., 1996; Lagae *et al*., 2010), those with symptomatic West syndrome with an identifiable cortical lesion are prone

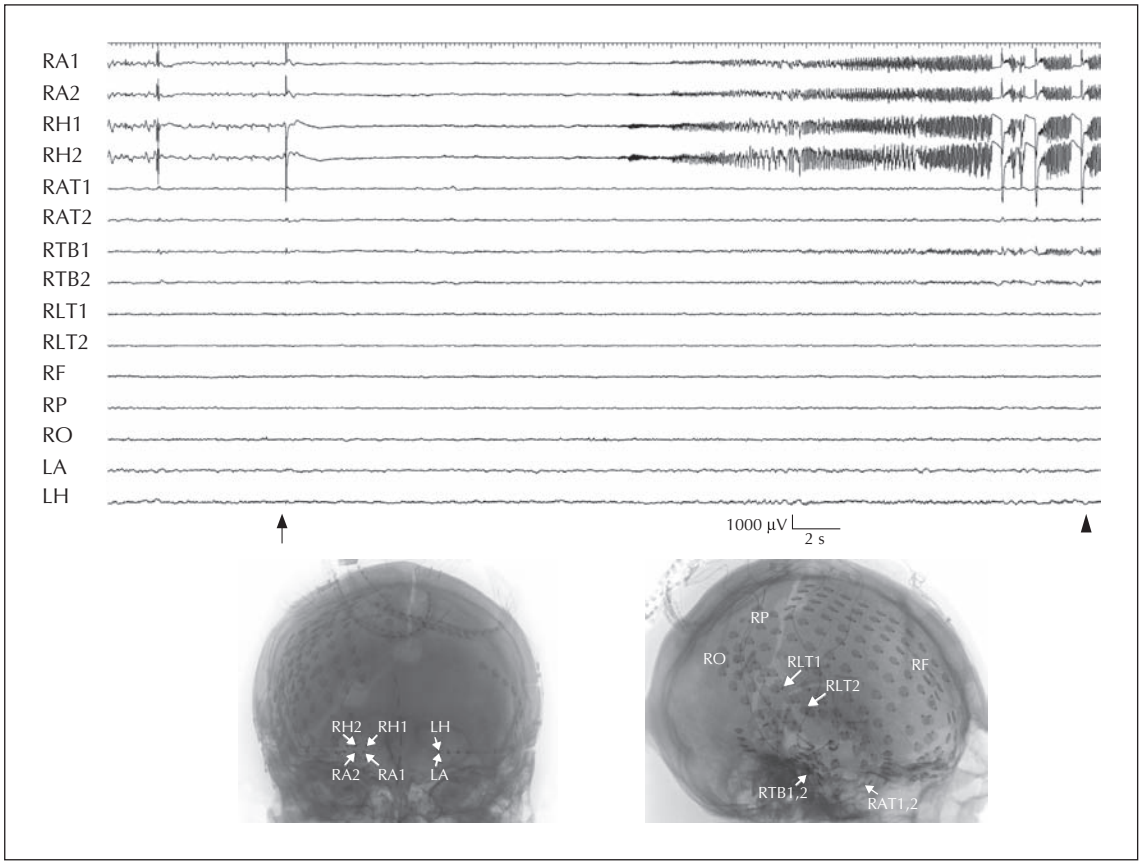

Figure 2. Invasive ictal EEG recording.
Low-amplitude, fast waves appeared in the right amygdala and hippocampus (arrow), followed by high-amplitude, sharp activity. A complex partial seizure began with motionless staring at the point indicated by the arrowhead. The epileptic discharges were almost completely restricted to the right temporal structures throughout the seizure.

