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ORIGINAL ARTICLE

Evaluation of dual pathology among drug-resistant epileptic patients with hippocampal sclerosis

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Abstract

Purpose Dual pathology (DP) is defined as simultaneous presence of hippocampal sclerosis (HS) and any other pathology in the brain. Since this is a less probed concept, we aimed to evaluate the frequency and characteristics of DP among drug-resistant epileptic patients with HS.

Methods This is a cross-sectional study conducted during 2007–2016 in Kashani Comprehensive Epilepsy Center, Isfahan, Iran. Patients with diagnosis of drug-resistant epilepsy and HS were enrolled in the study, and demographic data, seizure semiology, EEG findings, and MRI findings were collected. We compared these variables between three groups of DP, unilateral HS, and bilateral HS.

Results Of the 200 enrolled cases, 29 patients (14.5%) had DP and 21 patients (10.5%) had bilateral HS; the remaining patients had unilateral HS. The average age of patients with DP was 30.03, and 65.5% of them were male. Patients with DP had more EEG discharges from regional and multi-focal sites compared to unilateral HS (P value < 0.001). Also, complex partial seizure (CPS) was more commonly presented in patients with unilateral HS (96.8%). Comparison of disease characteristics between DP and bilateral HS showed no difference in most categories ($P > 0.05$).

Conclusions We found DP among 14.5% of our drug-resistant epileptic patients with HS. DP patients mostly presented with CPS and had high proportion of ictal and interictal EEG discharges from regional and multi-focal areas. Gliosis and focal cortical dysplasia were the most common pathologies among DP patients. Patients with DP showed a similar behavior to bilateral HS in many features.

Keywords Hippocampal sclerosis · Dual pathology · Drug-resistant epilepsy · Mesial temporal sclerosis

Introduction

Epilepsy is a common disease that approximately affects 65 million people worldwide [1]. Despite progresses in medical management of epilepsy and appropriate use of antiepileptic drugs, 30–40% of epileptic patients continue having seizures [2]. Hippocampal sclerosis is known as one of the reasons that could cause drug-resistant epilepsies [3].

Hippocampal sclerosis was first described in 1825 [4] and is histologically defined as a specific tissue pattern consisted of neuronal loss and gliosis [5]. It is the most common cause of temporal lobe seizures [6] with unknown prevalence [5], but responsible for 20% of epilepsies in adults [7] and a large proportion of epilepsy surgeries [8]. Hippocampal sclerosis can be validly diagnosed by magnetic resonance imaging (MRI) or through histological assessment [9].

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Hippocampal sclerosis accompanied by any other pathology in the brain is called dual pathology [5, 10]. This includes neoplasms, heterotopia, ischemic vascular lesions, brain atrophy, cysts, and other pathologies either in the temporal lobes or other brain regions [5, 10]. The prevalence of dual pathology is not known yet [11]; however, it is estimated that 5–20% of adult epilepsy surgery candidates have dual pathology [6, 12, 13]. Patients with dual pathology usually present with uncontrollable seizure. Resection of both pathologies is recommended to successfully eliminate seizures [5, 11, 14].

Despite the importance of dual pathology and its epidemiologic and clinical features, it is still vastly understudied [11]. Exploring dual pathology is valuable both for presurgical selection of suitable candidates and for understanding the pathogenesis of the condition [14–16]. In this study, we aimed to assess the characteristics of drug-resistant epileptic patients with dual pathology among drug-resistant epileptic patients with hippocampal sclerosis.

Methods

Participants

This was a retrospective study conducted during 2007–2016 in Kashani Comprehensive Epilepsy Center affiliated to Isfahan University of Medical Sciences, Iran. The inclusion criteria were defined as (1) patients with diagnosis of drug-resistant epilepsy, (2) having hippocampal sclerosis in an epilepsy-protocol MRI, and (3) complete medical history and seizure evaluation including ictal and interictal electroencephalography (EEG) and neuroimaging. The study was approved by the regional bioethics committee of Isfahan University of Medical Sciences.

