EPILEPSY

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Dear Doctor,

Greetings from Micro Labs. We are happy to bring you "EPILEPSY Newsletter'' which contains latest and interesting news in the field of Neuropsychiatry.

This issue contains:

- Clinical utility, safety, and tolerability in epilepsy patients of ultra-long-term monitoring with a novel subcutaneous electroencephalography
- Pregnancy and seizure outcomes in women with temporal lobe epilepsy and hippocampal sclerosis
- Diagnosis of functional seizures using nonictal electroencephalographic measures
- Case Report on Robot-Assisted Treatment of Secondary Epilepsy Due to Parasitic Infection

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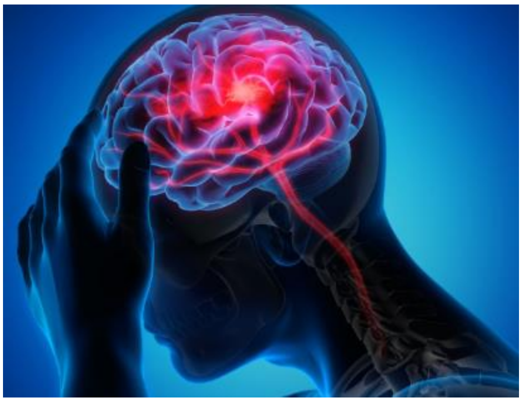
Clinical utility, safety, and tolerability in epilepsy patients of ultra-long-term monitoring with a novel subcutaneous electroencephalography

INTRODUCTION



In epilepsy care, tracking seizure counts reported by patients is crucial for evaluating the severity of the condition and making treatment decisions. Since therapies aim to reduce or stop seizures, precise seizure documentation is vital. This highlights the need for dependable and practical methods of detecting and quantifying seizures for extended monitoring in outpatient settings.[1] A new EEG recording device has been recently introduced, featuring a subcutaneous implant along with an external unit that enables inductive transfer of both data and power. This system is referred to as subcutaneous EEG (sqEEG).[2] The sqEEG device has proven capable of capturing EEG signals with satisfactory quality. Additionally, the signal has been shown to remain stable and retain its quality over several months of continuous recording.[1] There was limited information on the sensitivity, reliability, and safety of the sqEEG system for extended seizure monitoring in epilepsy patients, and more data are needed on its effectiveness in real-world clinical practice. This study aimed to evaluate the clinical utility, safety, and tolerability of ultra-long-term monitoring using a new sqEEG device in patients with epilepsy.

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Depending on the ictal EEG characteristics, EpiSight's sensitivity to identify seizures differed throughout patients. The ultra-long term sqEEG monitoring was both feasible and well-tolerated.

METHODS

This pilot study was conducted in a real-world setting. Five patients with drug-resistant focal epilepsy received sqEEG implants (one patient had bilateral implants). The inclusion criteria were: (1) patients reported at least one seizure per week, either self-reported or documented in a seizure diary within the three months before enrollment; (2) unilateral or bilateral seizure focus was confirmed by ictal electroclinical data from the epilepsy monitoring unit (EMU), consistent with clinical history and Magnetic resonance imaging (MRI) findings; and (3) the ictal EEG activity localized or spread to the temporal regions, where the sqEEG electrodes were implanted. In phase 1, researchers evaluated the sensitivity of sqEEG for seizure detection by recording seizures concurrently with scalp EEG in the EMU. The sqEEG data were analyzed visually (v-sqEEG) or using a semi-automatic algorithm (EpiSight; E-sqEEG). In phase 2,

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patients were monitored as outpatients for 3 to 6 months. The sqEEG data were reviewed monthly, comparing the results from v-sqEEG, E-sqEEG, and patient seizure diaries. Data from v-sqEEG were used to guide treatment adjustments. Throughout the study, side effects related to sqEEG were monitored and assessed.

RESULTS

In phase 1, v-sqEEG successfully identified all seizures recorded in the EMU for every patient, while E-sqEEG performed effectively for three patients. For the remaining two patients, E-sqEEG detected only a portion or none of their seizures, respectively. The sensitivity of E-sqEEG varied based on the ictal EEG characteristics. In phase 2, in patients #1, #2, and #5, v-sqEEG found 15, 29, and 33 seizures, respectively (Table 1). A 100% agreement in seizure detection between E-sqEEG and v-sqEEG was found in the same three patients from phase 1. However, for the other two patients (one with bilateral implants), the effectiveness of E-sqEEG compared to v-sqEEG ranged from 0% to 83%. The v-sqEEG revealed that all patients reported fewer seizures in their diaries than they experienced. Additionally, in 4 out of 5 patients, v-sqEEG indicated that treatment adjustments were ineffective or associated with an increase in seizures. The only observed side effect was an infection at the implantation site in one patient.

