



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:

1. **Study on neonatal brain MRI and short-term outcomes following acute provoked seizures**
2. **A Hospital-Based case-control study: Association of patent foramen ovale with epilepsy.**
3. **Lateralized Interictal Epileptiform Discharges and Postoperative Seizure Outcomes in Tuberous Sclerosis Complex Patients**
4. **Illustrative case of focal drug-resistant temporal lobe epilepsy associated with an ipsilateral anterior choroidal artery aneurysm**



Study on neonatal brain MRI and short-term outcomes following acute provoked seizures

INTRODUCTION

Acute symptomatic seizures, which happen one to three times per 1000 live births, are a frequent indicator of neurological dysfunction and brain damage in newborns ⁽¹⁾. In neonates with severe brain injuries, acutely provoked seizures are frequently the earliest indication of neurologic impairment. Neonatal seizures are most frequently caused by ischemic stroke, hypoxic-ischemic encephalopathy (HIE), or cerebral haemorrhage ⁽²⁾. Depending on the underlying condition, such as hypoxic-ischemic encephalopathy or new-born stroke, an MRI may reveal either normal results or significant abnormalities ⁽³⁾. This study was conducted on neonates with acute provoked seizures to test the concept that the cause and location of brain damage identified on an early newborn brain MRI after the onset of acute provoked seizures are related to seizure load and neurologic outcomes at hospital discharge.

METHODS

A prospective, multicentre cohort study was conducted on 236 infants with acutely provoked neonatal seizures. A neuroradiologist examined the MRIs to determine the site of the damage and the radiologic diagnosis. The following radiologic diagnoses were used to classify MRI studies: normal, hypoxic-ischemic encephalopathy (HIE), focal ischemic stroke (arterial, venous, or other aetiology), intracranial haemorrhage (ICH), probable infection, and "other"(FIGURE 1). Patients clinical information was gathered by chart review. Two primary clinical outcomes were collected: Electroencephalogram(EEG)-seizure burden categorized as low or high, and neurologic examination at discharge as normal or abnormal. Two secondary outcomes assessed were the presence of EEG only seizures and incomplete

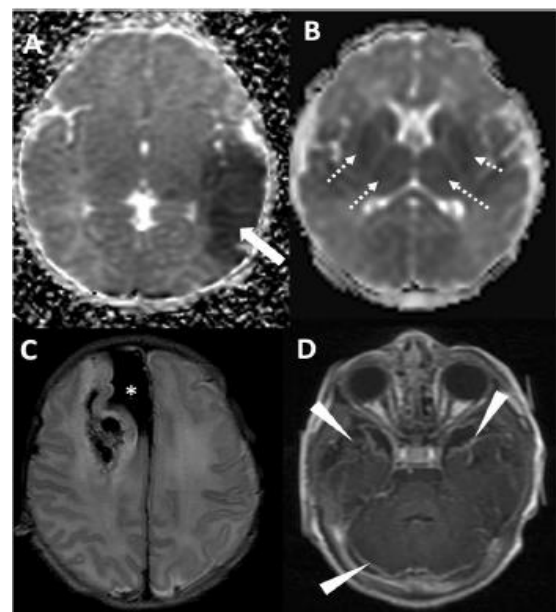
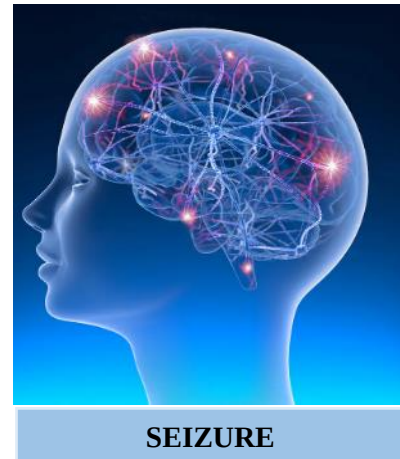


Figure 1 Radiologic diagnosis in the group of individuals with acute symptomatic seizures. A) The left middle cerebral artery area is shown on an axial ADC map as having an arterial ischemic stroke (White arrow). B) The deep gray nuclei and subcortical white matter show decreased diffusion on the axial ADC map in B, which is consistent with hypoxic ischemic damage. C) A substantial subpial haemorrhage may be seen in the medial right frontal lobe (asterisk) on axial T2 weighted imaging, along with right frontal lobe haemorrhage that is linked with it. D) Axial T1-weighted post-contrast imaging showing leptomeningeal enhancement in the presence of neonatal meningitis/intracranial infection.



response to antiseizure medication. MRI findings were analysed using multivariate logistic regression to study their association with outcomes.