Epilepsy was defined as having at least two unprovoked seizures, more than 24 h apart [11]. Drug-resistant epilepsy was defined as failure of adequate response (i.e., to achieve sustained seizure freedom) to two different appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) [17]. Hippocampal sclerosis was defined as seeing hippocampal atrophy accompanied by increased signal in T2 and FLAIR and decreased signal in T1 in MRI with epilepsy protocol [9].

Procedures

All the patients had undergone a comprehensive evaluation including neurological examination, neuroimaging (to identify any substrate-related lesion), and non-invasive EEG recording. MRI was performed using 1.5-T scanners with epilepsy protocol including coronal FLAIR. EEG was done using the international 10–20 system including T_1 and T_2 electrodes. Data regarding EEG was interpreted by experienced epileptologists, and neuroimaging findings were recorded by a single skilled neuroradiologist. We were not able to perform intracranial EEG in our center due to limited infrastructural and skills.

To report MRI-EEG concordance, we attributed EEG discharges to patient's pathological findings according to the scalp electrodes and seizure semiology. Therefore, an interpretation of findings about the estimated origin of epileptic discharges is reported, but not the actual origin.

MRI findings were also reported according to guidelines and suggested criteria for each pathology. Although the only definite way to confirm a radiologic diagnosis is histological assessment, we distinguished the two diagnoses of gliosis and FCD based on the following criteria [18–20]:"

1. Increased signal intensity on T2W images associated with volume loss and hemosiderin hypointense deposits on T2W weighted/gradient echo images and/or history of significant head trauma in patient where classified as gliosis, if there was no additional finding in favor of FCD including abnormal sulci/gyri and transmantle sign.
2. Lesions were classified as FCD if they met at least three of the following characteristics:

    a. Cortical thickening
    b. Blurring of white matter-gray matter junction with abnormal architecture of subcortical layer
    c. T2/FLAIR signal hyperintensity of white matter with or without the transmantle sign
    d. T2/FLAIR signal hyperintensity of gray matter
    e. Abnormal sulcal or gyral pattern
    f. Segmental and/or lobar hypoplasia/atrophy."

We also looked for patients with dual pathology and recorded data regarding the second pathology. Dual pathology is defined as hippocampal sclerosis accompanied by any other pathology including neoplasm, heterotopia, ischemic vascular lesions, brain atrophy, or other pathologies, either in temporal lobe or other lobes [5, 10]. Since the definition of dual pathology is still a matter of debate, we decided to consider all "second pathologies" that have been reported in similar studies as dual pathology [5, 10, 15].

All the cases were divided into three groups of dual pathology, unilateral hippocampal sclerosis, and bilateral hippocampal sclerosis. Demographic data, seizure characteristics, neuroimaging findings, and EEG findings were reported for each group and were compared between groups thereafter.

Statistical analysis

We used descriptive statistics to report means and frequencies. To compare the mean age between groups, we used independent sample *t* test or Mann-Whitney *U* test when applicable.

Chi-squared test was used to compare categorical variables between groups. Data analysis was performed using IBM SPSS 22 and a *P* value less than 0.05 was considered as significant.

Results

Patient's characteristics

Of all the 200 cases, 29 patients (14.5%) had dual pathology, 21 patients (10.5%) had bilateral hippocampal sclerosis, and the remaining patients (75%) had unilateral hippocampal sclerosis. The mean of age ± standard deviation (SD) among patients with dual pathology was 30.03 ± 10.13; 19 of the patients (65.5%) were male. The mean of age ± SD among patients with unilateral and bilateral hippocampal sclerosis were 36.14 ± 11.37 and 35.71 ± 11.70, respectively.

