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ORIGINAL ARTICLE

Temporal encephaloceles and coexisting epileptogenic lesions

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Abstract

Objective: This study was performed to identify coexisting structural lesions in patients with epilepsy and known temporal encephaloceles (TEs).

Methods: Forty-seven structural magnetic resonance imaging (MRI) scans of patients with epilepsy and radiologically diagnosed TEs were retrospectively reviewed visually and using an automated postprocessing software, the Morphometric Analysis Program v2018 (MAP18), to depict additional subtle, potentially epileptogenic lesions in the 3D T1-weighted MRI data. All imaging findings were evaluated in the context of clinical and electroencephalographical findings.

Results: The study population consisted of 47 epilepsy patients (38.3% female, n = 18). The median age at the time of the scan was 40 years (range 12–81 years). Twenty-one out of 47 MRI scans (44.7%) showed coexisting lesions in the initial MRI evaluation; in 38.3% (n = 18) of patients, those lesions were considered probably epileptogenic. After postprocessing, probable epileptogenic lesions were identified in 53.2% (n = 25) of patients. Malformations of cortical development had initially been reported in 17.0% (n = 8) of patients with TEs, which increased to 38.3% (n = 18) after postprocessing. TEs and other epileptogenic lesions were considered equally epileptogenic in 21.3% (n = 10) of the cases in the initial MR reports and 25.5% (n = 12) of the cases after postprocessing.

Significance: Temporal encephaloceles are a potential cause of MRI-negative temporal lobe epilepsy. According to our data, TEs can occur with other lesions, suggesting that increased awareness is also required in patients with lesional epilepsy. TEs may not always be epileptogenic; hence, their occurrence with other structural pathologies may influence the presurgical evaluation and surgical approach. Finally, TEs can be associated with malformations of cortical development, which may indicate a common developmental etiology of those lesions.

KEYWORDS
epilepsy surgery, focal cortical dysplasia, structural epilepsy, temporal encephaloceles, temporal lobe epilepsy

1 | INTRODUCTION

Encephaloceles are brain herniations through congenital or secondary skull bone defects. Developmental neural tube defects during pregnancy due to genetic or environmental factors,[1,2] as well as congenital mesodermal defects (congenital mesodermal defect theory),[3,4] have been suggested as theories for the pathogenesis of congenital encephaloceles, while secondary encephaloceles are usually acquired as a consequence of trauma, inflammation, or postsurgical conditions.[5–7]

Temporal encephaloceles (TEs) are associated with increased body mass index (BMI) and intracranial hypertension[4,8,9] and have been increasingly identified as a potential structural lesion in patients with temporal lobe epilepsy (TLE).[4–7,9–20] Although they have mostly been discussed as being frequently missed lesions in patients with magnetic resonance imaging (MRI)-negative TLE,[14,17,21] several neuroimaging and histopathological findings of reported cases have shown the coexistence of TEs with other epileptogenic lesions, such as hippocampal sclerosis and malformations of cortical development.[4,6,13,14,18,21–24]

Because TEs can also be asymptomatic,[20,25] it is challenging to decide on the most appropriate surgical method in refractory cases, especially if they occur as dual pathologies. Therefore, we reviewed the initial MRI reports and postprocessed MRI data of patients with epilepsy and already diagnosed TEs to identify coexisting epileptogenic lesions. In addition, we evaluated these findings in light of the clinical and electroencephalographical data obtained during the presurgical evaluation.

Key points

- Twenty-one out of 47 MRI scans (44.7%) showed coexisting lesions in the initial MRI evaluation.
- After MRI postprocessing, probable epileptogenic lesions were identified in 53.2% (n = 25) of patients with TEs.
- The BMI distribution of patients with TEs did not differ from the one expected according to the BMI distribution of the German population.

2 | METHODS

2.1 | Study design and clinical data

A total of 47 patients with epilepsy and radiologically diagnosed TEs were retrospectively reviewed for coexisting structural epileptogenic lesions. Twenty-four patients were treated at the Epilepsy Center Hessen in Marburg, Germany, between 2008 and 2021, and 23 epilepsy patients were treated at the Epilepsy Center Frankfurt Rhine-Main in Frankfurt am Main, Germany, between 2011 and 2020. Four patients were initially excluded due to not having a three-dimensional (3D) T1-weighted MRI scan, which was the minimum requirement for the postprocessing analysis presented below. The patient's epilepsy syndrome was determined by experienced epileptologists from each center during the presurgical assessment.[26] The majority of TEs were identified after the completion of the patients' presurgical evaluation during previous studies of our centers.[12,20] Consequently, in some cases, the decision of the surgical approach was not influenced by the identification of TEs. Moreover, to minimize methodical biases, we followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines.[27] The study was approved by the local ethics committee.

2.2 | Imaging

All patients underwent either 1.5 or 3T MRI imaging at the Epilepsy Center Hessen in Marburg, Germany, at the Epilepsy Center Frankfurt Rhine-Main in Frankfurt am Main, Germany, or at external departments of radiology between 2008 and 2021. As all MRI scans were acquired for clinical purposes, different MRI scanners were used. All patients included in this study had a 3D T1-weighted scan, a coronal cube fluid-attenuated inversion recovery (FLAIR), and an axial diffusion sequence. The initial MRI findings were reported by experienced neuroradiologists from each center.

2.3 | MRI postprocessing

The Morphometric Analysis Program (v2018, MAP18)[28,29] was used to postprocess MRI data to facilitate the

detection of malformations of cortical development such as focal cortical dysplasia (FCD). This software uses as input conventional MRI data and enables the visualization of FCD by analyzing the gray-white matter junction, the extension of the gray matter, and cortical thickness after comparing them with a control MR database.[29] All 47 3D T1-weighted structural MRI scans were validated by using the fully automated MAP18 running in MATLAB version R2020b (MathWorks).[28,29] The full processing pipeline was used to create 3D morphometric maps, including "extension image," "junction image," and "thickness image." The largest average from all 1.5 and 3T scanner T1-weighted images for children and adults was selected as the normal database for the analysis. The FCD probability map was used to evaluate probable coexisting FCD. This method is based on an artificial neural network using as input a 3D T1-weighted MRI scan and is estimated to detect FCD automatically with a sensitivity of 81.0% at a specificity of 84.3%.[30] The result maps of the analysis were visually inspected to identify lesions other than malformations of cortical development. In those cases, the results of MAP18 were considered as false positive for identifying FCD.

