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Magnetic Resonance Findings In First Unprovoked Seizure And The Patient's Progression To Epilepsy

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INTRODUCTION

Every year 23 to 64.1 out of 100000 people experience a single episode of unprovoked seizure (1). It is also estimated that 150000 adult cases of first unprovoked seizure happen annually in united states of America (2). Besides these statistics, seizure brings withering feelings, when somebody faces the condition. Moreover, it is reported that there is 21 to 45 percent risk of recurrence for a first unprovoked seizure within the first 2 years (3).

The condition become more complicated, when a diagnosis of epilepsy is made. It is reported that the incidence of epilepsy is higher in very young and very old adults; but it can affect patients at all ages. With this regard, the annual incidence of epilepsy is about 20 to 30 cases per 100000 (4). In fact, one in 26 people will develop epilepsy over the course of their lifetime (5). Furthermore, epilepsy brings a high burden for the society and the patient. Epileptic cases are banned to do some high-risk social activities and need proper and even life-long treatment. Annual cost of epilepsy is reported to be $8,412–$11,354. Along with this, the high burden of the psychologic effect should be addressed, too (6).

Taking into consideration all above mentioned timely and accurate diagnosis of epilepsy is important. Electroencephalography (EEG) is one of the first used modalities for the diagnosis of epilepsy; however, 10% of patients with confirmed diagnosis of epilepsy may never develop abnormal discharges in EEG, as these are usually evident during the attack episodes (7, 8). Moreover, even abnormal waves in EEG may not be indicative of a seizure or epilepsy (9). Nowadays, the gold standard diagnostic method for epilepsy is long-term video-EEG monitoring (VEM). Although, it is tried to make the VEM easier and more accessible, as there is outpatient VEM, todays. However, the high cost of this modality limits its valuable finding. The mean cost of inpatient and outpatient VEM in USA is reported to be $13,821 and $4,098, respectively (10).

Imaging also may play a role in the diagnosis of the cause of seizure and epilepsy. Computed tomography and magnetic resonance imaging (MRI) are both useful in the diagnosis of the seizure; however, MRI dose not pose harmful radiation. MRI can present epileptic and non-epileptic findings (11). However, further studies are needed to find relevant MRI features in first unprovoked seizure that finally diagnosed as epilepsy patient. The aim of our study is to assess the MRI findings of the patients with first unprovoked seizure and follow them to find out the proportion of the patients that develop epilepsy and try to correlate MRI findings with epilepsy development.

Material and methods

Study population and design

This prospective cohort study was conducted in military hospitals of Tehran, during 2021 and 2022. The studied population was the patients who referred with the presentation of the first unprovoked seizure (FUS) and they underwent magnetic resonance imaging (MRI). The diagnosis of FUS was made by an expert neurologist after the rule out of other conditions. Those with previous brain lesions, cerebrovascular accident (CVA), and trauma cases were excluded. Moreover, only adults aged 18 years old or more were included.

Data gathering, imaging, and follow up

Demographic data including age and gender of the patients were extracted. Moreover, the patients were asked for a full history, especially family history of seizure. Also, a full physical examination was conducted. According to the history and examination, the type of seizure and the side of lateralization were assessed. Moreover, two expert radiologists assessed the MRI of the patients to find any abnormality. The patients were followed for a further 6-month time, in order to find out whether they develop recurrence and final diagnosis of epilepsy according to the VEM.

Ethics

All the patients were provided with written informed consent and were free to leave the study whenever they want. Data of the patient were coded in order to be confidential. Moreover, ethics committee of Aja university of Medical Sciences approved study protocol.

Analysis

Data were entered in SPSS software version 20. Percent and frequency of the qualitative data and mean and standard deviation of the quantitative data were calculated. The frequency of different MRI findings regarding the diagnosis of epilepsy at the end of six-month follow up were assessed.

Result

Totally, 80 FUS cases were assessed. Among them, 62 (77.5%) were male and 18 (22.5%) were female. The mean age of the included cases was 29.96±9.32 old. Table 1 shows the details of gender, epilepsy family history, and age in the studied population.

