

# LATE ONSET TEMPORAL LOBE EPILEPSY DUE TO CEREBRAL HYPOPERFUSION: CASE REPORT

*EPILEPSIA DE LOBO TEMPORAL DE INÍCIO TARDIO DECORRENTE DE HIPOPERFUSÃO CEREBRAL: RELATO DE CASO*

*EPILEPSIA DE LÓBULO TEMPORAL DE INICIO TARDÍO DEBIDO A HIPOPERFUSIÓN CEREBRAL: RELATO DE CASO*

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## ABSTRACT

Temporal lobe epilepsy is the most common form of focal epilepsy. The main pathological substrate of refractory TLE is hippocampal sclerosis (HS). HS has been associated with prolonged febrile and recurrent seizures. Other known causes for hippocampal injury are head trauma, ischemia, stroke and Alzheimer's disease. The exact causes of HS remain unknown, although they are probably diverse and multifactorial. The patient with TLE had no risk factors for epilepsy. His first seizure occurred immediately after an abdominal surgery complicated by profuse bleeding and hypotension during the procedure. The MRI showed hippocampal atrophy, probably due to hippocampal hypoperfusion, given the temporal relationship between the seizures and surgery. The etiology of hippocampal infarcts is discussed in this article. In a study with animal model, cerebral hypoperfusion led to a pattern of epileptiform activity similar to that found in the human hippocampus.

**Keywords:** Epilepsy, temporal lobe; Hippocampus; Atrophy; Ischemia; Sclerosis.

## RESUMO

A epilepsia de lobo temporal (ELT) é a forma mais comum de epilepsia focal. O principal substrato patológico da ELT refratária é a esclerose hipocámpal (EH). A EH tem sido associada a crises febris prolongadas e convulsões recorrentes. Outras causas conhecidas de dano hipocámpal são: traumatismo cranioencefálico, isquemia, acidente vascular cerebral e doença de Alzheimer. As causas exatas da EH permanecem desconhecidas, apesar de serem provavelmente diversas e multifatoriais. O paciente com ELT não tinha fatores de risco de epilepsia. O paciente apresentou a primeira crise epiléptica no pós-operatório imediato de uma cirurgia abdominal complicada por sangramento profuso e hipotensão durante o procedimento. A RM evidenciou atrofia hipocámpal, provavelmente decorrente da hipoperfusão hipocámpal, dada a relação temporal das crises com o procedimento cirúrgico. A etiologia dos infartos hipocámpais é abordada neste artigo. Em um estudo com modelo animal, o hipofluxo cerebral levou a um padrão de atividade epileptiforme semelhante ao encontrado no hipocampo humano.

**Descritores:** Epilepsia de lobo temporal; Hipocampo; Atrofia; Isquemia; Esclerose.

## RESUMEN

La epilepsia de lóbulo temporal (ELT) es la forma más común de epilepsia focal. El principal sustrato patológico de la ELT refractaria es la esclerosis hipocámpal (EH). La EH ha sido asociada a crisis febriles prolongadas y convulsiones recurrentes. Otras causas conocidas de daño hipocámpal son: traumatismo craneoencefálico, isquemia, accidente vascular cerebral y enfermedad de Alzheimer. Las causas exactas de la EH permanecen desconocidas, a pesar de ser probablemente diversas y multifactoriales. El paciente con ELT no tenía factores de riesgo de epilepsia. El paciente presentó la primera crisis epiléptica en el postoperatorio inmediato de una cirugía abdominal complicada por sangrado profuso e hipotensión durante el procedimiento. La RM evidenció atrofia hipocámpal, probablemente debido a la hipoperfusión hipocámpal, dada la relación temporal de las crisis con el procedimiento quirúrgico. La etiología de los infartos hipocámpales es abordada en este artículo. En un estudio con modelo animal, el hipoflujo cerebral llevó a un estándar de actividad epileptiforme semejante al encontrado en el hipocampo humano.

**Descriptores:** Epilepsia de lóbulo temporal; Hipocampo; Atrofia; Isquemia; Esclerosis.

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## INTRODUCTION

### Temporal lobe epilepsy

Temporal lobe epilepsy, especially mesial temporal lobe epilepsy (MTLE), is the most common form of focal epilepsy. The main pathological substrate in refractory MTLE is hippocampal sclerosis (HS).<sup>1-3</sup> The causes of HS remain unknown, although they are probably diverse and multifactorial.

