ABSTRACT

BACKGROUND AND PURPOSE: Temporal encephaloceles are increasingly visualized during neuroimaging assessment of individuals with refractory temporal lobe epilepsy, and their identification could indicate an intracranial abnormality that may be related to a potential seizure focus. Careful review by an experienced neuroradiologist may yield improved detection of TEs, and other clinical, neurophysiologic, and radiologic findings may predict their presence.

MATERIALS AND METHODS: Data were reviewed retrospectively in patients at our institution who were presented at a multidisciplinary conference for refractory epilepsy between January 1, 2010, and December 31, 2016. Clinical, neurophysiologic, and imaging data were collected. An expert neuroradiologist reviewed the latest MR imaging of the brain in patients for whom one was available, noting the presence or absence of temporal encephaloceles as well as other associated imaging characteristics.

RESULTS: A total of 434 patients were reviewed, 16 of whom were excluded due to unavailable or poor-quality MR imaging. Seven patients had temporal encephaloceles reported on initial imaging, while 52 patients had temporal encephaloceles identified on expert review. MR imaging findings were more often initially normal in patients with temporal encephaloceles (P < .001), and detection of temporal encephaloceles was increased in patients in whom 3T MR imaging was performed (P < .001), the T2 sampling perfection with application-optimized contrasts by using different flip angle evolutions sequence was used (P < .001), or the presence of radiologic findings suggestive of idiopathic intracranial hypertension was noted. Seizure onset by scalp electroencephalogram among patients with temporal encephaloceles was significantly more likely to be temporal compared with patients without temporal encephaloceles (P < .001). A significant correlation between intracranial electroencephalogram seizure onset and patients with temporal encephaloceles compared with patients without temporal encephaloceles was not observed, though there was a trend toward temporal-onset seizures in patients with temporal encephaloceles (P = .06).

CONCLUSIONS: Careful review of MR imaging in patients with refractory temporal lobe epilepsy by a board-certified neuroradiologist with special attention paid to a high-resolution T2 sequence can increase the detection of subtle temporal encephaloceles, and certain clinical and neurophysiologic findings should raise the suspicion for their presence.

ABBREVIATIONS: EEG = electroencephalogram; RTLE = refractory temporal lobe epilepsy; SPACE = sampling perfection with application-optimized contrasts by using different flip angle evolutions; TE = temporal encephalocele

Temporal encephaloceles (TEs) are herniations of the brain parenchyma through the dura mater and skull that involve the temporal lobe, typically the anteroinferior aspect. Although spontaneous TEs are thought to be rare, the true prevalence is likely higher than recognized. Nevertheless, the true prevalence of small TEs remains largely unknown because they could be easily overlooked on standard imaging techniques. The literature has predominantly focused on CSF leaks in TEs, and only 27 cases of temporal lobe epilepsy involving encephaloceles were published before 2015. Since that time, a recent increase in cases of TEs in patients with refractory epilepsy has been observed. The prevalence of TEs among the largest case series has been 2%–4% of drug-resistant patients referred for epilepsy surgery evaluation, and TEs have been present in nearly 10% of patients with refractory temporal lobe epilepsy (RTLE), which have also accounted for 10% of surgical resections at some institutions. Furthermore, it has been previously reported that 16%–31% of pa-

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Patients with RTLE do not have a clearly identified lesion on routine MR imaging,18,19 and TEs have been observed more frequently in patients with RTLE who had previously normal MR imaging findings.16 Despite the increasing awareness of TEs in patients with refractory epilepsy, the rate at which TEs are overlooked in patients with RTLE remains unknown. We hypothesized that a substantial number of patients with RTLE have TEs that were not being reported on initial MR imaging interpretation and that careful review with special attention to a high-resolution T2 sequence may result in improved detection. We also suspected that other clinical, neurophysiologic, and radiologic factors would be associated with the presence of TEs and may provide radiologists and epileptologists with a greater index of suspicion so that careful scrutiny for TEs could be performed.

MATERIALS AND METHODS

The study was approved by the Medical University of South Carolina institutional review board and was compliant with the Health Insur-

FIG 1. A 43-year-old woman with refractory epilepsy, right temporal onset based on ictal scalp EEG. A, Axial T2 SPACE image shows right anterior temporal encephaloceles (white arrows). A partially empty sella turcica (B) and flattening of the globe at the insertion of the optic nerves (C) are also noted.

