Uncovering a Commonly Missed Cause of Drug-Resistant Epilepsy: A Case Report on Surgical Intervention for Hippocampal Sclerosis

Yong Yuan,MM[a],Yiping Tang,MM[a], Yongjun Gao,PhD[a], Jianxing Xu, MM[a], Xi Zhang, MM[b], Haiyan Tian,MB[c],Qiongmei Zhang,MB[c],Xu You, PhD[c*]

Affliated:

a Department of Neurosurgery, The Second Affiliated Hospital of Kunming Medical University, Kunming, Yunnan 650101, China
b Department of Neurosurgery, Chuxiong Yi Autonomous Prefecture Traditional Chinese Medicine Hospital, Chuxiong, Yunnan 675000, China
c Department of Neurology, Honghe Second People's Hospital, Honghe, Yunnan 654399, China

* Correspending author.
E-mail addresses: 15181127730@163.com

Abstract

Rationale:

This study aimed to present a case of drug-resistant epilepsy caused by hippocampal sclerosis (HS). Furthermore, this study highlights the critical role of standardized and precise surgical intervention in the management of drug-resistant epilepsy (DRE), thereby providing a valuable reference for similar cases.

Patient concerns:

A 19-year-old male was admitted with frequent generalized tonic-clonic seizures. Imaging studies revealed characteristic features of left-sided HS, including symmetric bilateral hippocampi on hippocampal thin-slice magnetic resonance imaging, reduced volume of the left hippocampus, signal hyperintensity on T2-FLAIR imaging, and enlargement of the adjacent temporal horn of the lateral ventricle.

Diagnoses:

The diagnosis of DRE was made.

Interventions:

The standard left anterior temporal lobectomy (ATL) was performed with the assistance of neuronavigation and intraoperative electrophysiological monitoring.

Outcomes:

The patient underwent a standard left ATL. Postoperative pathology confirmed that the resected HS tissue was brain tissue, with no evidence of tumor lesions. The patient showed significant improvement in symptoms postoperatively, with no complications, and was discharged smoothly. Follow-up at 2 months, including 2 electroencephalograms, showed no typical abnormal wave activity during both awake and sleep states, with no clinical seizures.

Lessons:

Hippocampal sclerosis-related DRE are prone to misdiagnosis. It is recommended that hippocampal thin-slice Magnetic Resonance Imaging (MRI) should be routinely performed for DRE. Neuronavigation and intraoperative electrophysiological monitoring play crucial roles in the implementation of standard ALT. The epilepsy surgery team should provide continuous postoperative rehabilitation counseling and support for the patient and family.

1. Introduction

Drug-resistant epilepsy (DRE) is a disorder defined by the International League Against Epilepsy in which seizures persist despite treatment with at least two appropriate and adequate antiepileptic drugs. About 20-30% of patients with epilepsy develop resistance to antiepileptic drugs, with varying clinical manifestations, which are closely related to the biological basis of the disease[1]. The etiology of DRE is complex, often involving structural, genetic, and metabolic factors[2, 3]. Among these causes, HS is one of the most common structural causes, particularly prevalent in patients with DRE[4, 5]. However, many clinicians lack awareness of DRE caused by HS, leading to missed diagnoses, which can severely impact the patient's condition and quality of life. In August 2024, we admitted a patient with DRE caused by left-sided HS. This report presents a detailed account of the patient's diagnostic evaluation, surgical treatment, and follow-up process, providing valuable reference for the standardized management of DRE.