Lesion and seizure characteristics and MRI findings

Among patients with dual pathology, 11 cases (37.9%) had right hippocampal sclerosis, 17 (58.6%) had left hippocampal sclerosis, and one patient (3.4%) had bilateral hippocampal sclerosis. The detailed list of second pathologies is displayed in Table 1. With respect to second pathology, 4 cases (13.8%) had focal cortical dysplasia, 4 cases had gliosis only, 3 cases (10.3%) had porencephaly, and 3 cases had both porencephaly and gliosis. Also, 3 patients had brain tumor and 3 patients had encephalomalacia. The mean ± SD age of onset of seizures among patients with dual pathology was 12.3 (10.9). Most patients reported having complex partial seizures (CPS) and simple motor seizures (SMS) (69% and 20.7%, respectively). Two patients (6.9%) presented with both CPS and SMS and one patient (3.4%) had aura and dialeptic seizures.

EEG findings

EEG findings showed focal ictal activities in 15 cases while interictal activities were mostly regional (10 cases). These findings are presented in Table 2. Moreover, EEG-MRI matching in ictal and interictal phase is presented in Tables 1 and 2. As stated earlier, the epileptogenic origins reported here are estimated regions according to scalp electrodes and seizure semiology.

Twenty-three patients (79.3%) had ictal discharges from hippocampal sclerosis, and 22 patients (75.9%) had interictal discharges from hippocampal sclerosis. One patient who had left hippocampal sclerosis and right occipital focal cortical dysplasia had right temporal discharges only from an origin unmatched with MRI findings in the ictal EEG. Thirteen cases had no discharge from their second pathologies in the ictal EEG. We observed discharges from origins unmatched with MRI findings in 8 cases in the ictal EEG and 11 cases in the interictal EEG. Finally, only 10 cases (34.5%) had discharges both from hippocampal sclerosis and second pathology in the ictal EEG.

Comparison of disease characteristics between patients with dual pathology and unilateral hippocampal sclerosis

The mean age ± SD in patients with dual pathology and unilateral hippocampal sclerosis were 30.03 ± 10.13 and 36.14 ± 11.37, respectively (*P* value = 0.008). Comparison of disease characteristics between patients with dual pathology and unilateral hippocampal sclerosis is presented in Table 2. We found that patients with dual pathology had more regional and multi-focal discharges in both ictal and interictal EEG compared to those with unilateral hippocampal sclerosis (*P* value < 0.001). Also, CPS was a more common presentation in patients with unilateral hippocampal sclerosis (96.8% compared to 69%, respectively) while simple motor seizures were more common in patients with dual pathology (20.7% compared to 4.7%, respectively) (*P* value < 0.001). Furthermore, patients with dual pathology had more discharges from a region unmatched with MRI findings in ictal EEG (27.5% compared to 13.4%) while the difference was not statistically significant in the interictal EEG (37.9% compared to 34.7%; *P* value = 0.736).

Comparison of disease characteristics between patients with dual pathology and bilateral hippocampal sclerosis

The mean age ± SD in patients with dual pathology and bilateral hippocampal sclerosis were 30.03 ± 10.13 and 35.71 ± 11.70, respectively (*P* value = 0.073). Results regarding comparison of disease characteristics between two groups are shown in Table 3. No statistically significant differences were found between two groups with respect to EEG discharges site in both ictal and interictal phases (*P* value > 0.05). Also, distribution of seizure semiology was not different in the two groups (*P* value > 0.05). We observed a statistically significant difference regarding seizure frequency between the two groups (*P* value = 0.019).