Table 1. Seizure count in EMU and during ultra long-term outpatient monitoring

Patient # (side of implantation)	Total usage, h (% of total monitoring time)	EMU: number of seizures recorded	EMU: number of seizures reported in patients' diary	EMU: concordance, Visual sqEEG/ visual scalp EEG	EMU: concordance, EpiSight/visual scalp EEG	Outpatient monitoring: number of seizures detected Episight/ visual sqEEG	Outpatient monitoring: concordance, Episight/visual sqEEG	Outpatient monitoring: Episight false positive	Outpatient monitoring: Episight false negativ
1 (right)	3356 (93%)	2	0	100%	100%	15/15	100%	0	0
2 (right)	2747 (88%)	3	1	100%	100%	29/29	100%	0	0
3 (right)	3626 (93%)	1	0	100%	0%	32/60	53.3%	3	28
3 (left)	2298 (89%) (implant explanted 14 weeks after start of study)	1	1	100%	100%	5/6	83%	0	1
4 (right)	3935 (94%)	5	2	100%	0%	0/160	0%	0	160
5 (right)	1934 (95%)	6	0	100%	100%	33/33	100%	0	0

EEG- electroencephalography; EMU- epilepsy monitoring unit; sqEEG- subcutaneous EEG

DISCUSSION

During phase 2, the average sensitivity of E-sqEEG for detecting six seizure types was 72.6% (with a range of 0–100%). This contrasts with the overall seizure detection sensitivity of 86% (range=69–100%) reported in a prior study involving 94 electrographic seizures.[3] The comparison between the Co-diary and v-sqEEG revealed that all patients recorded fewer seizures in their diaries than they experienced. This finding reinforces the commonly recognized issue of patients underreporting their seizures.[4,5] This observation was further supported in phase 1 of the present study, where patients did not document all the seizures that occurred in the EMU. A previous study on an individual patient highlighted the advantage of sqEEG over seizure diaries, as the patient recorded 22 seizures in an electronic diary, while an automatically assisted visual review of the sqEEG identified 32 seizures.[6]

CONCLUSION

The sqEEG system can reliably gather information on seizure activity when compared to standard scalp EEG recordings. Also, the EpiSight algorithm can offer useful insights into seizure counts for specific seizure types, with its sensitivity largely influenced by the most suitable candidates for implantation and ultra-long-term monitoring of epilepsy patients using the sqEEG system for up to 6 months was both feasible and well-tolerated.

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Pregnancy and seizure outcomes in women with temporal lobe epilepsy and hippocampal sclerosis

INTRODUCTION

Compared to medicine alone, surgical therapy before to pregnancy seems to offer a higher chance of seizure freedom. Despite having inadequate seizure control and unjustified conception, most women with TLE-HS can give birth to healthy children.

Epilepsy is a prevalent long-term neurological condition that was thought to impact 0.3% to 0.5% of pregnancies globally.[1] Managing seizures in pregnant women with epilepsy is essential to minimize the risks of obstetric complications.[2] Achieving seizure control during pregnancy poses a significant challenge for women, as anti-seizure medications (ASMs) are linked to a higher risk of major congenital malformations (MCMs) and neurodevelopmental delays in their children. This study specifically examines women with temporal lobe epilepsy and hippocampal sclerosis (TLE-HS) in three key areas: First, there is an ongoing debate about whether undergoing surgery before pregnancy can lower the risk of seizures during gestation.

Second, despite the typical drug resistance associated with temporal lobe epilepsy, continuous use of ASMs is often necessary. Third, the extent of increased seizure risk in this population remains unclear, and there was a lack of pregnancy-related data from developing countries. While temporal lobe epilepsy with hippocampal sclerosis (TLE-HS) often resists pharmacological treatments, surgery can potentially lead to seizure freedom.[3] So, this study was to examine pregnancy and seizure outcomes in women with TLE-HS and to identify factors that may predict seizure control.

METHODS

The West China Registry of Pregnancy of Women with Epilepsy (WCPR_EPi) was a single-center, prospective cohort study involving WWE. Women with TLE-HS were selected from this database, and their clinical profiles, ASM usage, and pregnancy outcomes were gathered from the registry records spanning from 2010 to 2023. The inclusion criteria for WWE included being aged 18 to 45 years and having a gestational age of 24 weeks or less. Seizure types were classified as focal to bilateral tonic-clonic seizures (FBTCS), focal impaired awareness seizures (FIAS), or focal onset aware seizures.