RESULTS

In neonates, cortical injury was found in 50% and deep gray injury in 38%. Radiologic etiologies included focal ischemic stroke (36%), HIE (28%), ICH (9%), suspected infection (7%) and other etiologies (12%). Compared to neonates with an abnormal MRI, those with a normal MRI had a decreased chance of having a high seizure load (14%) (TABLE 1). Children with a radiologic diagnosis of HIE had a higher likelihood of a high seizure burden. Conversely, those with radiologic diagnosis of “other” had a lower likelihood of a high seizure burden. ICH showed a trend towards high seizure burden. Cortical injury and deep gray injury were significantly associated with high seizure burden. In multivariate model, HIE, ICH and cortical injury remained independently associated with high seizure burden. Neonates with MRI evidence of HIE had a higher likelihood of abnormal neurologic examination. Neonates with a radiologic diagnosis of infection were also more likely to have abnormal neurologic examination at discharge. Deep gray injury on early MRI was assessed with abnormal discharge examination. In the multivariate model, a radiologic diagnosis of infection and deep gray injury remained independently associated with abnormal neurologic examination at discharge. Neonates with ischemic stroke had a lower likelihood of EEG-only seizures. Additionally, cortical injury was negatively associated with EEG-only seizures. The multivariate model confirmed that cortical injury still had a statistically significant negative association with EEG-only seizures. Neonates with normal MRI had a significantly lower likelihood of treatment-resistant seizures. HIE and cortical injury were significantly associated with treatment-resistant seizures. In the multi-variate model, HIE and cortical injury remained associated with treatment resistant seizures.

TABLE 1 ODDS OF HIGH SEIZURE BURDEN AND ABNORMAL NEUROLOGICAL EXAMINATION AT DISCHARGE IN CHILDREN WITH ACUTE PROVOKED NEONATAL SEIZURES

MRI Findings	High Seizure Burden		Abnormal Neuro Examination at Discharge	
	Minimally Adjusted*	Fully Adjusted/Multivariate	Minimally Adjusted	Fully Adjusted/Multivariate
Imaging Diagnoses				
Normal MRI (N = 22)	0.13 [0.04–0.45], p < 0.001		0.49 [0.16–1.5], p < 0.21	
HIE (N = 67)	2.4 [1.3–4.4], p < 0.006	2.7 [1.4–5.4], p < 0.003	2.2 [1.1–3.7], p < 0.02	
Ischemic Stroke (N = 84)	0.90 [0.52–1.6], p < 0.71		0.7 [0.4–1.3], p < 0.30	
Intracranial Hemorrhage (N = 62)	1.8 [0.96–3.4], p < 0.07	3.2 [1.6–6.5], p < 0.001	0.9 [0.45–1.7], p < 0.67	
Infection (N = 6)	2.5 [0.76–8.1], p < 0.13		4.2 [1.4–12.0], p < 0.008	3.9 [1.3–11.6], p < 0.01
Other diagnosis (N = 51)	0.44 [0.22–0.85], p < 0.02		0.75 [0.4–1.5], p < 0.43	
Injury Location				
Cortical Injury (N = 118)	2.9 [1.7–5.1], p < 0.001	3.5 [1.9–6.4], p < 0.001	1.5 [0.86–2.7], p < 0.16	
Deep Gray Injury (N = 89)	1.7 [1.0–3.0], p < 0.05		2.8 [1.6–5.0], p < 0.001	2.7 [1.6–5.0], p < 0.001
Other Injury Location (N = 61)	0.64 [0.35–1.2], p < 0.15		0.51 [0.26–1.03], p < 0.06	



DISCUSSION

In the present study, ICH was associated with high seizure burden ⁽²⁾. According to earlier research, acute symptomatic seizures may be linked to either intra- or extra-axial cerebral haemorrhage. Seizures are rarely related with subdural haemorrhage, which was not scored in this research ⁽⁴⁾. In present study, a neurological examination that was abnormal at discharge was linked to deep gray injury ⁽²⁾. Since damage to these structures is substantially linked to poor motor, cognitive, and linguistic outcomes in this group, these findings are congruent with the research on newborn HIE currently available ⁽⁵⁾.