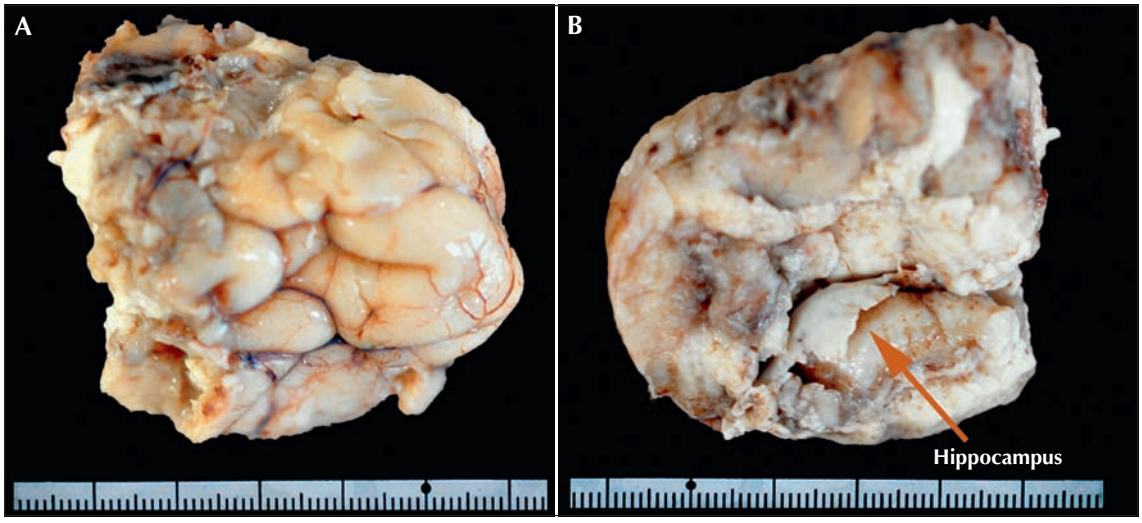

Figure 3. Right anterior temporal lobectomy.
Lateral (A) and mesial (B) view of the resected right anterior temporal lobe. The right hippocampus is indicated by the arrow.

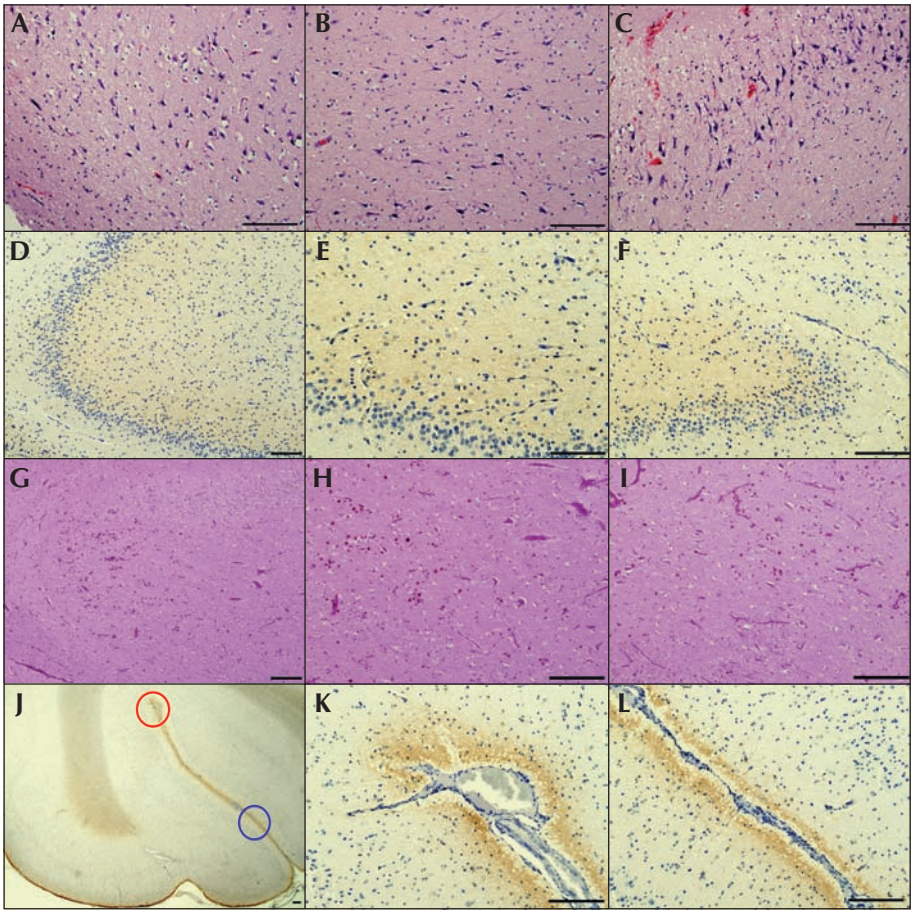

Figure 4. Pathological findings of the resected specimen.
(A-C) Haematoxylin-eosin (HE) staining of the hippocampus demonstrates minimum neuronal loss in CA1 (A), CA4 (B), and CA3 (C). (D-F) Glial fibrillary acidic protein (GFAP) staining of the hippocampus reveals minimum GFAP expression in the hippocampus (D: CA1; E: CA4; F: CA3). (G-I) Periodic acid-Schiff (PAS)-stained section of the hippocampus shows corpora amylacea deposition in CA1 and CA4 (G: CA1; H: CA4; I: CA3). (J-L) GFAP staining of the temporal lobe shows cortical gliosis. The areas within the red and blue circles in (J) correspond to panels (K) and (L), respectively. Scale bars: 100 μm.