2. Case report

A 19-year-old male was admitted in August 2024 due to 17 years of episodic limb convulsions associated with loss of consciousness. He first experienced a seizure at age 2 without obvious triggers, with seizure frequency gradually increasing thereafter. Over the past 15 years, he visited multiple hospitals and was prescribed various antiepileptic drugs, but his symptoms remained poorly controlled. In 2022, he visited our hospital where his medication was adjusted, and surgery was recommended. However, due to concerns about surgical risks, the family opted to continue with medication, taking oxcarbazepine 0.6g (twice daily) and valproic acid controlled-release tablets 500mg (twice daily). After medication adjustment, his

seizure frequency slightly decreased. However, since July 2024, his seizures significantly worsened, occurring 6-7 times per day, with each episode resulting in varying degrees of injury, seriously threatening his quality of life and safety. He sought surgical treatment at our hospital. Laboratory tests, including complete blood count, biochemical markers, coagulation function, and infectious disease screening, were all within normal limits. On physical examination, the patient was alert and responsive, with pupils equal and reactive to light (approximately 3.0mm in diameter). The neck was soft with no resistance, and limb muscle strength and tone were normal, with no positive pathological signs. Multiple contusions and abrasions were noted on the face and limbs, indicative of repeated falls.

Under the guidance of our department, the patient continued taking oxcarbazepine 0.6g (third times daily) to prevent seizures, while actively completing the necessary preoperative assessments. (2024-08-23) Routine head Magnetic Resonance Imaging (MRI) showed no intracranial abnormalities, and no changes were observed in the hippocampal plane (Fig. 1A, B, C). (2024-08-28) Hippocampal thin-slice MRI demonstrated symmetric bilateral hippocampi, with reduced volume of the left hippocampus, FLAIR imaging revealing signal hyperintensity, and enlargement of the adjacent temporal horn of the lateral ventricle, consistent with left hippocampal sclerosis (Fig. 1D, E, F). (2024-08-28) Electroencephalogram (EEG) showed a normal background with intermittent epileptiform discharges. During both awake and sleep states, abundant low, medium, and high-amplitude spikes, sharp waves, and spike (sharp) slow waves were observed. These activities exhibited short-to-medium rhythm, primarily in the left anterior temporal, middle temporal, and frontal regions, without clinical seizures.

(2024-09-04) The patient underwent a standard left ALT under general anesthesia. Meanwhile, the 3D reconstruction of the left HS area was generated using the neuronavigation system, providing the surgeon with a more intuitive visual representation (Fig. 2). Intraoperative electrophysiological monitoring revealed significant epileptiform discharges in the left temporal lobe leads. The resection area of the anterior temporal lobe was about 4.5 cm, performed under high-power microscopy. During the procedure, the hippocampal tissue was found to be firmer than normal tissue. The sclerotic hippocampal tissue was completely resected, and the post-resection view exposed the cerebral peduncles, brainstem, basal cisterns, and posterior cerebral arteries. (See Video, Supplemental Video, which demonstrated the brief procedure of ALT.)

(2024-09-05) Head computed tomography (CT) showed changes consistent with left ALT (Fig. 3A). The patient recovered well postoperatively and had the antiepileptic medication adjusted to oral oxcarbazepine 0.6g (twice daily) and levetiracetam 0.5g (twice daily). Postoperative pathology confirmed that the resected hippocampal sclerosis tissue was brain tissue with no evidence of tumor lesions (Fig. 3B,3C). (2024-09-23) Follow-up EEG showed abnormal background activity with occasional focal epileptiform discharges. The alpha waves in the left temporal region had lower

amplitude than the contralateral side, and low- to medium-amplitude delta and theta slow waves were mildly increased in the anterior head regions, particularly in the left frontal pole, frontal, central, and temporal areas, with higher amplitude compared to the contralateral side. Low- to medium- and high-amplitude sharp-slow complex waves were observed in both awake and sleep states, scattered across the leads, predominantly in the left frontal pole, frontal, and central regions, without clinical seizures. (2024-09-24) The patient was discharged as instructed.

(2024-10-28) The patient returned for follow-up, and the EEG showed mild background abnormalities, with no typical intermittent epileptiform discharges. The amplitude and frequency modulation of alpha waves were suboptimal, with lower amplitude in the left temporal region compared to the contralateral side. Low- to medium-amplitude theta slow waves were mildly increased in the anterior head regions, with amplitudes approximately symmetric on both sides. No typical abnormal wave discharges were observed in either awake or sleep states, and no clinical seizures occurred. Routine head MRI showed changes consistent with left ALT (Fig. 4A, B, C). (2024-12-06) The patient returned for follow-up again, and the EEG showed mild background abnormalities, with no typical intermittent epileptiform discharges. No typical abnormal wave discharges were observed in either awake or sleep states, and no clinical seizures occurred. Routine head MRI revealed changes consistent with ALT (Fig. 4D, E, F). During the follow-up period, the patient continued taking oxcarbazepine 0.6g (twice daily) and levetiracetam 0.5g (twice daily), with no seizures reported and significant improvement in quality of life.