RESULTS

Among the 2,320 WWE monitored, 47 pregnancies in women with TLE-HS were identified and analyzed. Of the participants, 9 women (19.1%) had been seizure-free in the year leading up to conception, and 8 of these women (88.9%) maintained seizure freedom throughout their pregnancies. About two-thirds of the women had no FBTCS in the year prior to conception, while a small group (8 women, 17%) experienced frequent focal impaired awareness seizures (FIAS), with more than one episode per week. During pregnancy, 19 pregnancies (40.4%) experienced a worsening of seizures, with 14 (29.8%) showing an increase in FBTCS and 9 (19.1%) experiencing more FIAS. Changes in seizure frequency are detailed in Figure 1. Seizure exacerbation occurred in 40.4% of pregnancies, while 34% of these pregnancies remained seizure-free. The factor linked to increased seizure activity during pregnancy was non-adherence to ASM (odds ratio [OR] = 7.00, 95% confidence interval [CI] 1.43–34.07, P = 0.016). The group that underwent surgery had a significantly higher rate of seizure freedom (OR = 6.87, 95% CI 1.02–46.23, P = 0.016) and a lower incidence of induced labor (0.0% vs. 26.5%, P = 0.047) compared to those treated only with medication. Cesarean sections were performed in 77.1% of cases due to seizure concerns, with similar rates for epilepsy-related (n=20) and obstetric causes (n=24). No major congenital malformations were reported.

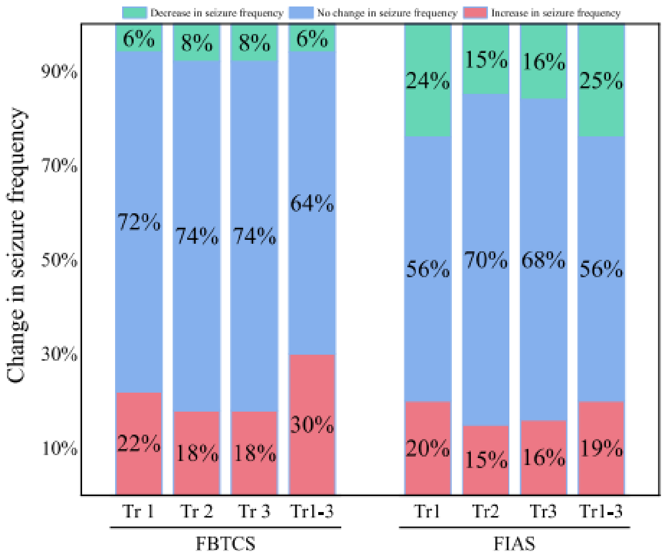

Figure 1. Variation in seizure frequency between the trimesters for two types of seizures. Tr-Trimester; FBTCS-Focal to bilateral tonic-clonic seizure; FIAS- Focal impaired awareness seizure.

DISCUSSION

In this study, most women with epilepsy (WWE-S) experienced improved seizure control during pregnancy compared to those receiving only ASMs. Hippocampal sclerosis (HS) was acknowledged as a primary condition that can be treated surgically, resulting in better seizure management, with a significant number of patients being able to successfully discontinue their ASMs. This underscores the importance of prompt intervention for this condition.[4]

CONCLUSION

Proper management of epilepsy in pregnant WWE is essential for the well-being of both the mother and the baby. This study suggested that women with TLE-HS may be at a higher risk of seizure exacerbation during pregnancy. However, the results indicate that this risk can be reduced through regular use of ASMs and careful consideration of surgical options prior to pregnancy when suitable.

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Diagnosis of functional seizures using nonictal electroencephalographic measures

INTRODUCTION

Using machine learning instead of individual features was significantly more effective, and it has the potential to be a very useful tool for FS diagnosis. Moreover, combining the frequency bands often increased the classifiers' accuracy, with delta and gamma consistently being the least effective EEG bands.