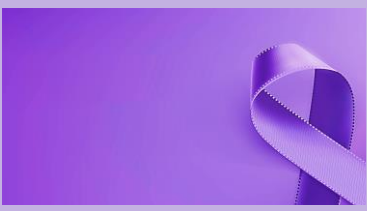
CONCLUSION

In neonatal acute provoked seizures, MRI findings of ICH or HIE and cortical injury were linked to high seizure burden. Atypical neurologic evaluation of discharge was linked to radiologic signs of infection and severe gray nuclei damage. These initial MRI findings can help in counselling parents about short-term outcomes for neonates with acute provoked seizures. Further research should explore the connection between brain MRI findings and neurodevelopmental outcomes after acute provoked neonatal seizures.

In neonatal acute provoked seizures, MRI findings of intracranial haemorrhage or hypoxic-ischemic encephalopathy and cortical injury were linked to high seizure burden. Radiologic evidence of infection and deep gray nuclei injury were associated with abnormal neurologic examination of discharge.

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A Hospital-Based case-control study: Association of patent foramen ovale with epilepsy.

INTRODUCTION

Epilepsy is a prominent neurological ailment, affecting around 69 million individuals globally ⁽¹⁾. Many epileptic patients lack access to efficient targeted treatment medicines and have unidentified aetiologies. Hypoxia and microembolism are brought on by the patent foramen ovale (PFO), which increases the risk of epilepsy and causes cerebral neurological impairment. When looking at the aetiology of CNS disorders in people with PFO, a right-to-left shunt (RLS) (mediated by the PFO) was a major factor in paradoxical embolisation, which raised the risk of stroke and migraine ⁽²⁾. Arterial blood gas assessment revealed that RLS might independently increase drug resistance risk in patients with epilepsy(PWEs) ⁽³⁾. The studies didn't compare PFO incidence in PWEs with healthy individuals. Also, the connection between PFO and seizure features was understudied. So this study was conducted to check PFO rates in PWEs and compared seizure traits in those with and without PFO.

METHODS

A Case-control study was conducted on 741 people with epilepsy(PWE) and 800 controls without epilepsy aged 18-55 years. All patients underwent contrast-transthoracic echocardiography (cTTE) with venous microbubble bolus and provocative maneuvers (Valsalva and coughing) to detect the presence of a PFO and its right-to-left shunt(RLS). Additionally, EEG and MRI results were recorded, with neuro-imaging considered "positive" when epileptogenic structural abnormalities were observed in brain MRI scans. These MRI scans were reviewed by expert neuroradiologists and epileptologists to identify subtle lesions. In order to account for congenital characteristics that can affect the likelihood of PFO, the study used multiple matching techniques and logistic regression to examine the risk of PFO in PWEs.

RESULTS

The prevalence of patent foramen ovale (PFO) was notably higher among individuals with epilepsy compared to healthy subjects (39.00% vs 24.25%). TABLE 1 shows detailed description of baseline characteristics after multiple imputation and the matched dataset under 1:1 ratio. PFO occurrence was also more frequent in the epilepsy group compared to the control group (35.87% vs 24.46%). Logistic regression analyses with adjustments, indicated that the risk of having PFO in individuals with epilepsy was 1.71 times that of controls. Upon controlling for potential confounders, it was observed that individuals with epilepsy had an elevated risk of having a higher grade of right-to-left shunt (RLS), with the risk increasing as the RLS grade rose. Additionally, among individuals with epilepsy, those with PFO had a



greater prevalence of migraine and drug-resistant epilepsy. The logistic regression analyses revealed that the risk of having PFO in individuals with drug-resistant epilepsy was 1.47 times higher compared to those without drug-resistant epilepsy. Similarly, the risk of having PFO in individuals with migraine was 2.54 times higher compared to those without migraine. These findings imply that PFO might contribute to the differences in clinical characteristics seen between patients with and without drug-resistant epilepsy or migraine.