2.4 | Statistical analysis

Continuous variables are presented as median (range), and categorical variables are presented as proportions. The distribution of patients across three different BMI groups was compared with the expected distribution based on population findings (BMI > 30 kg/m^2 = 21, 29%; BMI between 25 and 30 kg/m^2 = 35, 24%; BMI < 25 kg/m^2 = 43, 46%)[31] using the chi-square test. Quantitative variables were compared using the Student's *t* test. Wilson's 95% confidence intervals (CIs) were computed for the frequencies of the identified epileptogenic lesions in the initial MRI findings. All reported *P* values are based on two-sided tests; the level of statistical significance was set at $\alpha = 0.05$. Analyses were performed with SPSS Statistics 23.0.

2.5 | Definitions

During the presurgical evaluation, experienced epileptologists of each center had characterized the epilepsy syndrome according to the seizure semiology and interictal and ictal electroencephalographical data. All identified lesions known to cause epilepsy, including TEs, were considered "probably epileptogenic" if they appeared ipsilateral to the assumed epileptogenic zone (EZ) or if they were identified in patients with unclarified epilepsy syndromes. Developmental venous anomalies (DVAs) were not considered epileptogenic because there was no MRI evidence of their association with other malformations of cortical development or any evidence of DVA complications, which are the two main suggested reasons why DVAs are supposed to cause epilepsy.[32] Moreover, hydrocephalus was not considered a structural cause of epilepsy. Acquired lesions after the epilepsy onset were also not considered epileptogenic. FCD was identified on MRI if the following characteristics were shown: cortical thickening or thinning, blurring of the gray-white junction, abnormal sulcal or gyral pattern, local atrophy, transmantle sign or increased signal areas on T2- and FLAIR-weighted images.[31,33] As mentioned above, the FCD probability map was considered positive only in cases of suspicion of malformations of cortical development.

3 | RESULTS

3.1 | Study population, demographics, and clinical characteristics

A total of 47 patients with epilepsy (38.3% female, n = 18) and already identified TEs were included in this study. The median age at the time of the MRI scan was 40 years (range 12-81 years). All patients were diagnosed with focal epilepsy, 63.8% (n = 30) were diagnosed with TLE, 12.8% (n = 6) with extratemporal lobe epilepsy (ETLE), 8.5% (n = 4) with multifocal epilepsy, 12.8% (n = 6) with unclarified focal epilepsy, and 2.1% (n = 1) with both generalized epilepsy and TLE. The median BMI was 26 kg/m^2 (n = 45, range 17.30-49.80); this measure was available in 45 out of 47 patients. Specifically, 28.9% (n = 13) of the patients were obese (BMI > 30 kg/m^2), 28.9% (n = 13) had a BMI between 25 and 30 kg/m^2, and 42.2% (n = 19) had a BMI < 25 kg/m^2. The BMI distribution did not differ compared with the distribution expected for the German population ($P = .898$).[34]

Concerning the TE etiology, there were three patients with suggested secondary TEs: one patient had a positive history of infection (Table 1, case 25) and two had a positive history of trauma (Table 1, cases 44 and 45), while one had a positive history of trauma after epilepsy onset (Table 1, case 28). In this case, trauma was not considered the etiology of the TE. Moreover, one patient was diagnosed with idiopathic intracranial hypertension (Table 1, case 39) and one had an empty sella finding on MRI without clinical symptoms of benign intracranial hypertension (Table 1, case 40). Thus, in the majority of the patients, there was no recognizable acquired etiology for the TE, suggesting a congenital etiology.

TABLE 1 Overview of patient demographics and clinical and imaging findings

Case #	BMI (kg/m^2)	Age at MRI scan (years)	Epilepsy syndrome	# of TE/localization	History of trauma/ inflammation/ intracranial hypertension (yes/ no)	MRI findings other than TEs	Suspicion of FCD-MAP18 FCD MAP (p/n)/ localization	Epilepsy surgery (yes/no)/outcome/ TE removed (yes/no)	TE removed (yes/ no)/histopathology
1	<25	Early 20s	TLE R	2/1 AT R and 1 AIT L	No	DVA L frontal lobe	p/bitemporal	No/—/—	No/—
2	<25	Late 20s	TLE L	1/AT L	No	No	n/—	No/—/—	No/—
3	<25	Late 20s	TLE L	1/AIT R	No	No	p/R occipital	No/—/—	No/—
4	>30	Late 20s	TLE L	1/AT L	No	No	n/—	STLE L/Engel IA/yes	Yes/mild gliosis
5	25-30	Late 30s	TLE L	1/AT L	No	HS L	p/R frontal lobe	AHE/Engel IIA/no	No/—
6	<25	Late 30s	TLE L	1/AT L	No	No	n/—	TE resection L/Engel IA/yes	Yes/gliosis with astrocytosis
7	25-30	Early 30s	TLE R	1/AIT R	No	No lesion	p/R temporal	TE resection R/Engel IB/yes	Yes/mild gliosis and arachnoidal cell proliferation
8	25-30	Late 50s	TLE L	2/1 AIT R and 1 ALT L	No	Glioblastoma WHO grad IV L temporal lobe	n/— (false positive for leukoencephalopathy)	Glioblastoma resection/follow-up data not available/ no	No/—
9	>30	Late 30s	TLE and PLE	1/AIT L	No	Oligodendroglioma WHO II parietal lobe and MS lesions	n/— (false positive for glioma L parietal lobe and MS lesions)	Oligodendroglioma WHO II resection/ Engel IIIA/no	No/—
10	<25	Early 50s	TLE R	1/AT R	No	Posttraumatic lesion parietal lobe	p/R frontal and bitemporal	No/—/—	No/—
11	>30	Late 40s	TLE R	1/ALT R	No	DVA L parietal lobe	n/— (false positive for DVA L parietal lobe)	No/—/—	No/—
12	<25	Early 10s	TLE R	1/AIT L	No	HS R	p/bifrontal and right temporal	STLE R/Engel IA/no	No/—
13	>30	Late 20s	TLE L	2/AT R and L	No	No lesion	n/—	No/—/—	No/—
14	25-30	Early 50s	TLE R and L	1/AT L	No	No lesion	n/—	No/—/—	No/—
15	<25	Early 20s	FLE R	1/AIT L	No	No lesion	p/bifrontal	No/—/—	No/—
16	25-30	Early 40s	PLE L	2/ALT R and AIT L	No	FCD L parietal lobe	p/left parietal	No/—/—	No/—
17	<25	Early 10s	FLE R or bilateral	1/AIT R	No	No lesion	p/right frontal	No/—/—	No/—
18	>30	Late 20s	PLE and TLE R	1/AL L	No	Double cortex	p/double cortex	No/—/—	No/—
19	>30	Early 40s	FLE	1/AIL L	No	FCD L frontal lobe	p/bifrontal	No/—/—	No/—
20	25-30	Early 20s	TLE L	1/AIT L	No	No lesion	p/L frontal lobe	No/—/—	No/—
21	<25	Early 20s	TLE R	1/AIT L	No	Nodular heterotopia bitemporal	p/bitemporal	No/—/—	No/—
22	<25	Late 20s	TLE	2/AIT bitemporal	No	No lesion	n/—	No/—/—	No/—
23	<25	Early 50s	FLE R and TLE R	2/AL bitemporal	No	No lesion	p/bifrontal	No/—/—	No/—
24	<25	Early 30s	FLE	1/AIT	No	FCD R frontal lobe	n/—	No/—/—	No/—