Table 1. frequency of the gender, epilepsy family history, and mean age.

Feature		Statistic
Age (years; mean±SD)		29.96±9.32
Gender N (%)	Male	62 (77.5)
	Female	18 (22.5)
Epilepsy family history N (%)	Positive	6 (7.5)
	Negative	74 (92.5)

Table 2 shows the details of the type of diagnosed seizure in the cases. Most of the cases were generalized (50;62.5%) and convulsive (51;63.7%).

Table 2. type of diagnosed seizure in the cases.

Feature		Statistic
Type of epilepsy (focal/generalized) N (%)	Focal	30 (37.5)
	Generalized	50 (62.5)
Type of epilepsy (convulsive/non-convulsive) N (%)	Convulsive	51 (63.7)
	Non-convulsive	29 (36.3)

Table 3 shows the MRI findings of the included cases. The imaging was normal in 42 (52.5%)

cases. The most prevalent abnormal finding was small vessel ischemic changes that was found in 7 cases (8.8%). Table 2 shows the details.

Table 3. MRI findings of the included cases.

Feature		Statistic
MRI finding N (%)	Normal	42 (52.5)
	Small vessel ischemic changes	7 (8.8)
	Unspecified lesion	6 (7.5)
	White matter hyperintensity	5 (6.3)
	Gliosis/encephalomalacia	4 (5.0)
	Nonspecific T2 signal	3 (3.8)
	Cavernoma	2 (2.5)
	Focal cortical dysplasia	2 (2.5)
	Hippocampal structure asymmetry	2 (2.5)
	Developmental venous anomaly	1 (1.3)
	Demyelination	1 (1.3)
	Arachnoid cyst	1 (1.3)

During the follow up time, 22 cases (27.5%) were confirmed as epilepsy patients. Table 4 compares the MRI findings of the patients who developed epilepsy with those who did not. As it is evident there was a significant difference regarding this comparison (p=0.023).

Table 4. comparison of MRI findings of the patients who developed epilepsy with non-epileptic cases.

Feature		Epilepsy	Non-epilepsy	p value
MRI finding N (%)	Normal	9 (21.4)	33 (78.6)	0.023
	Small vessel ischemic changes	2 (28.6)	5 (71.4)	
	Unspecified lesion	1 (16.7)	5 (83.3)	
	White matter hyperintensity	0 (0.0)	5 (100.0)	
	Gliosis/encephalomalacia	4 (100.0)	0 (0.0)	
	Nonspecific T2 signal	1 (33.3)	2 (66.7)	
	Cavernoma	0 (0.0)	2 (100.0)	
	Focal cortical dysplasia	1 (50.0)	1 (50.0)	
	Hippocampal structure asymmetry	0 (0.0)	2 (100.0)	
	Developmental venous anomaly	1 (100.0)	0 (0.0)	
	Demyelination	0 (0.0)	1 (100.0)	
	Arachnoid cyst	0 (0.0)	1 (100.0)	