In bilateral hippocampal sclerosis group, five patients (23.8%) in ictal phase and six patients (28.6%) in interictal phase had discharges from a region unmatched with MRI findings in their EEG, which was not different with dual-pathology patients (*P* value > 0.05). Among patients with bilateral hippocampal sclerosis, nine (42.9%) and seven (33.3%) cases had ictal discharges from left and right hippocampal sclerosis, respectively. Only one patient had discharges from both sides of bilateral hippocampal sclerosis in

Table 1 The detailed list of first and second pathologies and EEG-MRI matching in dual-pathology patients

No.	Age	Sex	Hippocampal sclerosis	Second pathology	Ictal EEG and MRI matching	Interictal EEG and MRI matching
1	53	Female	Left	Right temporal tumor	With HS and SP	With HS and SP
2	20	Male	Right	Right temporal tumor	With HS and SP	With HS and SP
3	25	Male	Right	Right temporal focal cortical dysplasia	With HS and SP	With HS and SP
4	14	Female	Left	Right hemisphere leukomalacia	With SP	With SP and OU
5	16	Female	Left	Right hemisphere arachnoid cyst	With HS	With SP and OU
6	29	Male	Right	Right frontotemporal porencephaly and gliosis	With HS and SP	With HS and SP
7	37	Male	Right	Right frontotemporal atrophy	With HS and OU	With HS and OU
8	51	Male	Right	Right frontal gliosis	With HS and OU	With HS and OU
9	25	Male	Left	Right frontal gliosis	With HS and SP	With HS and SP
10	20	Female	Right	Right amygdala tumor	With HS and SP	With HS and SP
11	38	Female	Left	Right occipital focal cortical dysplasia	With OU	With HS and OU
12	31	Male	Left	Left temporoparietooccipital encephalomalacia	With SP and OU	With SP and OU
13	33	Male	Left	Left temporal porencephaly	With HS and SP	With HS, SP, and OU
14	35	Female	Right	Left temporal arachnoid cyst	With SP	With SP and OU
15	38	Female	Left	Left hemisphere porencephaly and gliosis	With HS and SP	With HS and SP
16	32	Male	Left	Left hemisphere encephalomalacia	With HS	With HS and OU
17	14	Male	Left	Left frontoparietal atrophy	With SP	With HS and SP
18	36	Male	Right	Left frontal porencephaly and gliosis	With HS and OU	With HS and OU
19	34	Male	Right	Left frontal porencephaly	With HS	With HS and SP
20	20	Male	Bilateral	Left frontal porencephaly	With HS and OU	With HS
21	25	Male	Left	Left frontal gliosis	With SP	With SP
22	33	Female	Left	Left frontal focal cortical dysplasia	With HS	With HS
23	32	Male	Right	Left frontal focal cortical dysplasia	With SP	With SP
24	26	Female	Left	Left frontal arachnoid cyst	With HS	With HS
25	42	Female	Left	Left fontal gliosis	With HS and SP	With HS and SP
26	22	Male	Left	Insular atrophy	With HS	With HS
27	44	Male	Right	Hydrocephalus	With HS	Normal EEG
28	26	Male	Left	General brain atrophy	With HS and OU	Normal EEG
29	20	Male	Left	Cerebellar atrophy	With HS and OU	With HS and OU

EEG electroencephalography, MRI magnetic resonance imaging, HS hippocampal sclerosis, SP second pathology, OU origin unmatched with MRI finding

the ictal EEG while six patients showed bilateral matching in the interictal EEG.

Discussion

Almost all the epidemiologic characteristics of dual pathology is still a matter of debate depending on the assumed definition [21]. Here, we observed that 14.5% of drug-resistant epileptic patients with hippocampal sclerosis had dual pathology. Cendes et al. reported the frequency of 15% for dual pathology among patients with lesional epilepsy [22]. Studying histopathological findings of 327 drug-resistant epileptic cases who had undergone epilepsy surgery showed only 18 dual-pathology cases (5.5%) [23]. Similarly, a study on surgical specimen of 33 cases with drug-resistant temporal lobe epilepsy showed dual or multiple pathologies in 48% of cases [16] and in review of surgical pathologies of 40 children with drug-resistant epilepsy who had undergone temporal lobectomies and neocortical resections, 12 patients (30%) with dual pathology were found [24]. Moreover, Levesque et al. found dual pathology among 30.3% of their cases with mesial temporal sclerosis [10]. Different definition of dual pathology [25], low diagnostic sensitivity of MRI [25, 26], and different target populations could explain the discrepancy on frequency of dual pathology.