TABLE 1 (Continued)

Case #	BMI (kg/m^2)	Age at MRI scan (years)	Epilepsy syndrome	# of TE/localization	History of trauma/ inflammation/ intracranial hypertension (yes/ no)	MRI findings other than TEs	Suspicion of FCD-MAP18 FCD MAP (p/n)/ localization	Epilepsy surgery (yes/no)/outcome/ TE removed (yes/no)	TE removed (yes/ no)/histopathology
25	25-30	Early 7s	TLE L	3/1 AIT R, 1 AT R and 1 ALT L	Inflammatory bacterial meningitis	FCD L amygdala	p/bifrontal	No/—/—	No/—
26	25-30	Late 40s	TLE L	1/AIT L	No	FCD L amygdala	n/—	No/—/—	No/—
27	<25	Early 20s	TLE R	3/1 AIT R, 1 AIL and 1 AT L	No	No lesion	p/right frontal	STLE R/Engel IA/yes	Yes/mild gliosis
28	<25	Early 30s	Not clarified	1/AT L	Trauma after epilepsy onset	Posttraumatic hemorrhagic lesions frontobasal right, frontal left and bitemporal	n/— (false positive for right frontobasal posttraumatic lesions)	No/—/—	No/—
29	<25	Early 30s	Not clarified	1/AIT L	No	No other lesion	n/—	No/—/—	No/—
30	<25	Early 40s	TLE L	1/AIT L	No	DVA R frontal lobe	n/—	No/—/—	No/—
31	25-30	Early 30s	FLE L	1/AIT L	No	No lesion	p/left frontal	No/—/—	No/—
32	25-30	Late 60s	Not clarified	2/1 AIT R and 1 AIT L	No	Hydrocephalus	n/—	No/—/—	No/—
33	>30	Early 50s	TLE L and R	2/1 AIT R and 1 AIT L	No	No other lesion	n/—	STLE L/Engel IIA/yes	Yes/glial and neuronal cell elements, partial neuronal hypoxic cell damage with a shrunken cell body, eosinophilic cytoplasm, and pyknotic nuclei
34	<25	Early 80s	Not clarified	2/1 ATL and 1 ATR	No	Postischemic lesion L frontal	n/—	No/—/—	No/—
35	>30	Late 40s	Not clarified	1/AT R	No	No lesion	n/—	No/—/—	No/—
36	>30	Early 60s	TLE R	1/AIT R	No	FCD R mesiotemporal	n/—	No/—/—	No/—
37	25-30	Late 40s	Generalized and TLE left	1/AIT L	No	No lesion	n/—	No/—/—	No/—
38	–	Early 60s	TLE L	2/ 1 ALT and 1 AIT L	No	HS L	n/—	No/—/—	No/—
39	>30	Early 40s	TLE R	2/1 AIT L and 1 AIL R	Idiopathic intracranial hypertension	Epidermoid Cyst L temporal	n/—	No/—/—	No/—
40	–	Early 40s	TLE L	2/1 AT L and 1 AT R	No	No lesion/empty sella	n/—	No/—/—	No/—
41	25-30	Early 40s	OLE	1/AIT R	No	Postischemic lesions bi-occipital	p/left frontal	No/—/—	No/—

(Continues)

TABLE 1 (Continued)

Case #	BMI (kg/m^2)	Age at MRI scan (years)	Epilepsy syndrome	# of TE/localization	History of trauma/ inflammation/ intracranial hypertension (yes/ no)	MRI findings other than TEs	Suspicion of FCD-MAP18 FCD MAP (p/n)/ localization	Epilepsy surgery (yes/no)/outcome/ TE removed (yes/no)	TE removed (yes/ no)/histopathology
42	<25	Early 50s	TLE bds	1/AT L	No	No lesion	n/–	No/–/–	No/–
43	>30	Late 30s	TLE R	2/ 1 AIT R and 1 AT R	No	No lesion	n/–	STLE R without hippocampectomy/ Engel IB /yes	Yes/brain tissue with hypoxic cell damage and heterotopic white matter neurons.
44	25-30	Early 50s	TLE L	1/AIT L	Trauma by meningioma resection and radiotherapy	Osteoma and meningioma L parieto-temporo-occipital	n/–	Meningioma resection/ Engel IIC/no	No/–
45	>30	Late 30s	TLE R	2/ 2 AIT L	Trauma	Posttraumatic lesions bitemporal and R frontobasal	n/– (false positive for posttraumatic lesions)	No/–/–	No/–
46	>30	Early 40s	TLE L	1/AT L	No	No lesion	n/–	STLE L/Engel IIA/yes	Yes/brain tissue with fibrous elements
47	<25	Early 40s	Not clarified	2/1 AT L and 1 AT R	No	DVA L temporal lobe	n/–	No/–/–	No/–