3. Discussion

3.1 Drug-resistant epilepsy and hippocampal sclerosis

Patients with drug-resistant epilepsy（DRE） account for one-third of all epilepsy cases[6], and this group often suffers from brain damage[7], loss of social function, cognitive impairment, and a higher mortality rate[8]. Hippocampal sclerosis(HS) is a key pathological basis for DRE, particularly prominent in patients with temporal lobe epilepsy[9]. MRI plays a central role in detecting epileptogenic lesions in DRE, HS often presents as atrophy and signal hyperintensity, typically more pronounced on the side of the epileptogenic focus[10]. However, in this case of temporal lobe epilepsy with a 17-year history, the patient visited multiple hospitals and was treated with various antiepileptic drugs. Despite several routine head MRIs, no intracranial abnormalities were detected. This raises the question of whether the lack of recognition was due to insufficient awareness among healthcare providers or limitations in imaging technology, leading to the under-identification of the hippocampus, an important anatomical structure. Therefore, in clinical practice, we should emphasize the use of hippocampal thin-slice MRI for DRE patients, with particular attention to the signal characteristics of this anatomical structure on T2-FLAIR imaging, in order to minimize the risk of missing diagnoses of DRE caused by HS.

3.2 Drug-resistant epilepsy and surgical intervention strategies

Common surgical treatments for DRE include selective amygdalohippocampectomy and ALT. These 2 surgical techniques have distinct characteristics. Selective amygdalohippocampectomy primarily targets lesions in the hippocampus and its associated areas, aiming to alleviate or control seizures by resecting the epileptogenic focus. In contrast, ALT involves a broader resection of the temporal lobe, typically used for epilepsy foci that involve extensive brain regions[11]. Although these 2 surgical methods differ in indications, surgical scope, and associated risks, they have both been shown to significantly reduce or completely eliminate seizures and effectively improve the quality of life for patients[12, 13]. One study had shown that for patients with DRE, follow-up evaluations of anterior temporal lobectomy and selective amygdalohippocampectomy were conducted at 6 months, 1 year, and 2 years. The results indicated that the efficacy of ALT in improving symptoms was 82.4%, 72.1%, and 55.0%, respectively[14]. These data further support the superiority of ALT over selective amygdalohippocampectomy in controlling seizures, highlighting its more significant long-term benefits and better seizure control. In ALT, the combination of intraoperative electrophysiological monitoring and neuronavigation enables real-time adjustment of the resection boundaries, allowing precise localization of the epileptogenic focus while minimizing damage to normal brain tissue, thereby ensuring optimal treatment outcomes[15, 16].

3.3 Anterior temporal lobectomy and prognosis

2 years ago, the patient's family expressed concerns about the high surgical risks. We will now further discuss the surgical risks and potential complications associated with ALT. 1.Visual field defects are one of the most common complications .Peripheral visual field defects are often unnoticed by patients, but extensive field loss can significantly impact daily activities, particularly driving ability[17].2. Language and memory deficits are common sequelae. While most patients experience some recovery in memory function, a small subset may develop persistent memory issues, affecting cognitive function[18]. Some patients may experience long-term psychosocial issues, including varying degrees of psychiatric symptoms, such as depression and mania[19]. One study show that depression is more common after left-sided ALT, while mania is more frequent after right-sided lobectomy[20]. Although rare, severe pain-related complications, such as trigeminal neuralgia, may occur following ALT[21]. This patient did not experience any of the complications above. We believe that age was the patient's greatest advantage. Additionally, regular postoperative follow-up by our epilepsy surgery team with the patient's family was a key factor in ensuring a positive prognosis. One study found that regardless of seizure outcomes, depression and mental fatigue can negatively impact the patient's quality of life. Therefore, it is important to consider this during preoperative counseling and postoperative follow-up with patients and their families[22].