Likewise, different definition, methodology, and study populations have led to various findings regarding the frequency of second pathologies in dual-pathology cases. We found left hippocampal sclerosis among more than half of our dual-pathology cases. With respect to second pathologies, focal cortical dysplasia was seen in four cases (13.8%), single

Table 2 Comparison of disease characteristics in patients with dual pathology and unilateral hippocampal sclerosis

Category		Dual (no (%))		Unilateral hippocampal sclerosis (no (%))		*P* value
Sex	Female	10 (34.5%)		71 (47.3%)		0.203
	Male	19 (65.5%)		79 (52.7%)		
Hippocampal sclerosis site	Right	11 (37.9%)		70 (46.7%)		0.058
	Left	17 (58.6%)		80 (53.3%)		
	Bilateral	1 (3.4%)		0		
Seizure Semiology	Complex partial seizure	14 (48.3%)		127 (90.1%)		*< 0.001*
	Complex partial seizure + SG	6 (20.7%)		10 (6.7%)		
	Simple motor seizure	2 (6.9%)		0		
	Simple motor seizure + SG	4 (13.8%)		7 (4.7%)		
	Complex partial seizure + Simple motor seizure	2 (6.9%)		0		
	Aura + dialeptic	1 (3.4%)		0		
	Others	0		5 (3.4%)		
Seizure frequency	Daily	4 (14.3%)		25 (16.7%)		0.162
	Weekly	7 (25%)		53 (35.3%)		
	Monthly	6 (21.4%)		39 (26%)		
	Annual	3 (10.7%)		5 (3.3%)		
	Variable	8 (28.6%)		28 (18.7%)		
		Ictal EEG	Interictal EEG	Ictal EEG	Interictal EEG	
EEG discharges site of origin	Focal	15 (51.7%)	9 (31%)	132 (88%)	95 (63.3%)	*< 0.001*
	Regional	8 (27.6%)	10 (34.5%)	8 (5.3%)	12 (8%)	
	Multi-focal	6 (20.7%)	8 (27.6%)	10 (6.7%)	39 (26%)	
	Normal	0	2 (6.9%)	0	4 (2.7%)	
EEG-MRI matching (no (%))	With HS	7 (24.1%)	4 (13.8%)	130 (86.7%)	95 (63.3%)	*< 0.001*
	With HS and SP	9 (31%)	10 (34.5%)	0	0	
	With SP	5 (17.2%)	2 (6.9%)	0	0	
	With HS and OU	6 (20.7%)	6 (20.7%)	16 (10.7%)	49 (32.7%)	
	With SP and OU	0	3 (10.3%)	0	0	
	With HS, SP, and OU	1 (3.4%)	2 (6.9%)	0	0	
	With OU	1 (3.4%)	0	4 (2.7%)	3 (2%)	
	None	0	2 (6.9%)	0	3 (2%)	

EEG electroencephalogram, MRI magnetic resonance imaging, HS hippocampal sclerosis, SP second pathology, OU origin unmatched with MRI finding, SG secondary generalization, $P < 0.05$ indicates statistically significant difference

gliosis in four patients, gliosis and porencephaly in three patients, and single porencephaly in three patients. Also, three patients had brain tumor and three patients had encephalomalacia. Cortical dysplasia is the most common reported pathology associated with hippocampal sclerosis [5]. Among 38 surgically evaluated cases with dual pathology, cortical dysplasia accounted for almost half of lesions and 26% of cases had tumors [13]. We believe that lower number of cortical dysplasia in our study is due to either cortical dysplasia may not be detectable in MRI [27] or cortical dysplasia may look like gliosis in MRI when it is associated with neuronal and glial proliferation [28]. Thus, patients with cortical dysplasia may either be underestimated/undiagnosed or misdiagnosed in our study.