Abbreviations: AHE, amygdalohippocampectomy; AIL, anterior inferior lateral; AIT, anterior inferior temporal; ALT, anterior lateral temporal; AT, anterior temporal; BMI, Body Mass Index; DVA, developmental venous anomaly; ETLE, extratemporal lobe epilepsy; FLE, frontal lobe epilepsy; HS, hippocampal sclerosis; L, left; LE, lesionectomy; MS, multiple sclerosis; OLE, occipital lobe epilepsy; PLE, parietal lobe epilepsy; R, right; SF, seizure- free; STLE, standard temporal lobectomy; TE, temporal encephalocele; TLE, temporal lobe epilepsy.

3.2 | Initial imaging findings

After visual reading, in 21 out of 47 MRI scans (44.7%, 95% CI 30.2%-59.9%) of the patients with TEs, there were initially other lesions reported as follows: hippocampal sclerosis in 6.4% (n = 3), malformations of cortical development in 17.0% (n = 8), tumors in 8.5% (n = 4), and other acquired lesions such as traumatic or ischemic lesions in 12.8% (n = 6). In 38.3% (n = 18) of the cases; the identified MRI lesion was concordant with the assumed EZ. As stated in section 2.5, DVAs were not considered potentially epileptogenic; they were identified in 8.5% (n = 4) of patients of the study population. TEs were ipsilateral to the assumed EZ in 72.3% (n = 34) of the patients. Bilateral TEs were identified in 27.7% (n = 13) of the patients. There were no statistically significant differences in BMI between patients with unilateral and bilateral TEs ($P = .972$). In 51.1% (n = 24) of the patients, TEs were the only lesion suspected to cause seizures, while in 21.3% (n = 10) of the patients, TEs and other MRI lesions were equally considered as probably epileptogenic. In 17.0% (n = 8) of the patients, the identified MRI lesion was the only assumed structural cause of epilepsy, and in 10.6% (n = 5) of the patients, neither TE nor any other lesion was concordant with the EZ.

3.3 | Postprocessing findings

Overall, 38.3% (n = 18) of 3D T1-weighted structural MRI scans showed a positive FCD probability map, 51.1% (n = 24) were negative, and 10.6% (n = 5) were considered false positives for identifying FCD after visual inspection of the results. The FCD probability map was false positive in one patient for periventricular leukoencephalopathy (Table 1, case 8), in one patient with multiple sclerosis lesions and glioma of the left parietal lobe (Table 1, case 9), in one patient for a DVA (Table 1, case 11), and in two patients for posttraumatic lesions (Table 1, cases 28 and 45). In 25.5% (n = 12) of the patients, those findings were concordant with the assumed EZ and in 12.8% (n = 6) of the patients not concordant with the EZ. Overall, considering both the initial MRI findings and the results of the MAP18 analysis, in 53.2% (n = 25) of the patients, there were lesions other than TEs and they were considered as the probable cause of structural epilepsy. In 10.6% (n = 5) of the patients, the lesions identified in both MRI and MAP18 analysis were not in accordance with the assumed EZ, and in 36.2% (n = 17) of the patients, there were no other lesions identified except for the TE. After evaluating all structural lesions identified and the TEs with the findings of the presurgical evaluation, TEs were the only probable epileptogenic lesion in 42.6% (n = 20) of the patients, while the other structural lesions were the only probable structural cause in 27.7% (n = 13) of the patients. Both TEs and lesions identified based on MRI and MAP18 analysis could be considered epileptogenic in 25.5% (n = 12) of the patients. Finally, in 4.3% (n = 2) of the patients, none of the imaging findings matched with the other results of the presurgical evaluation. Representative images of the above-mentioned results are presented in Figures 1 and 2.

3.4 | Epilepsy surgery-related data

Overall, 25.5% (n = 12) of the patients were surgically treated because of refractory epilepsy. In 58.3% (n = 7) of those patients, the TE was removed and was in all cases concordant with the assumed EZ without any other structural lesions found on the initial MRI evaluation (Table 1, cases 4, 6, 7, 27, 33, 43, and 46). Three patients remained seizure-free after surgery (Engel IA): one after TE resection without removing the hippocampus (Table 1, case 6) and two after a standard temporal lobectomy (STLE) including hippocampal resection (Table 1, cases 4 and 27) after a median follow-up of 60 months (range 24-96). MAP18 analysis was negative for cases 4 and 6 (Table 1), while, in case 27, FCD probability map was positive but not concordant with the EZ (Table 1). Two patients had isolated auras after surgery (Engel IB): one after right TE resection (Table 1, case 7), with a positive FCD probability map of the right temporal lobe, and one after right STLE excluding hippocampus (Table 1, case 43), with a negative FCD probability map. Moreover, two patients had rare disabling seizures (Engel IIA) after STLE, including hippocampal resection (Table 1, cases 33 and 46). In both of those cases, there were no other lesions identified in the postprocessing analysis. The histopathological findings of the removed TEs showed only gliosis and no other pathologies. In one case, heterotopic white matter neurons were identified additionally to the gliosis (Table 1, case 43). The detailed histopathological findings of the removed TEs are presented in Table 1.