FIG 2. A 50-year-old woman with refractory epilepsy, left temporal onset based on ictal scalp EEG. A, Axial T2 SPACE image shows bilateral anterior temporal encephaloceles (white arrows) and enlarged Meckel caves. B, Coronal T2 SPACE image shows a cribriform plate meningocele.

MR Imaging Protocol

All patients underwent MR imaging on either a 1.5 Avanto or Aera or 3T Skyra or Verio (Siemens, Erlangen, Germany) system according to a protocol optimized for patients with epilepsy. The 3T epilepsy protocol was updated in the second half of 2013 to include sagittal T2 FLAIR (TI, 1800 ms; TE, 387 ms; TR, 5000 ms) and sagittal T2 (TE, 408 ms; TR, 3200 ms) sampling perfection with application-optimized contrasts by using different flip angle evolutions (SPACE; Siemens) sequences of the whole brain with section thickness of 0.9 mm and voxel size of 0.9 × 0.9 × 0.9 mm, which were subsequently reconstructed in axial and coronal planes.

Image Analysis

Imaging was reviewed by a single reader (M.Y.), a board-certified neuroradiologist with 3 years of experience, who was blinded to the clinical history and radiology report at the time of imaging review. All MRIs had been initially read by a group of board-certified neuroradiologists with an experience range of 1–12 years. MR imaging of 418 patients was retrospectively reviewed with particular attention paid to the anterior temporal lobes. The number, size, and location of osseous dural defects of the middle cranial fossa with unequivocal extension of brain parenchyma into the defect (Fig 1A) were recorded. In addition, the presence or absence of an empty or partially empty sella, enlarged Meckel cave, cribriform plate meningocele, and optic nerve protrusion into the globes was documented (Figs 1 and 2). The height of the pituitary gland was classified into 5 categories using the system of Yuh et al.20 We considered categories III (moderate concavity of the superior pituitary) and IV (severe concavity of the superior pituitary) as a partially empty sella and category V (enlarged sella without visible pituitary) as an empty sella. The width of the Meckel cave was measured on a coronal T2-weighted sequence and was considered enlarged if >7 mm.21
Seizure onsets were determined from neurophysiologic data and were based on interpretations of the ictal scalp electroencephalogram (EEG) and intracranial EEG. Three hundred eighty-seven patients had available ictal scalp EEGs. Fifty-five patients had intracranial monitoring, one of whom did not have seizures recorded. Patients were categorized by a board-certified epileptologist (Z.M.C.) on the basis of seizure onset as temporal (defining laterality when present), nontemporal (ie, either generalized or extratemporal onset), or nonlocalizable. Patients were only classified as having nonlocalizable onset if none of the recorded seizures could be clearly localized. One patient with an intracranial EEG was found to have independent temporal and extratemporal (nontemporal) seizure onset.

Statistical Analysis

All demographic and radiologic findings are presented as mean ± SD for continuous variables or as median (25th, 75th percentiles) and were tested using a Wilcoxon rank sum test. To assess their statistical association with TEs, we conducted a t test for continuous variables and a χ² test for categoric variables. Wilcoxon rank sum tests and Fisher exact tests were used when appropriate. The McNemar test was used to assess the relationship between retrospective review and initial determination of TEs. All analyses were conducted using SAS, Version 9.4 (SAS Institute, Cary, North Carolina). Statistical significance was assessed at α = .05.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Total</th>
<th>TEs (n = 52)</th>
<th>Without TEs (n = 136)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>43.3 ± 13.5</td>
<td>43.3 ± 12.1</td>
<td>36.4 ± 13.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BMI</td>
<td>28.7 (24.1–35.4)</td>
<td>36.9 (30.0–40.7)</td>
<td>27.7 (23.9–33.7)</td>
<td>&lt;.001b</td>
</tr>
<tr>
<td>Age at onset (yr)</td>
<td>15.0 (6.0–29.0)</td>
<td>35.0 (29.0–45.0)</td>
<td>14.0 (5.0–22.0)</td>
<td>&lt;.001b</td>
</tr>
<tr>
<td>Years with epilepsy</td>
<td>16.0 (7.0–27.0)</td>
<td>4.5 (2.0–9.5)</td>
<td>17.0 (9.0–28.0)</td>
<td>&lt;.001b</td>
</tr>
<tr>
<td>Male</td>
<td>176 (42.1%)</td>
<td>9 (17.3%)</td>
<td>167 (45.6%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Radiologic findings