4. Conclusion

In conclusion, DRE caused by HS should be diagnosed and intervened early, ALT play a crucial role in improving treatment outcomes and patient prognosis. This case further highlights the importance of clinicians being highly vigilant for HS, a commonly missed etiology, and taking timely surgical intervention. However, the study had several limitations: 1) The follow-up period was only slightly over 2 months. Although the patient's clinical symptoms were fully controlled, he continued taking antiepileptic drugs; 2) More postoperative data from patients with DRE caused by HS were needed to support these findings.

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Author contributions

Conceptualization: Yong Yuan.

Data curation: Xu You, Yong Yuan.

Formal analysis: Xu You, Yiping Tang.

Funding acquisition: Yong Yuan.

Investigation: Yongjun Gao.

Project administration: Yong Yuan.

Software: Jianxing Xu, Xi Zhang, Qiongmei Zhang.

Supervision: Yong Yuan.

Validation: Yiping Tang, Yongjun Gao.

Writing – original draft: Xu You, Yong Yuan,Haiyan Tian.

Writing – review & editing: Yong Yuan, Yiping Tang, Yongjun Gao, Jianxing Xu, Xi Zhang, Xu You

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have influenced the work reported in this study.

Informed written consent was obtained from the patient for the publication of this case report and accompanying images.

All data generated or analyzed during this study are included in this article.

Abbreviations:

HS= hippocampal sclerosis; DRE= drug-resistant epilepsy； ALT=anterior temporal lobectomy; MRI= Magnetic Resonance Imaging; CT = computed tomography;

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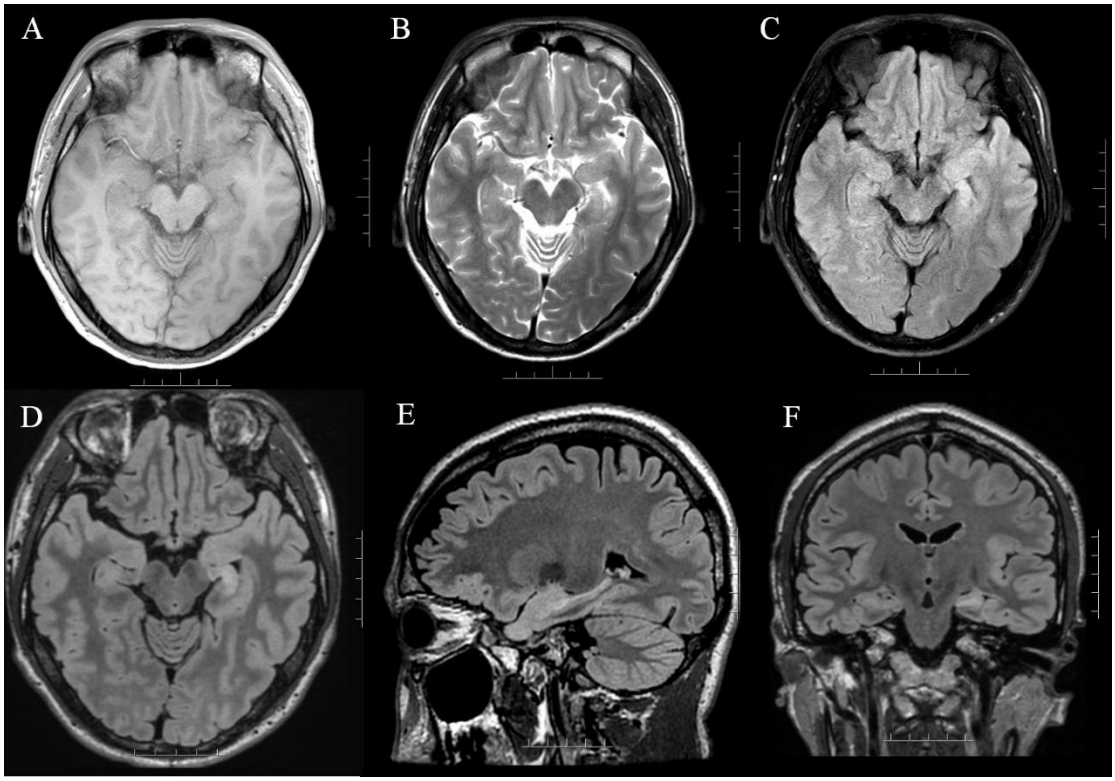