For the other surgically treated patients, 41.7% (n = 5) of the patients were surgically treated for other lesions identified on the initial MRI evaluation without removing the TE (Table 1, cases 5, 8, 9, 12, and 44). One patient remained seizure-free (Engel IA) after undergoing a right STLE because of hippocampal sclerosis contralateral to the identified TE, which was not considered epileptogenic. In this patient, the FCD probability map was positive in the frontal lobes bilaterally as well as in the right temporal lobe, which was removed surgically as well by the right STLE (Table 1, case 12). One patient underwent a selective amygdalohippocampectomy of left hippocampal sclerosis without removing the TE and experienced rare seizures after surgery (Engel IIA), with a follow-up of

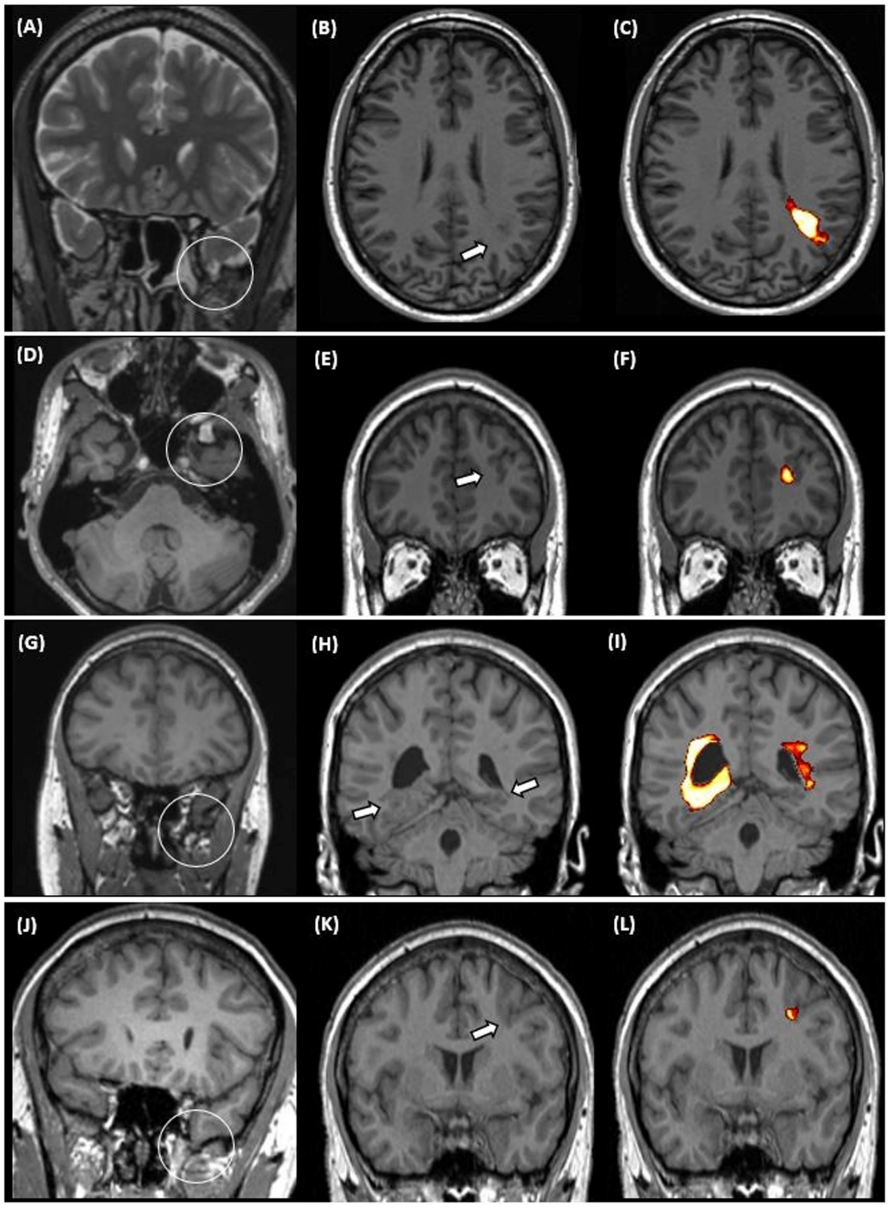

FIGURE 1 Representative images of patients with temporal encephaloceles (TEs) and malformations of cortical development. A, Coronal T2-weighted magnetic resonance imaging (MRI) sequence showing a left (L) TE, B, axial T1-weighted MRI with transmantle dysplasia of the L parietal lobe and C, axial representation of the positive focal cortical dysplasia (FCD) probability map of a patient with extratemporal lobe epilepsy (ETLE) (Table 1, Patient 16). D, Axial T1-weighted MRI sequence representing a L TE, E, coronal T1-weighted MRI sequence with abnormal sulcal pattern and blurring of the L frontal lobe and F, coronal representation of the positive FCD probability MAP of a patient with TLE L and ipsilateral TE (Table 1, Patient 20). G, Coronal T1-weighted MRI with L TE, H, coronal T1-weighted MRI sequence showing bitemporal nodular heterotopia and I, coronal representation of the positive FCD probability map of a patient with right (R) TLE and L TE (Table 1, Patient 21). J, Coronal T1-weighted MRI sequence representing a L TE, K, coronal T1-weighted MRI sequence representing cortical thickening of L frontal lobe and L, coronal representation of the positive FCD probability map of a patient with ETLE (Table 1, Patient 31). FCD, focal cortical dysplasia; L, left; R, right; TE, temporal encephalocele; TLE, temporal lobe epilepsy

60 months (Table 1, case 5). Finally, three other patients were surgically treated because of tumors—two due to gliomas and one due to meningioma—which were considered the most probable epileptogenic lesions. For one patient, there were no follow-up data available (Table 1, case 8), while the other two had seizures after surgery (Table 1, Engel IIIA for case 9 and Engel IIC for case 44).