Gliosis is frequently seen in dual pathology patients and mainly has traumatic or ischemic origin [25]. The high prevalence of traumatic brain injury in Iran [29] could be a reason for the high frequency of gliosis in our cases. Porencephalic cysts are one of the rare pathologies associated with hippocampal sclerosis [25]. Other associated pathologies are arachnoid cysts, vascular malformations, hydrocephalus, and others [13, 22, 25]. We also had one case of cerebellar atrophy with left HS that seemed to have no epileptogenic activity originating from his cerebellum. The epileptogenicity of cerebellum has been a matter of debate with both confirming and disproving arguments [30]. In addition, cerebellar atrophy could happen as a consequence of chronic epilepsy [31].

Table 3 Comparison of disease characteristics in patients with dual pathology and bilateral hippocampal sclerosis

Category		Dual (no (%))		Bilateral hippocampal sclerosis (no (%))		*P* value
Sex	Female	10 (34.5%)		9 (42.9%)		0.547
	Male	19 (65.5%)		12 (57.1%)		
Seizure semiology	Complex partial seizure	14 (48.3%)		15 (71.4%)		0.211
	Complex partial seizure + SG	6 (20.7%)		2 (9.5%)		
	Simple motor seizure	2 (6.9%)		0		
	Simple motor seizure + SG	4 (13.8%)		1 (4.8%)		
	Complex partial seizure + Simple motor seizure	2 (6.9%)		0		
	Aura + Dialeptic	1 (3.4%)		0		
	Others	0		3 (14.4%)		
Seizure frequency	Daily	4 (14.3%)		0		*0.019*
	Weekly	7 (25%)		11 (52.4%)		
	Monthly	6 (21.4%)		5 (23.8%)		
	Annual	3 (10.7%)		0		
	Variable	8 (28.6%)		5 (23.8%)		
		Ictal EEG	Interictal EEG	Ictal EEG	Interictal EEG	
EEG discharges site of origin	Focal	15 (51.7%)	9 (31%)	12 (57.1%)	8 (38.1%)	> 0.05
	Regional	8 (27.6%)	10 (34.5%)	5 (23.8%)	2 (9.5%)	
	Multi-focal	6 (20.7%)	8 (27.6%)	4 (19%)	10 (47.6%)	
	Normal	0	2 (6.9%)	0	1 (4.8%)	
EEG-MRI matching (no (%))	With HS	7 (24.1%)	4 (13.8%)	13 (61.9%)	14 (66.7%)	*< 0.05*
	With HS and SP	9 (31%)	10 (34.5%)	0	0	
	With SP	5 (17.2%)	2 (6.9%)	0	0	
	With HS and OU	6 (20.7%)	6 (20.7%)	4 (19%)	6 (28.6%)	
	With SP and OU	0	3 (10.3%)	0	0	
	With HS, SP, and OU	1 (3.4%)	2 (6.9%)	0	0	
	With OU	1 (3.4%)	0	4 (19%)	0	
	None	0	2 (6.9%)	0	1 (4.8%)	

EEG electroencephalogram, MRI magnetic resonance imaging, HS hippocampal sclerosis, SP second pathology, OU origin unmatched with MRI finding, SG secondary generalization, $P < 0.05$ indicates statistically significant difference

With respect to seizure frequency, we found that half of patients with bilateral hippocampal sclerosis had experienced weekly seizures compared to 25% in dual-pathology group. Patients with bilateral hippocampal sclerosis had no daily seizures while 14% of dual pathology cases reported to experience daily seizures. Overall, no difference was observed between dual pathology and unilateral hippocampal sclerosis here, but the distribution of seizure frequency was different in bilateral hippocampal sclerosis. Levesque et al. found no association between dual pathology and seizure frequency [10], while Bocti et al. reported that dual-pathology patients, especially those with cortical dysplasia, develop more frequent seizures [32].