Functional seizures (FS), also known as psychogenic nonepileptic seizures, appear similar to epileptic seizures (ES) in clinical presentation but are not caused by epileptic electrical activity in the brain.[1] FS are frequently misdiagnosed, with an accurate diagnosis typically taking around 7 years. Since antiepileptic drugs do not effectively treat FS, patients who are misdiagnosed often suffer from the side effects of these medications without gaining any real benefit.[2] At present, the gold standard for diagnosis involves admitting patients for simultaneous video and electroencephalography (EEG) monitoring.[3] While this method is reliable, it has several limitations. Interictal (seizure-free) EEG abnormalities have been observed in patients with FS, but no single biomedical signal can reliably distinguish FS from epilepsy. The use of machine learning to analyze nonictal EEG may help address these limitations and assist clinicians. Previous research has shown that statistical, time domain, and frequency domain measures analyzed with machine learning can differentiate FS EEGs from those of epilepsy and healthy individuals, although in small study groups.[2] This analysis aimed to determine whether it is possible to reliably distinguish between FS and epilepsy using these measures in combination with machine learning classifiers, applied to a larger sample size than previous studies. Additionally, the study will assess the diagnostic effectiveness of these features and EEG frequency bands to identify the most useful inputs for the models.

METHODS

This preliminary study explored the use of seizure-free EEG signals combined with machine learning to differentiate individuals with FS from those with epilepsy. The dataset comprised interictal and preictal EEG recordings from 48 FS patients (mean age = 34.76 ± 10.55 years, 14 males) and 29 epilepsy patients (mean age = 38.95 ± 13.93 years, 18 males). Various statistical, temporal, and spectral features from the five EEG frequency bands were extracted and analyzed using threshold accuracy, five machine learning classifiers, and two feature important methods.

RESULTS

The highest classification accuracy from thresholding was 60.67%. However, temporal features performed the best, with machine learning models achieving the highest balanced accuracy of 95.71% when all frequency bands were combined, using a support vector machine classifier. Machine learning results for temporal features showed an average balanced accuracy of 82.78% and a peak accuracy of 95.71%. Combining the frequency bands led to an improvement of 9%, compared to 14% for statistical features and 12% for temporal features. The delta band was the lowest performer, followed by gamma. Table 1 outlines the importance of each band for different feature groups, with temporal features scoring the highest, particularly in the theta and alpha bands, followed by statistical and spectral features.

Table 1. A summary of the average feature values for each feature group's bands

Statistical features		Temporal features		Spectral features	
Band	**Mean±SD**	**Band**	**Mean±SD**	**Band**	**Mean±SD**
Theta	2.56±5.5	**Theta**	3.18±6.8	**Broad**	1.69±2.4
Beta	2.14±4.4	**Alpha**	3.15±5.0	**Alpha**	1.02±2.1
Alpha	2.09±4.8	**Beta**	2.77±4.3	**Theta**	0.79±1.7
Broad	1.56±2.6	**Broad**	1.94±2.4	**Beta**	0.79±1.1
Gamma	1.03±1.9	**Gamma**	1.78±4.0	**Gamma**	0.57±0.8
Delta	0.95±1.4	**Delta**	1.42±3.1	**Delta**	0.47±0.7

DISCUSSION

Noel et al. discovered that resting-state EEGs of individuals with FS exhibited higher Lempel–Ziv complexity (LZC) values compared to those with epilepsy.[4] In this study, significant differences were identified in 13 EEG channels, with FS patients showing a higher mean LZC than epilepsy patients in all but one channel, aligning with the findings of Noel et al. Additionally, two studies have compared the spectral power between FS and epilepsy patients.

One of these studies reported that individuals with temporal lobe epilepsy had higher mean delta activity compared to those with FS.[5] Another study found that patients with FS exhibited greater gamma power compared to those with epilepsy.[4] Although this study did not measure power directly, it did analyze band energy, finding statistically significant differences in most channels. Overall, band energy was higher for FS across all five bands, except in the prefrontal regions for the theta, alpha, and beta bands. As a result, this study does not align with the findings of Bernasconi et al. but is consistent with those of Noel et al.

CONCLUSION

Machine learning proved to be significantly more effective than relying on individual features and could serve as a valuable tool in diagnosing FS. Additionally, integrating the frequency bands enhanced the accuracy of the classifiers in most instances, with delta and gamma consistently being the lowest-performing EEG bands.