4 | DISCUSSION

Temporal encephaloceles have been discussed as subtle, potentially epileptogenic lesions that are usually missed in patients with MRI-negative TLE.[14,17,21] However, in our study, 44.7% of the patients with known TEs presented initially positive MRI findings other than TEs, which exceeds

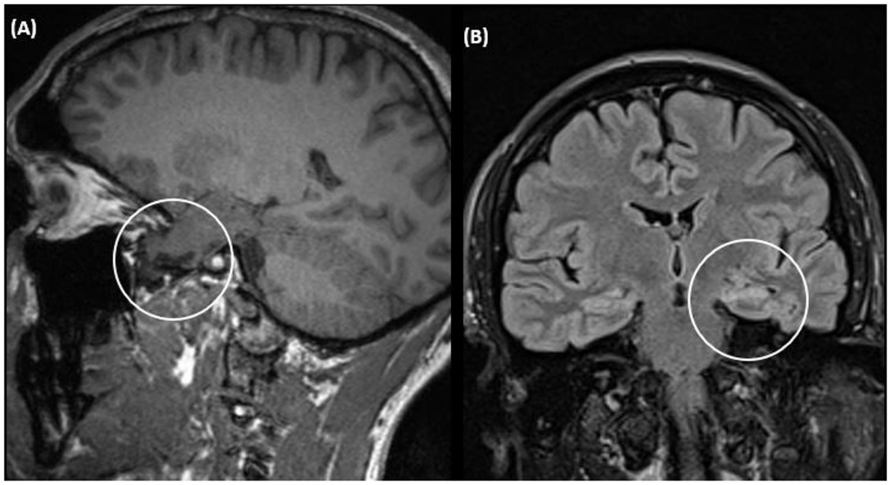

FIGURE 2 A, Sagittal T1-weighted image with a left temporal encephalocele and B, coronal flair with ipsilateral hippocampal sclerosis of a patient with left temporal lobe epilepsy (Table 1, Patient 5)

the expected 2.4% of incidental findings in the healthy population[35] as well as the 25% of identified epileptogenic lesions in patients with an initial diagnosis of epilepsy.[36] In 38.3% of the patients, those lesions were concordant with the assumed EZ. After evaluating the postprocessing results, 53.2% of the patients had positive imaging findings other than TEs that were considered as a potential epileptogenic lesion. The initial MRI reports showed epileptogenic lesions concurrent with the TE in 21.3% (n = 10) of the patients and in 25.5% (n = 12) of the patients after the postprocessing analysis. The above results suggest the importance of increased awareness for identifying TEs in lesional epilepsy, as they might also be associated with other epileptogenic lesions and might even be an indicator for dual pathologies.

Dual structural pathologies may influence the decision process for finding the most appropriate surgical therapy and are one of the main reasons of epilepsy surgery failure.[37] Such coexisting pathologies have already been reported in neuroimaging and histopathological findings of patients with TEs, with the most etiologically interesting being the coexistence with malformations of cortical development.[4,6,13,14,18,21–23] In our study population, hippocampal sclerosis was found in 6.4% (n = 3) of the patients, while malformations of cortical development were radiologically reported in 17.0% (n = 8) of the patients and in 38.3% (n = 18) of the patients after the postprocessing analysis. Although the pathomechanism remains poorly understood, this may indicate a common underlying developmental etiology of both congenital TEs and malformations of cortical development during embryogenesis.

Dual pathologies have been reported in histopathological findings in previous case series and have shown the coexistence of TEs with heterotopia and malformations of cortical development.[4,21,22,38] In this study population, histopathology showed heterotopic white matter neurons in one patient (Table 1, case 43), while gliosis has been found in most cases. Gliosis around the TE has been described in the majority of reported histopathological findings of epilepsy patients in the literature.[7,14,22,39] Similarly, in case series of patients without epilepsy, histopathology has shown neuroglial tissue covered by leptomeninges, large astrocytes and in some cases chronic inflammation and fibrous tissue.[40,41] Nevertheless, the common histopathological findings of TEs in patients with and without epilepsy complicate the understanding of the TE epileptogenesis and indicate the need for further histopathology studies to provide insight into the pathomechanisms of these lesions.

Concerning the TE etiology of this cohort, most of the patients did not have a known history of a secondary TE, such as trauma and infection, or clinical and imaging findings of intracranial hypertension, such as empty sella. Furthermore, although increased BMI is known to be associated with TEs,[4,5,42,43] the BMI distribution across groups in our study population did not differ from the one expected according to the BMI distribution of the German population.[34] Although epilepsy patients have been reported to have higher BMI than the general population,[44] this was not the case in the current study population, as mentioned above. Those findings suggest that the majority of the TEs had a congenital etiology.

Generally, surgical treatment of patients with TE and drug-resistant epilepsy seems to be beneficial in refractory TLE regardless of the surgical approach.[39] In line with the literature, the surgically treated patients of our study population showed an improved seizure outcome either after TE lesionectomy or after STLE, excluding or including mesiotemporal structures (Table 1, cases 4, 6, 7, 27, 33, 43, and 46). None of the patients surgically treated for TEs showed other coexisting structural pathologies on the initial MRI evaluation. In such cases, further invasive electroencephalographic evaluation may be necessary in order to avoid unnecessary resections, because TEs are not always epileptogenic.

The present study has certain limitations, mostly due to its retrospective nature. For this reason, we followed the STROBE guidelines to minimize methodical biases.[27] Moreover, we based this study on imaging findings and postprocessing MRI analysis to identify epileptogenic lesions. Despite the high estimated sensitivity and specificity of the FCD probability map, it is a complementary method for evaluating MRI scans during the presurgical evaluation, probably leading to false positive results. Finally, although this is the largest reported cohort of patients with TEs, the sample size should be considered for the interpretation of statistical results.

5 | CONCLUSION

The presence of TEs should be considered not only in MRI-negative epilepsy, but also in lesional epilepsy. In refractory patients, the decision for further evaluation with invasive electroencephalographic techniques or for the most appropriate surgical method should be made highly individualized. Furthermore, the association of TEs with malformations of cortical development may suggest a common developmental and genetic etiology of those lesions. TEs might even be an indicator for dual pathologies, MRIs should, therefore, be inspected carefully, and semiautomated morphometric analysis tools may be used to exclude further lesions in this patient population in order to achieve the best postsurgical outcome. Genetic studies of patients with TEs might help to better understand the pathomechanism of those lesions. Finally, TEs occur in patients with normal BMI and they should not be underestimated in those patients.