to partial seizures originating from that cortical lesion. These patients often have partial seizures as well as epileptic spasms during the clinical period of West syndrome (Ohtsuka *et al.*, 1996; Kobayashi *et al.*, 2001) and their cortical lesion may play a role in the generation of both West syndrome and localisation-related epilepsy. Children with cryptogenic late-onset epileptic spasms were also reported; they had associated focal seizures and predominant temporo-frontal EEG abnormalities (Eisermann *et al.*, 2006). Clear evidence to support this possibility was not found in the surgical specimen of the current patient, but the finding of diffuse gliosis in the temporal cortex may be related to epileptogenicity for both West syndrome and subsequent MTLE. We were not able to find any other reported cases of West syndrome caused by strictly mesial temporal lesions.

In some patients, no brain lesions are revealed by neuroimaging despite the occurrence of partial seizures following West syndrome, as was true for the current patient. It has been reported that the occurrence of MTLE has a close causative relationship with complicated febrile seizures in infancy and early childhood (French *et al.*, 1993). However, to the best of our knowledge, there are no other reports of MTLE caused by West syndrome and, therefore, it is an unlikely possibility that West syndrome (a type of epileptic encephalopathy) induced epileptogenicity in the previously normal mesial temporal structures.

As for the current case, no decisive evidence has been obtained to determine whether pathology involving the mesial temporal structures was present from the onset of West syndrome, though the presence of diffuse intense gliosis in the temporal cortex may suggest this possibility. This patient with cryptogenic West syndrome and subsequent MTLE represents a previously unreported case of great interest regarding the pathophysiology and pathogenesis of these two types of epileptic syndromes. □

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References

Bell ML, Rao S, So EL, *et al*. Epilepsy surgery outcomes in temporal lobe epilepsy with a normal MRI. *Epilepsia* 2009; 50: 2053-60.

Berkovic SF, McIntosh AM, Kalnins RM, *et al*. Preoperative MRI predicts outcome of temporal lobectomy: an actuarial analysis. *Neurology* 1995; 45: 1358-63.

Eisermann MM, Ville D, Souf et C, *et al*. Cryptogenic late-onset epileptic spasms: an overlooked syndrome of early childhood? *Epilepsia* 2006; 47: 1035-42.

Elsharkawy AE, Alabbasi AH, Pannek H, *et al*. Long-term outcome after temporal lobe epilepsy surgery in 434 consecutive adult patients. *J Neurosurg* 2009; 110: 1135-46.

French JA, Williamson PD, Thadani VM, *et al*. Characteristics of medial temporal lobe epilepsy: I. Results of history and physical examination. *Ann Neurol* 1993; 34: 774-80.

Immonen A, Jutila L, Muraja-Murro A, *et al*. Long-term epilepsy surgery outcomes in patients with MRI-negative temporal lobe epilepsy. *Epilepsia* 2010; 51: 2260-9.

Jackson GD, Kuzniecky RI, Cascino GD. Hippocampal sclerosis without detectable hippocampal atrophy. *Neurology* 1994; 44: 42-6.

Keller JN. Age-related neuropathology, cognitive decline, and Alzheimer s disease. *Ageing Res Rev* 2006; 5: 1-13.

Kobayashi K, Ohtsuka Y, Ohno S, *et al*. Clinical spectrum of epileptic spasms associated with cortical malformation. *Neuropediatrics* 2001; 32: 236-44.

Lagae L, Verhelst H, Ceulemans B, *et al*. Treatment and long-term outcome in West syndrome: the clinical reality. A multicentre follow-up study. *Seizure* 2010; 19: 159-64.

Ohtsuka Y, Murashima I, Asano T, Oka E, Ohtahara S. Partial seizures in West syndrome. *Epilepsia* 1996; 37: 1060-7.

Radhakrishnan A, Radhakrishnan K, Radhakrishnan VV, *et al*. Corpora amylacea in mesial temporal lobe epilepsy: clinicopathological correlations. *Epilepsy Res* 2007; 74: 81-90.

Téllez-Zenteno JF, Dhar R, Wiebe S. Long-term seizure outcomes following epilepsy surgery: a systematic review and meta-analysis. *Brain* 2005; 128: 1188-98.

Wiebe S, Blume WT, Girvin JP, Eliasziw M. Effectiveness and Efficiency of Surgery for Temporal Lobe Epilepsy Study Group. A randomized, controlled trial of surgery for temporal lobe epilepsy. *N Engl J Med* 2001; 345: 311-8.

Wieser HG; ILAE Commission on Neurosurgery of Epilepsy. ILAE Commission Report. Mesial temporal lobe epilepsy with hippocampal sclerosis. *Epilepsia* 2004; 45: 695-714.