One third of patient with TLE treated with antiepileptic drugs do not respond to medication.<sup>4</sup> In refractory cases, surgical treatment should be considered. Anterior temporal lobectomy is the most common surgery for epilepsy and is superior to drug treatment and other types of surgery in controlling seizures.<sup>5,6</sup>

### Hippocampal sclerosis

HS is a pathological finding observed for over 100 years with a specific pattern of neuronal loss in subregions of the hippocampal formation and other medial temporal structures.<sup>7</sup> HS has been associated with prolonged febrile<sup>8-10</sup> and recurrent seizures, but the relationship between repeated seizures and hippocampal atrophy is not well known.<sup>11</sup>

There are also other known causes of hippocampal injury such as head trauma, ischemia, stroke and Alzheimer's disease.<sup>12</sup>

Another etiology discussed in recent studies is hippocampal infarcts. When ischemia reaches large hippocampal areas it is associated with clinical symptoms of cognitive impairment or epilepsy. The susceptibility to ischemia found in this region, leading to neuronal degeneration, is influenced by risk factors that are not well known, but the size of the lesion is directly correlated with the clinical presentation.<sup>13</sup>

The excitotoxic damage related to seizure activity during the ischemia may also contribute to early injury of hippocampal neurons and can lead to dysfunction of extrahippocampus regions too. In an animal model study, the occlusion of four-vessels led to a pattern of epileptiform activity similar to that found in human hippocampus, prefrontal and perirhinal cortex, areas that are also susceptible to ischemia.<sup>14</sup>

We describe in this case report a patient with no previous risk factors for TLE, who had his first seizure during the postoperative period, following a large abdominal surgery. MRI images showed signs of HS. We discuss here the possible mechanism that could be related to HS.

### Case report (results)

We present a case of a 65 years old patient, male, who underwent an azygo-portal disconnection in September 2007 due to schistosomiasis associated with portal hypertension and esophageal varices. During surgery, the left gastric vein and artery, as well as, the esophagus varices and splenic artery were ligated. Splenectomy was not performed. Due to the presence of collateral circulation, patient presented profuse bleeding that was planned to be performed in the same surgical procedure.

After the operation, he developed episodes characterized by nonspecific malaise followed by loss of consciousness and right-handed automatisms, without postictal symptoms. These episodes recurred, occurring approximately seven times per month. In May 2013, there was an increase in seizure frequency to three times per week and 100 mg per day of phenobarbital was started. In November 2013, he was seen for the first time in our Epilepsy clinic. He complained of somnolence, without

significant improvement in seizure control. Neurologic exam was normal. He had arterial hypertension and had no previous risk factors for epilepsy.

MRI was performed and showed bilateral hippocampal atrophy, more pronounced on left side, as well as, hyperintense signal in T2 and FLAIR images in the left amygdala and hippocampus. There was no abnormal hyperintensity in the right hippocampus. Inter-ictal EEG showed infrequent epileptiform activity and frequent slow waves in the left temporal region. carbamazepine was initiated and phenobarbital was slowly withdrawn. Patient was diagnosed with TLE and continues with an average of three focal dyscognitive seizures per day due to noncompliance.

## DISCUSSION

This case describes a late-onset temporal lobe epilepsy,<sup>15</sup> with typical semiology, MRI and EEG features. In this case, there is a well-established temporal relationship between seizure onset and a major abdominal surgery with profuse bleeding and hypovolemia. Patient had no other risk factors for epilepsy, suggesting a causal relationship between the procedure and seizure onset.

In a study performed in rats, the model of four-vessels occlusion causing cerebral ischemia with monitoring by implanted electrodes in CA1, prefrontal and perirhinal cortex, identified reduced amplitude of alpha and occurrence of spikes during occlusion. During the first hours of reperfusion the majority of animals developed seizures.<sup>14</sup> As the mesial temporal lobe region is poorly irrigated, any significant reduction of blood flow in this area may cause an early ischemic injury, explaining the occurrence of seizures. We hypothesize that a similar mechanism might have occurred in the case reported herein. Due to profuse bleeding this patient probably became hypotense and presented brain hypoperfusion, leading to ischemia of the mesial temporal lobe structures. Therefore, as described in the animal model, the patient presented seizures during the first hours of reperfusion.

Hippocampal injury can lead to increased levels of neurogenesis and high concentration of neurotrophic factors that appear to be beneficial in acute hippocampal dysfunction. However, in the chronic phase of injury, abnormal synaptogenesis and new neurons that arise in this area may lead to aberrant reorganization of synapses and progressive loss of GABAergic inhibition, generating sustained decline in neurogenesis and inflammation, which are deleteric and potentially epileptogenic.<sup>12</sup> The ongoing changes occurring overtime may explain the clinical deterioration of the patient after a few years of insult. Unfortunately, the patient had no neuroimaging studies prior to surgery in order to compare the hippocampus signal and volume. Investigation was not performed in the early postoperative period, which limits the etiological evaluation.

The literature shows that stem cells of the nervous system used in the early injured hippocampus in an animal models with minor injuries from toxic substances, brain trauma, and status epilepticus may have therapeutic value in preventing the development of temporal lobe epilepsy, depression and memory dysfunction. This can be attributed to potential mechanisms of functional recovery mediated by these cells<sup>12</sup> and represents hope for curative treatment for similar future cases.

## FINAL CONSIDERATIONS

The correlation between temporal lobe epilepsy and hippocampal sclerosis is well established in the literature for over 100 years, however the causes of hippocampal sclerosis are not yet well defined. Studies with animal models as well as

clinical follow-ups are essential to help us better understand this relationship. This knowledge would be important in the prevention of secondary MTLE and maybe in the development of more specific therapeutic options based on the mechanism of injury.

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