DISCUSSION

The present study indicated a high occurrence of PFO in epilepsy patients, particularly those with drug-resistant epilepsy or migraine and individuals with epilepsy had an elevated risk of having a higher grade of right-to-left shunt (RLS)⁽¹⁾. Numerous studies have linked PFO

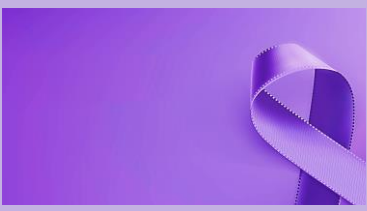
with migraine, and we found that PWEs shared some clinical traits with PFOs, including aura and drug-resistant epilepsy. Numerous studies have suggested that migraine and epilepsy may be two distinct clinical manifestations of the same neurophysiological process and share a similar pathophysiological basis. There are other thoughts that could explain our findings, even if there isn't any proof right now that these heart anomalies are present in our patients. One possible cause of hypoxemia is a PFO, which can result in the mixing of oxygenated arterial blood in the left atrium with deoxygenated venous blood from the right atrium⁽⁴⁾.

CONCLUSION

The study indicated a high occurrence of PFO in epilepsy patients, particularly those with drug-resistant epilepsy or migraine. These findings offer important insights into the connection between PFO and epilepsy, possibly influencing how these conditions are managed.

The study indicated High occurrence of patent foramen ovale in epilepsy patients, particularly those with drug-resistant epilepsy or migraine.

TABLE 1- BASELINE CHARACTERISTICS OF COMPLETE DATASET AND MATCHED DATASET UNDER 1:1 RATIO						
Variables	COMPLETE DATASET			1:1 matched dataset		
	Epilepsy patients (n = 741)	Health people (n = 800)	P- value	Epilepsy patients (n = 368)	Health people (n = 368)	P- value
Age	29.82 (23.90, 39.00)	40.00 (32.00, 49.00)	0.001	35.00 (29.00, 48.94)	36.00 (30.00, 46.00)	0.191
BMI	22.76 (19.98, 24.79)	23.46 (21.36, 25.81)	0.001	22.88 (20.17, 25.22)	22.86 (20.82, 24.99)	0.781
Gender, male	337 (45.48)	219 (27.38)	0.001	121 (32.88)	119 (32.34)	0.937
Ethnic minorities	31 (4.18)	149 (18.63)	0.001	27 (7.34)	46 (12.50)	0.026
Smoke	70 (9.45)	92 (11.50)	0.219	47 (12.77)	45 (12.23)	0.911
Alcohol	61 (8.23)	86 (10.75)	0.111	37 (10.05)	43 (11.69)	0.554
Birth hypoxia	52 (7.02)	0 (0.00)	0.001	0 (0.00)	0 (0.00)	0.999
Preterm birth	17 (2.29)	20 (2.50)	0.923	8 (2.17)	6 (1.63)	0.787
Febrile convulsion	93 (12.55)	9 (1.13)	0.001	1 (0.27)	9 (2.45)	0.026
Congenital anomaly	37 (4.99)	0 (0.00)	0.001	0 (0.00)	0 (0.00)	0.999
PFO	289 (39.00)	194 (24.25)	0.001	132 (35.87)	90 (24.46)	0.001
RLS grade			0.001			0.001
Without	452 (61.00)	606 (75.75)		236 (64.13)	278 (75.54)	
I Grade	128 (17.27)	32 (4.00)		49 (13.33)	16 (4.35)	
II Grade	88 (11.88)	46 (5.75)		43 (11.69)	23 (6.25)	
III Grade	73 (9.85)	116 (14.50)		40 (10.87)	51 (13.86)	



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Lateralized Interictal Epileptiform Discharges and Postoperative Seizure Outcomes in Tuberous Sclerosis Complex Patients