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Case Report on Robot-Assisted Treatment of Secondary Epilepsy Due to Parasitic Infection

INTRODUCTION

The use of surgical robots in different neurosurgery specialties is expected to increase. Utilizing frameless stereotactic neurosurgical robot-assisted technology has significant implications given the benefits it

Sparganosis is a zoonotic infection caused by the plerocercoid or second-stage larvae (sparganum) of pseudophyllidean tapeworms that inhabit the tissues of their hosts.[1] When sparganum enters the human body, it typically causes a parasitic infection that results in lesions in the subcutaneous or muscle tissues. However, a small number of sparganum can invade the human brain, leading to chronic active inflammation following central nervous system (CNS) invasion. This invasion can cause a range of neurological symptoms, including epileptic seizures, sensory disturbances, and headaches in patients, a condition referred to as cerebral sparganosis.[2] Cerebral sparganosis is an extremely rare zoonotic disease and is considered the most severe form of sparganosis. Seizures are often reported as the most prevalent symptom in individuals affected by cerebral sparganosis.[3] This case report discusses a case of secondary epilepsy resulting from cerebral sparganosis, highlighting the use of robot-assisted frameless stereotactic technology and intraoperative stereotactic electroencephalography (SEEG) monitoring in neurosurgery.

CASE PRESENTATION

A 24-year-old male patient was admitted to the hospital with a history of left limb twitching that had persisted for over a year. His first seizure occurred a year back, characterized by sudden rigidity in the left upper arm, accompanied by numbness and a crawling sensation, as well as visual field loss, lasting about one minute. For the past 2 months, the patient experienced five similar seizures, each lasting approximately one minute and accompanied by visual field defects. Following these episodes, he reported headaches that lasted about an hour. Last month, he had another seizure while awake, which presented as twitching in the left limbs (both upper and lower), backward head tilting, leftward gaze, and left mouth droop. These symptoms subsided after about two minutes, but the headache lasted several hours before gradually easing. He was then referred to a local hospital, where a magnetic resonance imaging (MRI) scan of his head revealed abnormal signals in the right precentral gyrus, leading to a diagnosis of secondary epilepsy. The patient began treatment with sodium valproate sustained-release tablets at a dosage of 0.5 g twice daily for a week before gradually reducing and eventually stopping the medication on his own. Then, the patient experienced a relapse of similar seizures, this time presenting as five consecutive cluster seizures occurring 2 to 3 minutes apart. He showed motor weakness in the left upper limb, scoring 3 out of 5 on the manual muscle test (MMT). A plain cerebral MRI revealed patchy mixed signal shadows in the right fronto-parietal lobe, particularly in the precentral gyrus, characterized by slightly prolonged T1 and T2 signals with areas of short T2 signals, along with significant surrounding edema. In the right parietal and occipital lobes, some lesions exhibited low signal intensity