<table>
<thead>
<tr>
<th>Findings</th>
<th>Total</th>
<th>TEs (n = 52)</th>
<th>Without TEs (n = 136)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal initial MRI</td>
<td>157 (37.6%)</td>
<td>31 (59.6%)</td>
<td>126 (34.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>MRI magnet = 3T</td>
<td>341 (81.8%)</td>
<td>50 (96.2%)</td>
<td>291 (79.7%)</td>
<td>.002c</td>
</tr>
<tr>
<td>SPACE was used</td>
<td>175 (41.9%)</td>
<td>37 (71.2%)</td>
<td>138 (37.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Abnormal Meckel cave</td>
<td>11 (2.6%)</td>
<td>5 (9.6%)</td>
<td>6 (1.6%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Abnormal sella turcica</td>
<td>98 (23.4%)</td>
<td>48 (92.3%)</td>
<td>50 (13.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Papilledema, yes</td>
<td>9 (2.2%)</td>
<td>6 (11.5%)</td>
<td>3 (0.8%)</td>
<td>&lt;.001c</td>
</tr>
</tbody>
</table>

Seizure localization

<table>
<thead>
<tr>
<th>Seizure Localization</th>
<th>Total</th>
<th>TEs (n = 52)</th>
<th>Without TEs (n = 136)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal</td>
<td>223 (57.6%)</td>
<td>46 (90.2%)</td>
<td>177 (52.7%)</td>
<td>&lt;.001c</td>
</tr>
<tr>
<td>Nonlocalizable</td>
<td>102 (26.4%)</td>
<td>5 (9.8%)</td>
<td>97 (28.9%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nontemporal</td>
<td>62 (16.0%)</td>
<td>0 (0.0%)</td>
<td>62 (16.0%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

icEEG

<table>
<thead>
<tr>
<th>icEEG</th>
<th>Total</th>
<th>TEs (n = 52)</th>
<th>Without TEs (n = 136)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>No seizures</td>
<td>1 (0.9%)</td>
<td>1 (12.5%)</td>
<td>0 (0.0%)</td>
<td>.06c</td>
</tr>
<tr>
<td>Temporal</td>
<td>34 (63.0%)</td>
<td>7 (87.5%)</td>
<td>27 (58.7%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nontemporal</td>
<td>11 (20.4%)</td>
<td>0 (0.0%)</td>
<td>11 (23.9%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Nonlocalizable</td>
<td>7 (13.0%)</td>
<td>0 (0.0%)</td>
<td>7 (15.2%)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Temp + extratemp</td>
<td>1 (0.9%)</td>
<td>0 (0.0%)</td>
<td>1 (2.2%)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Note: icEEG indicates intracranial EEG. BMI, body mass index; temp, temporal; extratemp, extratemporal.

a Results of the analysis are presented as mean ± SD for continuous variables and No. (%) for categoric variables unless otherwise noted. To assess statistical associations, we conducted a t test for continuous variables and a χ² test for categoric variables unless otherwise noted.

b Descriptive statistics are presented as median (25th, 75th percentiles) and were tested using a Wilcoxon rank sum test.

c Test conducted was a Fisher exact test.

RESULTS

Identification of Temporal Encephaloceles

Among the 418 patients with refractory epilepsy who had MR imaging available, 52 (12.5%) were found to have TEs on retrospective review, while only 7 (1.7%) had TEs identified on initial interpretation. Among the 52 patients with TEs, 19 TEs were unilateral (10 with left only, 9 with right only) and 33 TEs (63.5%) were bilateral. A total of 192 TEs (95 on the right and 97 on the left) were identified. There was an overall agreement of 89.2% between the retrospective reviewer and the initial interpretation. However, only 13.5% of patients were eventually discovered to have at least 1 TE on initial review (P < .001). All 7 TEs detected on initial interpretation were on scans that included a T2 SPACE sequence. There was no statistically significant difference between the size of TEs detected on the initial interpretation and TEs only detected on retrospective review.

Clinical Characteristics, Radiologic Findings, and Seizure Localization

Demographic, radiologic, and neurophysiologic data are summarized in the Table. Comparisons of clinical characteristics between subgroups with or without TEs differed significantly in regard to age, sex, body mass index, age at epilepsy onset, and years with epilepsy. MR imaging findings were more often initially normal in patients with TEs (P < .001), and a strong association was noted among patients with TEs for whom MR imaging was acquired using a 3T magnet (P = .002) and a T2 SPACE sequence (P < .001). The presence of an enlarged Meckel cave (P < .001), an empty or partially empty sella (P < .001), or findings suggestive of papilledema (P < .001) was also significantly associated with the presence of TEs. There was no significant difference found between laterality (unilateral TE percentage versus bilateral TE percentage) and an enlarged Meckel cave (10.5% versus 9.1%, P = 1.00), an empty or partially empty sella (89.5% versus 93.9%, P = .62), or papilledema (5.3% versus 15.2%, P = .40). Ictal scalp EEG was significantly more likely to localize seizure onset as temporal in patients with TEs (P < .001). Among the 54 patients who underwent intracranial monitoring, localization of seizure onset did not achieve statistical significance (P = .06), though all patients with TEs for whom seizures were recorded during intracranial monitoring had seizures localized as temporal-onset.