INTRODUCTION

Tuberous sclerosis complex(TSC) is an uncommon neurological condition caused by variations in the TSC1 or TSC2 genes. Around 80% of individuals with TSC experience seizures that are difficult to treat⁽¹⁾. The scalp Electroencephalogram(EEG) is a non-invasive technique that holds potential for detecting focal epileptic seizures prior to surgical treatment⁽²⁾. Previous studies indicated that scalp EEG results have the ability to anticipate the likelihood of being seizure-free after undergoing anterior temporal lobectomy. Moreover, individuals who underwent surgery on the temporal lobe and displayed unilateral interictal epileptic discharge(IEDs) experienced more favourable surgical results compared to those with bilateral IEDs^(3,4). There is a lack of evidence concerning the impact of IEDs on extended seizure results. This research aimed to investigate how IEDs are linked to long-term seizure outcomes after surgery and clinical attributes among patients with Tuberous Sclerosis Complex(TSC).

METHODS

A retrospective study was conducted on 82 patients with Tuberous Sclerosis who underwent epilepsy surgery. The main pre-operative assessments included neurological exams, genetic tests, computed tomography (CT), magnetic resonance imaging (MRI), F-fluorodeoxyglucose (FDG) PET, scalp video-EEG recordings and IQ tests. MRI scans showed cortical tubers. PET scans were done. Experts confirmed tuber identification. Patients had surgical procedures that involved removing brain tissue, such as lobectomy, tuberectomy and combined tuberectomy. Surgical results were evaluated using ILAE criteria: seizure freedom (ILAE type 1), focal seizures only (ILAE type 2), fewer seizures (ILAE type 3), over 50% reduction (ILAE type 4), minor changes (ILAE type 5) and significant increase (ILAE type 6). Outcomes were split into seizure freedom(SF) and no-seizure freedom(No-SF) categories. The link between patient traits and surgical results were studied. Characteristics impact on 1-year, 5-year and 10-year post-surgery seizure outcomes was examined. The connection between interictal epileptiform discharges (IEDs) and post-surgery seizures were investigated. Differences in traits were analysed across 4 IED patterns.

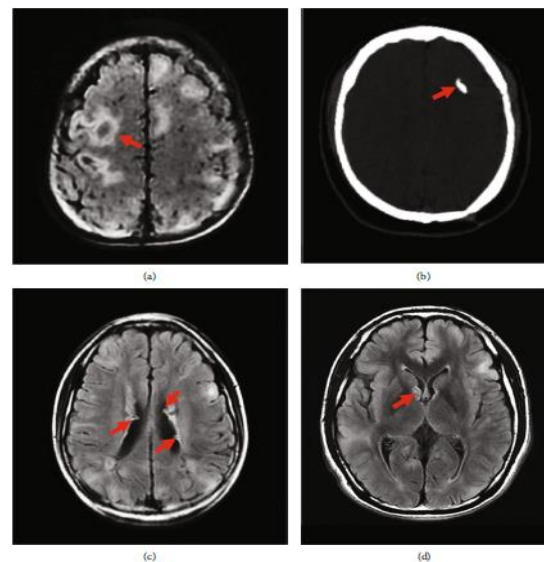


Figure 1 Typical imaging features of tubers in TSC patients shown by the red arrows (a) Cyst-like tubers. (b) Calcified tubers. (c) SEN. (d) SEGA.



RESULTS

TSC patients had various IED patterns: focal (14.6%), lateralized (37.8%), multifocal (17.1%) and generalized (30.5%). Post-surgical outcomes were evaluated at 1,5 and 10 years. Interictal scalp video-EEG, ASM and tubers are related to seizure outcomes at 1-year. For 5 and 10 years, scalp video-EEG and epileptogenic tubers were linked to surgical outcomes. Focal, lateralized and generalized IEDs were associated with postsurgical seizure freedom at 1 year. Lateralized IEDs also linked to freedom at 5 and 10 years. Patients with lateralized IEDs had better long-term freedom than those with other patterns. Seizure frequency was lower in focal and lateralized IEDs than in generalized or multifocal (TABLE 1). Lateralized IEDs correlated with fewer epileptogenic tubers. No associations found with gene variants, IQ or others. Patients with lateralized IEDs had fewer calcified tuber appearance. The common imaging types of epileptogenic tubers in TSC patients are shown in FIGURE 1.