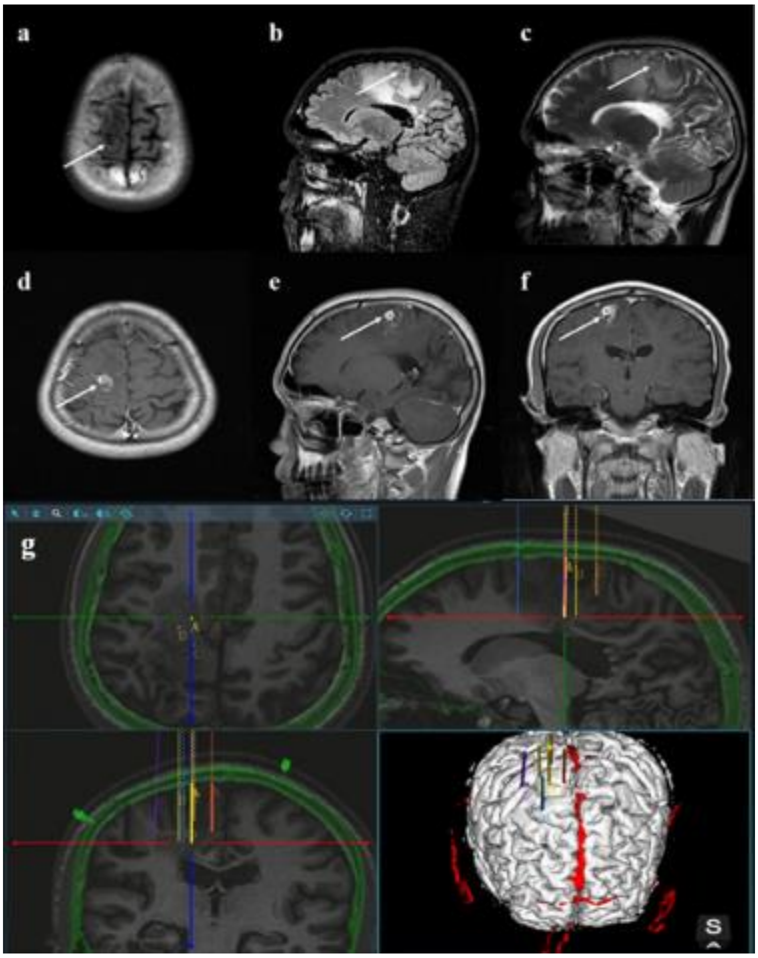

Figure 1. Axial (a), sagittal (b), and sagittal (c) T2-weighted preoperative magnetic resonance imaging scans. axial (d), sagittal (e), and coronal (f) preoperative T1-weighted MRI images enhanced with contrast are shown. To carry out the surgical plan for lesion biopsy and resection in functional areas, neurosurgery robot-assisted frameless stereotactic technology was utilized (g).

while others showed high signal intensity, suggesting potential softening lesions (Fig. 1a–c). Enhanced brain MRI imaging revealed a heterogeneous nodular mixed signal shadow in the right precentral gyrus, surrounded by a large area of edema. Some lesions in the right parieto-occipital lobe showed low signal intensity, while others exhibited high signal intensity, indicating possible softening lesions in that region (Fig. 1d–f). Video electroencephalogram (VEEG) results showed occasional atypical sharp wave components with medium amplitude (46–78 μV) at around 5.4 Hz in the right frontal area during light sleep, with no other abnormalities detected. A thorough inquiry into the patient's history revealed a habit of consuming raw food while working in a coastal area and a past trauma to the right occipital region over a decade prior. After a comprehensive multimodal assessment and multidisciplinary discussion, the diagnosis was established as 1) space-occupying lesions in the right frontal and parietal lobes; 2) space-occupying lesions in the right occipital lobe; 3) secondary epilepsy: Jacksonian epilepsy without loss of consciousness. The lesions in the right frontal and parietal lobes were highly suspected to be caused by a parasitic infection. The patient and his family opted for stereotactic intracranial lesion biopsy technology, utilizing both framed and frameless stereotactic techniques. The epilepsy team employed robot-assisted frameless stereotactic technology. Following the procedure, the patient was prescribed praziquantel for anthelmintic therapy along with sodium valproate sustained-release tablets at a dosage of 0.5 g twice daily for seizure management. During a two-year follow-up, the patient scored 29 on the mini-mental state examination (MMSE) and 28 on the Montreal cognitive assessment (MoCA), indicating no cognitive dysfunction post-surgery. His scores on the Hamilton Depression Rating Scale (17 items) and the Hamilton Anxiety Rating Scale (14 items) were 1 and 3, respectively, suggesting no post-surgical depression or anxiety. The patient reported a quality-of-life score of 89.47 on the Epilepsy Inventory-31 (QOLIE-31) scale. Two years after the operation, follow-up MRI scans showed complete removal of the right frontal and parietal epileptic lesions without the appearance of new similar brain lesions. Additionally, there was a significant reduction in the edema surrounding the lesions. Throughout regular follow-up visits at the outpatient department of the hospital's epilepsy center, the patient remained seizure-free. The subsequent plan for adjusting anti-seizure medication (ASM) involved gradually reducing the dosage until the patient could stop taking the medication altogether.

DISCUSSION

Compared to traditional craniotomy surgery, robot-assisted neurosurgery technology offers unique benefits as well as some limitations. The advantages of this technology can be categorized into three main areas: (1) improving surgical precision, reducing human errors, and increasing operative safety; (2) shortening the duration of surgery, boosting operational efficiency, and reducing physician fatigue; and (3) automating the creation and simulation of optimal surgical plans, which simplifies and streamlines the surgical process.[4] Nonetheless, there are several drawbacks to this technology. For example, the high cost of the equipment could limit its adoption in certain areas and hospitals. Additionally, it necessitates that surgeons have a specific level of technical skill and considerable experience. Currently, its applications are somewhat restricted and primarily pertain to specific types of surgeries.[5] Studies have confirmed the cost-effectiveness of robot-assisted surgery.[5] However, the accessibility of this technology remains restrained, particularly in areas where it may not be easily accessible.

CONCLUSION

This case has enhanced the understanding of cerebral sparganosis. Additionally, it's important to note that for patients with symptomatic epilepsy due to cerebral sparganosis, the skilled application of frameless stereotactic neurosurgical robot-assisted technology, along with effective teamwork, can be highly beneficial. This approach facilitates the precise identification and removal of epileptic lesions, resulting in favorable outcomes, such as achieving seizure freedom without neurological deficits.

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