DISCUSSION

Our study, which represents the largest cohort of patients with TEs and refractory epilepsy to date, to our knowledge, demonstrates that the detection of TEs in patients with refractory epi-
The presence of TEs on review was significantly more common in patients with seizures of temporal onset on ictal scalp EEG, and none of the 52 patients identified were found to have extratemporal- or generalized-onset seizures on ictal scalp EEG. This proclivity of patients with TEs to have coexistent temporal lobe epilepsy has been observed in smaller studies, and suggests that even if TEs are not structurally epileptogenic, the presence of TEs may at least represent a surrogate marker for a propensity toward temporal lobe epilepsy and thus may be of localizing value. While some patients with TEs had seizures that were poorly localized on ictal scalp EEG, it is unclear whether these patients simply had temporal-onset seizures that were not clearly localized or whether some proportion of these poorly localized seizures is nontemporal in origin. Although the localizing data from ictal intracranial EEG did not achieve statistical significance, there appeared to be a trend toward patients with TEs having temporal-onset seizures, and all patients with TEs in whom seizures were detected were found to have temporal-onset seizures. However, these results were limited by the sample size. Larger intracranial studies are required to further evaluate the localizing value of TEs and to determine to what extent TEs may be epileptogenic. While there are little data available to determine whether or how much TEs constitute epileptogenic lesions, the literature has supported good clinical outcomes in cases in which surgical resection was performed. Additionally, seizures were found in 2 patients, both of whom had involvement of the area around the TEs at seizure onset, though there was synchronous or near-rapid spread to the hippocampus. Large case series have reported bilateral TEs in 14%–30% of patients with TEs and epilepsy, compared with 63.5% of patients in our study. It is conceivable that many patients may have bilateral TEs that may be overlooked without careful scrutiny and without an available high-resolution T2 sequence. While the presence of bilateral TEs does appear to be a relatively common phenomenon among patients with TEs, Saavalainen et al also found that 3 of 5 patients with bilateral TEs who underwent epilepsy surgery were seizure-free at follow-up; this finding suggests that not all TEs are likely epileptogenic. We suspect that while not all TEs are likely epileptogenic, their relatively common presence in patients with RTLE (along with their scarcity among patients with extratemporal or generalized epilepsy) suggests that a subset of TEs may lie within or contribute to the epileptogenic zone. However, the scope of our present study was limited to examining the presence of TEs and associated factors, while other studies may provide more insight as to their epileptogenicity. 

This study has several limitations. Due to its retrospective nature, no healthy control group was available, though patients with nontemporal seizures were used for comparison. Additionally, the use of an expert MR imaging reviewer is susceptible to rater-dependent bias. This could be mitigated by multiple-expert re-
view, with assessment to ensure appropriate interrater agreement; however, the development of guidelines may be necessary to facilitate a consensus among reviewers regarding what constitutes clinically relevant TEs in patients with epilepsy. Other than 1 patient who had a lumbar puncture with an elevated opening pressure, the remainder of patients with TEs included in the study did not undergo lumbar puncture to evaluate idiopathic intracranial hypertension. The association between idiopathic intracranial hypertension, TE, and temporal lobe epilepsy will require investigation in future studies. The localization of seizures was limited by the absence of seizures on intracranial EEGs in many patients, and larger studies with more patients undergoing intracranial monitoring should be able to confirm or refute our findings on the basis of the localizing data from ictal scalp EEG. Further studies to determine the frequency of TEs in the general population, the epileptogenicity of TEs, and outcomes of various treatment modalities are needed to better understand the relevance of and necessary approach to TEs.

CONCLUSIONS
Careful inspection of MR imaging with special attention paid to the high-resolution T2 sequence (T2 SPACE in our study) in patients with RTLE by a board-certified neuroradiologist can increase the detection of subtle TEs, which may be a source of focal refractory seizures. Certain clinical and neurophysiologic findings should raise suspicion for the presence of TEs, though further studies are necessary to determine their epileptogenicity and response to individual therapies.


REFERENCES