TABLE 1 The relationship between IED patterns and clinical characteristics in TSC patients.										
IED patterns	Gene variant		Seizure frequency			Number of ASMs				IQ
	TSC1	TSC2	1-3/w	4-10/w	>10/w	1	2	3	4	
Focal	2 (22.2)	7 (77.8)	6 (50)	3 (25)	3 (25)a	2 (16.7)	4 (33.3)	4 (33.3)	2 (16.7)	59.6 (35-71)
Lateralized	4 (17.4)	19 (82.6)	12 (38.7)	15 (48.4)	4 (12.9)b,c	5 (16.1)	14 (45.2)	9 (29.0)	3 (9.7)	57.1 (39-93)
Multifocal	2 (16.7)	10 (83.3)	2 (14.3)	5 (35.7)	7 (50)	2 (14.3)	5 (35.7)	4 (28.6)	3 (21.4)	56.9 (31-42)
Generalized	3 (15)	17 (85)	2 (8)	7 (28)	16 (64)	1 (4)	10 (40)	8 (32)	6 (24)	57.1 (30-86)

DISCUSSION

This study showed that Focal, lateralized and generalized IEDs were associated with postsurgical seizure freedom. Seizure frequency was lower in focal and lateralized IEDs than generalized or multifocal⁽¹⁾. Studies had indicated that individuals with focal epileptic activity might not consistently encounter seizure freedom after removing the specific zone where seizures begin. Additionally, there are instances where regions near the seizure-onset zone could also initiate epileptic seizures⁽⁵⁾. The revised clinical guidelines from European experts for treating epilepsy in patients with TSC indicated that achieving seizure freedom is more likely when surgical resection extends beyond the edges of tubers⁽⁶⁾

CONCLUSION

This study suggests a connection between IEDs and outcomes after epilepsy surgery in TSC patients. Lateralized IEDs were linked to favourable long-term outcomes and milder epilepsy symptoms. Thus, lateralized IEDs could serve as a valuable indicator for predicting TSC patient’s prognosis after epilepsy surgery. This research is expected to have significant implications for the medical treatment of TSC patients.

Lateralized interictal epileptic discharge(IEDs) were linked to favourable long-term outcomes and milder epilepsy symptoms. Thus, lateralized IEDs could serve as a valuable indicator for predicting Tuberous Sclerosis Complex patient’s prognosis after epilepsy surgery.



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Illustrative case of focal drug-resistant temporal lobe epilepsy associated with an ipsilateral anterior choroidal artery aneurysm

INTRODUCTION

Focal epilepsy is a significant category within pediatric drug-resistant epilepsy (DRE), impacting around 1% of children. Although focal epilepsies in kids are frequently linked to cortical developmental malformations and mild epilepsy-related neuroepithelial tumors, additional pathological conditions could also play a role in causing epilepsy⁽¹⁾. Aneurysms in the anterior choroidal artery (AChA) are not common, making up around 2-5% of all aneurysms within the brain⁽²⁾. The exact occurrence of aneurysms in the same side of the brain as drug-resistant epilepsy is not clear. Because there's a lack of available literature describing how to make surgical decisions, plan surgeries and handle the specific details of cases involving both DRE and intracranial aneurysms, the case of a 14-year-old girl with treatment-resistant seizures in the temporal lobe was presented. She was found to have an aneurysm in the internal carotid artery (ICA) on the same side.

CASE PRESENTATION

A 14-year-old, female patient presented to hospital with DRE associated with a left temporal lesion. Seizure onset was at approximately 4 years of age, with episodes of behavioural change and a scared look with her right arm shaking that could progress to bilateral tonic-clonic movements. These episodes occurred approximately 1 to 2 times per month. Her IQ was extremely low, with better visual-spatial processing than reasoning, verbal skills and executive function. She faced attention difficulties due to dysfunction in the frontotemporal systems. Despite trying three antiepileptic medications, her seizures persisted, prompting a referral to epilepsy surgery evaluation. During long-term EEG monitoring, left temporal slowing was observed

between seizures, and seizure onset was mainly in the left temporal region. MRI showed a faint T2-weighted hyperintense lesion in the left anterior temporal lobe, extending into mesial structures with subtle contrast enhancement along the uncus (FIG 1 A, B). An aneurysm near the uncus enhancement, originating from the left anterior choroidal artery was seen on Magnetic