Figure 1. Routine head MRI: T1-weighted image (A), T2-weighted image (B), and T2-FLAIR image (C) showed no obvious abnormalities in the hippocampus; Hippocampal thin-slice MRI: T2-FLAIR axial image (D), sagittal image (E), and coronal image (F) showed symmetric bilateral hippocampi, with reduced volume of the left hippocampus and signal hyperintensity on FLAIR imaging. MRI = Magnetic Resonance Imaging.

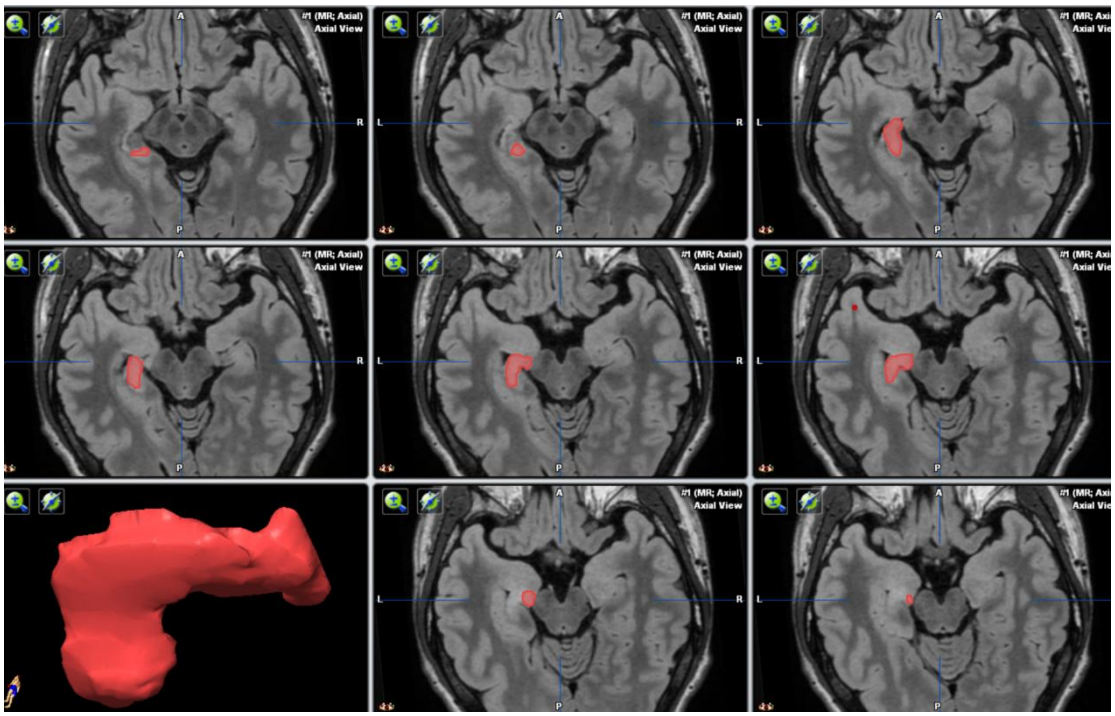

Figure 2. The left HS area was delineated using the neuronavigation system, enabling the 3D reconstruction of the HS region， "L" represents left and "R" represents right. HS = hippocampal

sclerosis.