In each group dual pathology and bilateral hippocampal sclerosis showed similar seizure semiology with CPS as seen in almost 80% of patients, while CPS accounted for 90% of seizure semiology reported in unilateral hippocampal sclerosis. On the other hand, SMS was seen in about 20% of dual pathology case, but only 5% of patients with unilateral and bilateral hippocampal sclerosis. Dual-pathology patients with SMS had mostly unilateral hippocampal sclerosis (both on right and left hemispheres) with different second pathologies (porencephaly, gliosis, atrophy, leukomalacia, focal cortical dysplasia) on different brain regions (frontotemporal, temporoparietal, right hemisphere, frontal). We could not identify any hint to differentiate features between these patients based on their seizure semiology, but presumably, SMS is a more common finding in dual pathology compared to hippocampal sclerosis. To the best of our knowledge, no information is available in the literature regarding comparison of seizure semiology between these groups.

With respect to ictal and interictal EEG, we found more similarities between dual pathology and bilateral hippocampal sclerosis. Dual-pathology patients had more ictal and interictal

epileptic activities from regional and multi-focal sources compared to patients with unilateral hippocampal sclerosis. Comparably, Cendes et al. reported no difference in ictal and interictal EEG findings between two groups of dual and not dual pathology [22]. Hippocampal sclerosis can also contribute to developing epileptogenicity in brain [16], which could add new epileptic zones to the possibly epileptogenic second pathologies and consequently to two or more sources of electric discharges, which was also observed in our cases.

Discharges from an origin unmatched with MRI findings were also more frequent in dual-pathology and bilateral hippocampal sclerosis patients. This is explainable by more frequent brain lesions in these patients and therefore more secondary generalization and epileptogenesis [16]. This adds more complexity to management of patients with dual pathology and bilateral hippocampal sclerosis, especially surgically, and should be noted.

In our dual-pathology group, all brain tumors and most gliosis and encephalomalacia pathologies seemed to be epileptogenic. In comparison, less than one fourth of cases with brain atrophy had discharges from their second pathologies. Brain atrophy could be a result of epilepsy, especially intractable type [33]. It is controversial to include brain atrophy as the second pathology or a consequence of epilepsy, but according to our data, these cases have less similarity with other dual-pathology cases and might not be considered as dual pathology in future studies.

These findings show that the epileptogenic zones in cases with dual pathology may be different with respect to their lesions and they should be managed differently in clinics. Also, considering the epileptogenicity of most dual pathologies, the surgical removal of the epileptogenic lesion may be an efficacious treatment. Here, we could not compare the epileptogenicity of these pathologies due to the small number of dual pathology cases; however, more studies are needed in the future to fill this gap.

In this study, we were limited due to inadequate evaluation of the surgical outcome in our cases since a small number of them underwent epilepsy surgery, lack of data on the factors that are suggested previously to be associated with developing dual pathology such as febrile convulsion, evaluation of the patients' pathologies based on their MRI which is less accurate compared to histopathological studies, and using a 1.5-T scanner which is associated with higher false negative rates for both hippocampal sclerosis and dual pathologies. Despite these limitations, the study covers a distinct target population pathologically and epidemiologically and presents findings in clinically applicable setting.

Conclusion

We found dual pathology among 14.5% of our drug-resistant epileptic patients with hippocampal sclerosis. Dual-pathology patients mostly presented with CPS and had high proportion of ictal and interictal EEG activities from regional and multi-focal areas. Gliosis and focal cortical dysplasia were the most common pathologies among dual-pathology patients. Also, patients with dual pathology experienced more simple motor seizures and had more ictal EEG activities from regional and multi-focal sites in the brain compared to patients with unilateral hippocampal sclerosis. We found a similar behavior in patients with dual pathology and those with bilateral hippocampal sclerosis regarding seizure characteristics (except for higher frequency of SMS in dual pathology) and EEG findings. Further studies are requited in the future to confirm our findings.

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