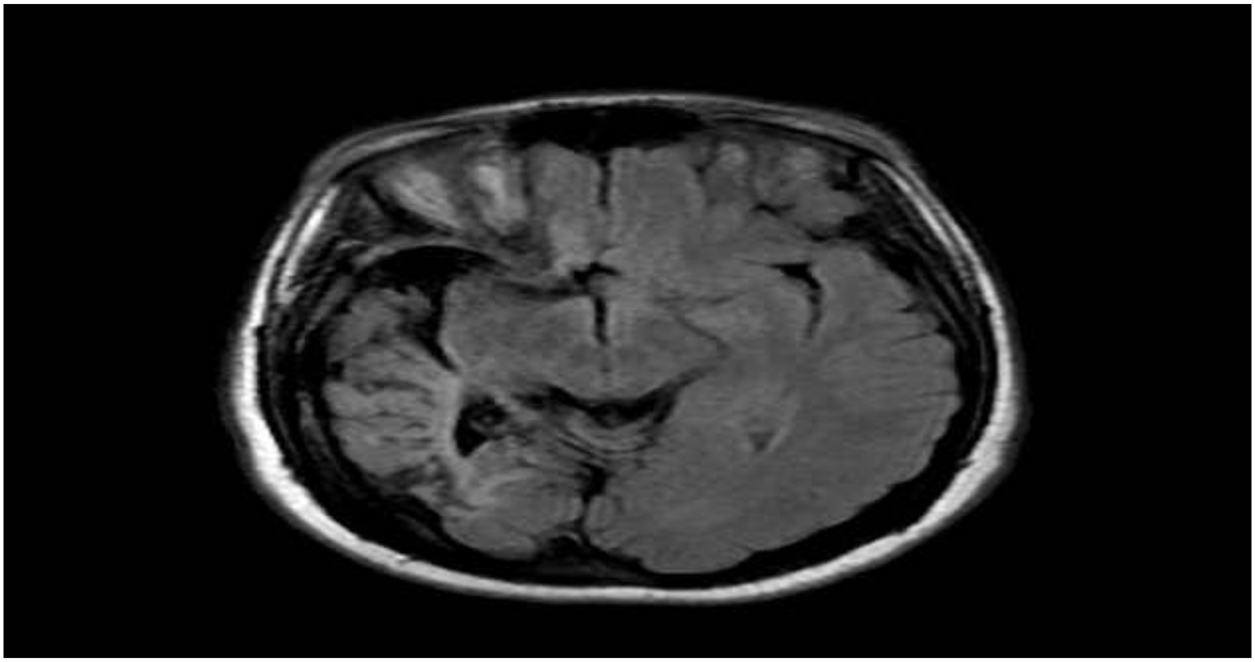

Figure 1. A magnetic resonance sequence showing gliosis

Discussion

The diagnosis of epilepsy is still a challenging task. Besides being challenging for the physicians, it is time and money consuming that poses a burden on the patients and the health system (12). The first approach to a patient with a seizure is to find a specific origin for the abnormal brain activity. But sometimes, there is no found origin and the patient is diagnosed, as a first unprovoked seizure case. In this situation, usually, the first approach is to take an electroencephalogram (EEG). However, EEG has several limitations, as it is believed that routine EEG usually assesses the superficial summation of excitatory and inhibitory actions of the cortex and the changes may be epileptic deep inside the brain. Moreover, nearly large electrical changes should be posed in the brain that can be detected with EEG. The reported specificity and sensitivity of routine EEG are 25-56% and 78-98%, respectively (13). Due to this low accuracy and limitations regarding the routine EEG, long term monitoring EEG (LTM) is developed with this regard. There are different benefits in using LTM, it can be used in case of diagnosing paroxysmal neurological attacks, rule out of nocturnal epilepsy and parasomnia or psychogenic non-epileptic seizures, assessment of candidates for epilepsy surgery, and definition of seizure type (14). Moreover, a recent meta-analysis proposed a sensitivity of 70% and specificity of 40% for long-term video-electroencephalographic monitoring (15), which is not high enough.

In fact, the diagnosis is usually made based on different clinical and para-clinical findings. Imaging can be helpful, too. MRI is clearly superior to CT in detection of epileptogenic abnormalities in patients with first-ever unprovoked seizure, in particular mesial temporal sclerosis and malformations of cortical development. MRI can even detect the lesions that a CT scan may miss (16). Ho et al. (17) found that 29 percent of their population had epileptogenic lesion including stroke, post-traumatic, or neoplastic lesions. Moreover, they proposed that 49% of their studied population developed epilepsy within a year and 55% of them were diagnosed as epilepsy cases after 2 years. This rate was 27.5% for our studied sample during 6 months. Chen et al. (18) proposed that using three dimensional MRI, 24.6% of their cases had abnormal findings. They proposed that 7 cases had encephalomalacia, 4 had brain contusions, 4 had infarctions, 2 had cerebral hemorrhages, 6 cases had hippocampal sclerosis, 6 cases had focal cortical dysplasia and 2 cases had other abnormalities. There was a relationship in their study between abnormal MRI finding and seizure recurrence. Our study showed that 47.5% of the cases had abnormal findings.