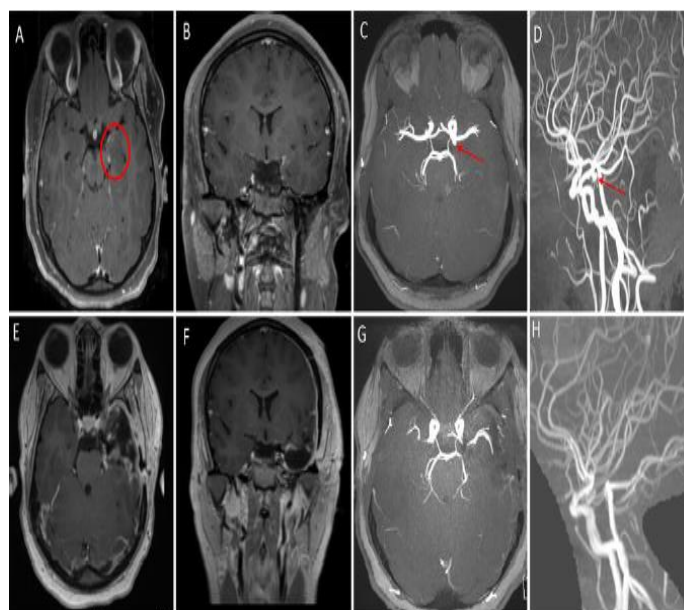


Figure 1 A left anteromesial temporal lesion with subtle contrast enhancement along the medial and superomesial uncus is shown on preoperative axial (A) and coronal (B) T1-weighted, contrast-enhanced magnetic resonance (MR) images. A 4-mm left AChA aneurysm is shown on preoperative axial (C) and sagittal three-dimensional (3D) reconstruction (D) MRA images. Axial (E), coronal (F), and sagittal (3D reconstruction) T1-weighted, contrast-enhanced MR images taken three weeks after a left craniotomy for lesion excision and clip ligation of a left AChA aneurysm are shown.



resonance angiography(MRA) (FIG 1 C, D). Functional MRI (fMRI) indicated left-dominant language and memory, while visual and motor functions were bilateral. A multidisciplinary conference agreed on surgery to resect the left temporal epileptic foci and clip the left anterior choroidal artery (AChA) aneurysm. The surgery involved resecting the lesion and clipping the aneurysm. After surgery, the patient resumed her home antiseizure medications (levetiracetam, oxcarbazepine, zonisamide) and had no lasting neurological issues except for a slight right superior quadrantanopia. MRI and MRA at 3 weeks post-operatively showed complete lesion resection and aneurysm clipping. No new lasting neurological problems arose post-surgery, and her vision improved. A year later, she remains seizure-free, experiencing better cognitive productivity at school, though still facing reading and speech comprehension challenges. She continued antiseizure medications as recommended.

DISCUSSION

This case presented a 14-year-old girl with treatment-resistant seizures in the temporal lobe who was found to have an aneurysm in the internal carotid artery(ICA) on the same side⁽¹⁾. Although it's uncertain how common drug-resistant focal epilepsies are in connection with aneurysms in children, focal epilepsy stands as the prevailing type of epilepsy among children⁽³⁾. Aneurysms in children are not common and can pose a greater challenge for treatment compared to those in adults. This is due to variations in size, where they are located in the brain, how they present clinically, and the resulting outcomes⁽⁴⁾.

CONCLUSION

For individuals with focal drug-resistant epilepsy(DRE) and a nearby intracranial aneurysm, a combined surgical method that includes both removal and ligation can be employed. It's important to carefully consider the timing of the surgery and neuroanesthetic factors to ensure the procedure's safety and effectiveness.

For individuals with focal drug-resistant epilepsy(DRE) and a nearby intracranial aneurysm, a combined surgical method that includes both removal and ligation can be employed.

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