AUTHOR CONTRIBUTIONS

Panagiota-Eleni Tsalouchidou involved in study concept and design, data analysis and interpretation, statistical analysis, and manuscript writing and revision. Johann Philipp Zoellner played a major role in data acquisition and interpretation and manuscript revision. Annika Kirscht played a major role in data acquisition and interpretation. Christina Julia Mueller and Georgios Chatzis involved in data interpretation, statistical analysis, and manuscript revision. Christopher Nimsky played a major role in data acquisition and manuscript revision. Maximilian Schulze, Elke Hattingen, and Felix Rosenow played a major role in data acquisition, analysis, and interpretation. Thomas M. Freiman involved in study concept and design and manuscript revision. Adam Strzelczyk, Sven Fuest, and Katja Menzler played a major role in data acquisition and manuscript revision. Susanne Knake involved in study concept and design and played a major role in data acquisition, analysis and interpretation, and manuscript revision.

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CONFLICT OF INTEREST

Christopher Nimsky is a scientific consultant for Brainlab. Adam Strzelczyk reports personal fees and grants from Angelini Pharma/Arvelle Therapeutics, Desitin Arzneimittel, Eisai, GW Pharmaceuticals, Marinus Pharma, Medtronic, UCB, UNEEG Medical, and Zogenix. All other authors have no conflict of interest to disclose with respect to this study.

DATA AVAILABILITY STATEMENT

Anonymized data will be shared with any qualified investigator upon request.

ETHICAL APPROVAL

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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REFERENCES

1. Siffel C, Wong LYC, Olney RS, Correa A. Survival of infants diagnosed with encephalocele in Atlanta, 1979-98. Paediatr Perinat Epidemiol. 2003;17(1):40–8.
2. Copp AJ, Greene NDE. Neural tube defects-disorders of neurulation and related embryonic processes. Wiley Interdiscip Rev Dev Biol. 2013;2(2):213–27.
3. Alonso RC, de la Peña MJ, Caicoya AG, Rodriguez MR, Moreno EA, de Vega Fernandez VM. Spontaneous Skull Base Meningoencephaloceles and cerebrospinal fluid fistulas. Radiographics [Internet]. 2013;33(2):553–70. https://doi.org/10.1148/rg.332125028
4. Urbach H, Jamneala G, Mader I, Egger K, Yang S, Altenmüller D. Temporal lobe epilepsy due to meningoencephaloceles into the greater sphenoid wing: a consequence of idiopathic intracranial hypertension? Neuroradiology. 2018;60(1):51–60.
5. Wind JJ, Caputy AJ, Roberti F. Spontaneous encephaloceles of the temporal lobe. Neurosurg Focus. 2008;25(6):E11.
6. Byrne RW, Smith AP, Roh D, Kanner A. Occult middle fossa encephaloceles in patients with temporal lobe epilepsy. World Neurosurg [Internet]. 2010;73(5):541–6. https://doi.org/10.1016/j.wneu.2010.01.018