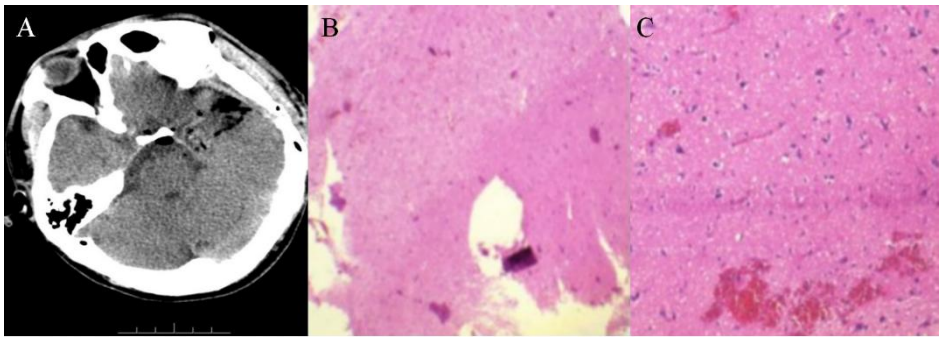

Figure 3. Postoperative head CT showed changes consistent with left temporal lobectomy, with no significant hemorrhage in the surgical area (A). Postoperative pathology report indicated that the resected HS tissue was brain tissue, with no evidence of tumor lesions (B, C). CT = computed tomography, HS = hippocampal sclerosis.

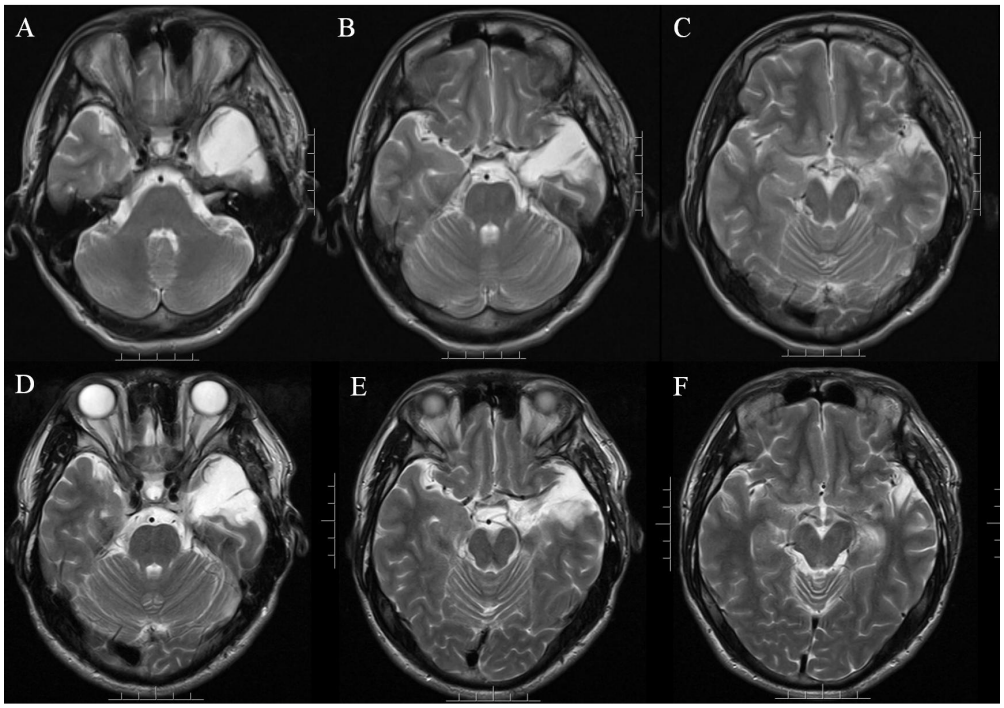

Figure 4. The patient underwent a follow-up head MRI on 2024-10-28, where T2-weighted images showed the surgical resection area (Fig. A, B, C). A subsequent follow-up MRI on 2024-12-06 (3 months post-surgery) revealed a clearer depiction of the resection area, with enhanced visibility of the left middle cerebral artery flow void in the surgical site (Fig. D, E, F). MRI = Magnetic Resonance Imaging.

Keywords:
Case report， Drug-resistant epilepsy, Hippocampal sclerosis, Anterior temporal

lobectomy