All the gliosis cases in our study were finally diagnosed as epilepsy cases. Hakami et al. (19) also reported that gliosis was the most common epileptogenic lesion in their study. They assessed the final diagnosis of first unprovoked seizure and among 764 patients that underwent MRI, 343 (45.0%) had an abnormal MRI. This finding consisted half of the epileptogenic lesions in MRI images. This finding can even happen in 18% of the cases with no evident history of trauma, stroke, or surgery. They also proposed that 52 percent of the epileptic seizure cases had normal MRI findings. Moreover, in case of non-epileptic lesions However, they did not compare the findings between epilepsy cases and non-epileptic patients.

The problem with the high rate of normal findings in MRI may be due to the low resolution of conventional MRI. Taking different sequences like T1 or T2 weighted and also FLAIR MRI can help with this regard. diffusion tensor imaging (DTI) is another modality that can be helpful in detecting subtle changes of the cortices (17, 20, 21). There are also other neuroimaging methods that can help the diagnosis of epilepsy like volumetric assessment of hippocampus (22). However, few studies regarding other neuroimaging techniques in diagnosing epilepsy have been conducted (23-25). Our study tried to find the MRI changes in first unprovoked seizure and their relationship with epilepsy development. Although some changes like Gliosis/encephalomalacia was associated with epilepsy development, due to the high number of normal brain MRI cases, we should declare that conventional MRI has a restriction in the diagnosis of epilepsy.

Conclusion

We found that many first unprovoked seizure patients, who developed epilepsy during our follow up time, had a normal MRI. However, some MRI findings like gliosis or encephalomalacia were more common in epileptic cases. In fact, the researchers should assess other neurological findings to point out a diagnostic clue for epilepsy.

REFERENCE

1. Jiménez-Villegas MJ, Lozano-García L, Carrizosa-Moog J. Update on first unprovoked seizure in children and adults: a narrative review. Seizure. 2021;90:28-33.
2. Krumholz A, Wiebe S, Gronseth GS, Gloss DS, Sanchez AM, Kabir AA, et al. Evidence-based guideline: management of an unprovoked first seizure in adults: report of the guideline development subcommittee of the American academy of neurology and the american epilepsy society: evidence-based guideline. Epilepsy currents. 2015;15(3):144-52.
3. Ebrahimi M, Shirzadeh M, Foroughipour M, Zamani Moghadam H, Najaf Najafi M, Foroughian M. Pathological EEG Findings in the Patients with the First Seizure Admitted to the Emergency Department. Reviews in Clinical Medicine. 2019;6(3):98-103.
4. Maloney EM, O'Reilly ÉJ, Costello DJ. Causes and classification of first unprovoked seizures and newly-diagnosed epilepsy in a defined geographical area-an all-comers analysis. Seizure. 2021;92:118-27.
5. Strawbridge LM, Schultz AM, Liverman CT, England MJ. Epilepsy across the spectrum: promoting health and understanding: National Academies Press; 2012.
6. Beghi E, Giussani G, Nichols E, Abd-Allah F, Abdela J, Abdelalim A,