7. Abou-Hamden A, Lau M, Fabinyi G, Berkovic SF, Jackson GD, Anne Mitchell L, et al. Small temporal pole encephaloceles: a treatable cause of "lesion negative" temporal lobe epilepsy. Epilepsia. 2010;51(10):2199–202.
8. Martinez-Poles J, Toledano R, Jiménez-Huete A, García-Morales I, Aledo-Serrano Á, Anciones C, et al. Epilepsy associated with temporal pole Encephaloceles: an unrecognized manifestation of idiopathic intracranial hypertension? Clin Neuroradiol. 2021;31(3):575–9.
9. Manjubashini D, Kiran M, Akshaya S, Nagarajan K. Intrasphenoidal Encephalocele with spontaneous cerebrospinal fluid rhinorrhea in idiopathic intracranial hypertension: need for clarity in terminology and imaging delineation. World Neurosurg [Internet]. 2019;132:129–33. https://doi.org/10.1016/j.wneu.2019.08.186
10. Morone PJ, Neimat JS, Weaver KD, Wanna GB, Sweeney AD, Carlson ML, et al. Temporal lobe encephaloceles: a potentially curable cause of seizures. Otol Neurotol. 2015;36(8):1439–42.
11. Fountas KN, Smith JR, Jenkins PD, Murro AM. Spontaneous motor cortex encephalocele presenting with simple partial seizures and progressive hemiparesis. Case report and review of the literature. Neurosurg Focus. 2005;19:E10.
12. Paule E, Freiman TM, Strzelczyk A, Reif PS, Willems LM, Wagner M, et al. Characteristics of bilateral versus unilateral temporal encephalocele-associated epilepsy. Seizure. 2019;71:13–9.
13. Aquilina K, Clarke DF, Whless JW, Boop FA. Microencephaloceles: another dual pathology of intractable temporal lobe epilepsy in childhood. J Neurosurg Pediatr. 2010;5(4):360–4.
14. Saavalainen T, Jutila L, Mervaala E, Kälviäinen R, Vanninen R, Immonen A. Temporal anteroinferior encephalocele. Neurology. 2015;85(17):1467–74.
15. Wilkins RH, Radtke RA, Burger PC. Spontaneous temporal encephalocele. Case report. J Neurosurg. 1993;78(3):492–8.
16. Gasparini S, Ferlazzo E, Pustorino G, Ascoli M, Cianci V, Sueri C, et al. Epileptogenic role of occult temporal encephalomeningocele. Neurology. 2018;90(14):1–4.
17. Campbell ZM, Hyer JM, Lauzon S, Bonilha L, Spampinato MV, Yazdani M. Detection and characteristics of temporal encephaloceles in patients with refractory epilepsy. Am J Neuroradiol. 2018;39(8):1468–72.
18. Faulkner HJ, Sandeman DR, Love S, Likeman MJ, Nunez DA, Lhatoo SD. Epilepsy surgery for refractory epilepsy due to encephalocele: a case report and review of the literature. Epileptic Disord. 2010;12:160–6.
19. Shimada S, Kunii N, Kawai K, Usami K, Matsuo T, Uno T, et al. Spontaneous temporal pole encephalocele presenting with epilepsy: report of two cases. World Neurosurg [Internet]. 2015;84(3):867.e1–6. https://doi.org/10.1016/j.wneu.2015.04.028
20. Tsalouchidou PE, Mintziras I, Biermann L, Krause K, Bergmann MP, Belke M, et al. Temporal encephaloceles in epilepsy patients and asymptomatic cases: size may indicate epileptogenicity. Epilepsia. 2021;62(6):1354–61.
21. Toledano R, Jiménez-Huete A, Campo P, Poch C, García-Morales I, Gómez Angulo JC, et al. Small temporal pole encephalocele: a hidden cause of "normal" MRI temporal lobe epilepsy. Epilepsia. 2016;57(5):841–51.
22. Panov F, Li Y, Chang EF, Knowlton R, Cornes SB. Epilepsy with temporal encephalocele: characteristics of electrocorticography and surgical outcome. Epilepsia. 2016;57(2):e33–8.
23. Bannout F, Harder S, Lee M, Zouros A, Raghavan R, Fogel T, et al. Brain sciences epilepsy surgery for skull-base temporal lobe encephaloceles: should we spare the hippocampus from resection? Brain Sci. 2018;8:42.
24. Lo BWY, Kulkarni AV, Rutka JT, Jea A, Drake JM, Lamberti-Pasculli M, et al. Clinical predictors of developmental outcome in patients with cephaloceles: clinical article. J Neurosurg Pediatr. 2008;2(4):254–7.
25. Benson JC, Lane J, Geske JR, Gompel JV, Krecke KN. Prevalence of asymptomatic middle cranial fossa floor pits and encephaloceles on MR imaging. Am J Neuroradiol. 2019;40(12):2090–3.
26. Rosenow F, Bast T, Czech T, Feucht M, Hans VH, Helmstaedter C, et al. Revised version of quality guidelines for presurgical epilepsy evaluation and surgical epilepsy therapy issued by the Austrian, German, and Swiss working group on presurgical epilepsy diagnosis and operative epilepsy treatment. Epilepsia. 2016;57(8):1215–20.
27. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. Int J Surg [Internet]. 2014;12(12):1495–9. https://doi.org/10.1016/j.ijsu.2014.07.013
28. Wagner J, Weber B, Urbach H, Elger CE, Huppertz HJ. Morphometric MRI analysis improves detection of focal cortical dysplasia type II. Brain. 2011;134(10):2844–54.
29. Huppertz HJ, Grimm C, Fauser S, Kassubek J, Mader I, Hochmuth A, et al. Enhanced visualization of blurred gray-white matter junctions in focal cortical dysplasia by voxel-based 3D MRI analysis. Epilepsy Res. 2005;67(1–2):35–50.
30. David B, Kröll-Seger J, Schuch F, Wagner J, Wellmer J, Woermann F, et al. External validation of automated focal cortical dysplasia detection using morphometric analysis. Epilepsia. 2021;62(4):1005–21.
31. Kabat J, Król P. Focal cortical dysplasia - review. Polish J Radiol. 2012;77(2):35–43.
32. Dussaule C, Masnou P, Nasser G, Archambaud F, Cauquil-Michon C, Gagnepain JP, et al. Can developmental venous anomalies cause seizures? J Neurol. 2017;264(12):2495–505.
33. Colombo N, Tassi L, Galli C, Citterio A, Lo Russo G, Scialfa G, et al. Focal cortical dysplasias: MR imaging, histopathologic, and clinical correlations in surgically treated patients with epilepsy. Am J Neuroradiol. 2003;24(4):724–33.
34. Dibonaventura M, Nicolucci A, Meincke H, Le LA, Fournier J. Obesity in Germany and Italy: prevalence, comorbidities, and associations with patient outcomes. Clinicoecon Outcomes Res. 2018;10:457–75.
35. Morris Z, Whiteley WN, Longstreth WT, Weber F, Lee YC, Tsushima Y, et al. Incidental findings on brain magnetic resonance imaging: systematic review and meta-analysis. BMJ (Online). 2009;339(7720):547–50.
36. Salmenperä T, Könönen M, Roberts N, Vanninen R, Pitkänen A, Kälviäinen R. Hippocampal damage in newly diagnosed focal epilepsy: a prospective MRI study. Neurology. 2005;64(1):62–8.
37. Harroud A, Bouthillier A, Weil AG, Nguyen DK. Temporal lobe epilepsy surgery failures: a review. Epilepsy Res Treat. 2012;2012:1–10.
38. de Souza JPSAS, Mullin J, Wathen C, Bulacio J, Chauvel P, Jehi L, et al. The usefulness of stereo-electroencephalography (SEEG) in the surgical management of focal epilepsy associated

with "hidden" temporal pole encephalocele: a case report and literature review. Neurosurg Rev. 2017;41(1):347–54.
39. Ramos-Fresnedo A, Domingo RA, McGeary RC, Sirven JI, Feyissa AM, Tatum W, et al. Encephalocele-associated drug-resistant epilepsy of adult onset: diagnosis, management, and outcomes. World Neurosurg [Internet]. 2021;151:91–101. https://doi.org/10.1016/j.wneu.2021.04.121
40. Martinez-Lage JF, Sola J, Casas C, Poza M, Almagro MJ, Girona DG. Atretic cephalocele: the tip of the iceberg. J Neurosurg. 1992;77(2):230–5.
41. Xue L, Gehong D, Ying W, Jianhua T, Hong Z, Honggang L. Annals of diagnostic pathology nasal meningoencephalocele: a retrospective study of clinicopathological features and diagnosis of 16 patients. Ann Diagn Pathol [Internet]. 2020;49:151594. https://doi.org/10.1016/j.anndiagpath.2020.151594
42. Woodworth BA, Prince A, Chiu AG, Cohen NA, Schlosser RJ, Bolger WE, et al. Spontaneous CSF leaks: a paradigm for definitive repair and management of intracranial hypertension. Otolaryngol Head Neck Surg [Internet]. 2008;138(6):715–20. https://doi.org/10.1016/j.otohns.2008.02.010
43. Grinblat G, Dandinarasaiah M, Prasad SC, Piras G, Piccirillo E, Fulcheri A, et al. Temporal bone Meningo-encephalic-herniation: etiological categorization and surgical strategy. Otol Neurotol. 2018;39(3):320–2.
44. Steinhoff BJ, Neusüss K, Thegeder H, Reimers CD. Leisure time activity and physical fitness in patients with epilepsy. Epilepsia. 1996;37(12):1221–7.

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