et al. Global, regional, and national burden of epilepsy, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. The Lancet Neurology. 2019;18(4):357-75.
7. Normark MB, Erdal J, Kjær TW. Video electroencephalography monitoring differentiates between epileptic and non-epileptic seizures. Danish Medical Bulletin. 2011;58(9):A4305-A.
8. Yaraki PT, Yeyao JY, AlKhateeb M, Astrada MAA, Lapalme-Remis S, Mirsattari SM. EEG and MRI Abnormalities in Patients With Psychogenic Nonepileptic Seizures. Journal of Clinical Neurophysiology. 2022:10.1097.
9. Benbadis SR, Beniczky S, Bertram E, MacIver S, Moshé SL. The role of EEG in patients with suspected epilepsy. Epileptic Disorders. 2020;22(2):143-55.
10. Slater JD, Eaddy M, Butts CM, Meltser I, Murty S. The real-world economic impact of home-based video electroencephalography: the payer perspective. Journal of Medical Economics. 2019;22(10):1030-40.
11. Kim SE, Lee BI, Shin KJ, Ha SY, Park J, Park KM, et al. Characteristics of seizure-induced signal changes on MRI in patients with first seizures. Seizure. 2017;48:62-8.
12. Shoeibi A, Ghassemi N, Khodatars M, Jafari M, Moridian P, Alizadehsani R, et al. Applications of epileptic seizures detection in neuroimaging modalities using deep learning techniques: methods, challenges, and future works. arXiv preprint arXiv:210514278. 2021.
13. Smith SJM. EEG in the diagnosis, classification, and management of patients with epilepsy. Journal of Neurology, Neurosurgery & Psychiatry. 2005;76(suppl 2):ii2-ii7.
14. Duun-Henriksen J, Baud M, Richardson MP, Cook M, Kouvas G, Heasman JM, et al. A new era in electroencephalographic monitoring? Subscalp devices for ultra–long-term recordings. Epilepsia. 2020;61(9):1805-17.
15. Kobulashvili T, Kuchukhidze G, Brigo F, Zimmermann G, Höfler J, Leitinger M, et al. Diagnostic and prognostic value of noninvasive long-term video-electroencephalographic monitoring in epilepsy surgery: A systematic review and meta-analysis from the E-PILEPSY consortium. Epilepsia. 2018;59(12):2272-83.
16. Poirier SE, Kwan BY, Jurkiewicz MT, Samargandy L, Iacobelli M, Steven DA, et al. An evaluation of the diagnostic equivalence of 18F-FDG-PET between hybrid PET/MRI and PET/CT in drug-resistant epilepsy: A pilot study. Epilepsy Research. 2021;172:106583.
17. Ho K, Lawn N, Bynevelt M, Lee J, Dunne J. Neuroimaging of first-ever seizure: contribution of MRI if CT is normal. Neurology: Clinical Practice. 2013;3(5):398-403.
18. Chen T, Si Y, Chen D, Zhu L, Xu D, Chen S, et al. The value of 24-hour video-EEG in evaluating recurrence risk following a first unprovoked seizure: A prospective study. Seizure. 2016;40:46-51.
19. Hakami T, Mcintosh A, Todaro M, Lui E, Yerra R, Tan KM, et al. MRI-identified pathology in adults with new-onset seizures. Neurology. 2013;81(10):920-7.
20. Crocker CE, Pohlmann-Eden B, Schmidt MH. Role of neuroimaging in first seizure diagnosis. Seizure. 2017;49:74-8.
21. Pohlmann-Eden B, Newton M. First seizure: EEG and neuroimaging following an epileptic seizure. Epilepsia. 2008;49:19-25.
22. Tai X, Bernhardt B, Thom M, Thompson P, Baxendale S, Koepp M, et al. Neurodegenerative processes in temporal lobe epilepsy with hippocampal sclerosis: Clinical, pathological and neuroimaging evidence. Neuropathology and applied neurobiology. 2018;44(1):70-90.

23. Tranvinh E, Lanzman B, Provenzale J, Wintermark M. Imaging evaluation of the adult presenting with new-onset seizure. American Journal of Roentgenology. 2019;212(1):15-25.
24. Salinsky M, Wong VS, Motika P, Meuse J, Nguyen J. Emergency department neuroimaging for epileptic seizures. Epilepsia. 2018;59(9):1676-83.
25. Coryell J, Gaillard WD, Shellhaas RA, Grinspan ZM, Wirrell EC, Knupp KG, et al. Neuroimaging of early life epilepsy. Pediatrics. 2018;142(3).