



Temporal Encephaloceles and Epileptogenicity: Does Size Matter?

Temporal encephaloceles in epilepsy patients and asymptomatic cases: Size may indicate epileptogenicity

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Objective: This study was undertaken to identify temporal encephaloceles (TEs) and examine their characteristics in patients with temporal lobe epilepsy (TLE) and extratemporal lobe epilepsy (ETLE), as well as in asymptomatic cases. **Methods:** Four hundred fifty-eight magnetic resonance imaging scans were examined retrospectively to identify TE in 157 patients with TLE, 150 patients with ETLE, and 151 healthy controls (HCs). **Results:** At least one TE was identified in 9.6% of the TLE patients ($n = 15$, 95% confidence interval [CI] = 5.3%–15.3%), in 3.3% of patients with ETLE ($n = 5$, 95%, CI = 1.1%–7.6%), and in 2.0% of the HCs ($n = 3$, 95% CI = .4%–5.7%), indicating a significantly higher frequency in patients with TLE compared to ETLE and HC subjects ($p = .027$, $p = .005$). Examining the characteristics of TEs in both asymptomatic and epilepsy patients, we found that TEs with a diameter of less than 6.25 mm were more likely to be asymptomatic, with a sensitivity of 91.7% and a specificity of 73.3% (area under the curve = .867, 95% CI = .723–1.00, $p = .001$). **Significance:** Temporal encephaloceles may occur without presenting any clinical symptoms. Patients with TLE show a higher frequency of TEs compared to the ETLE and HC groups. According to our study, TE size could be used to suggest potential epileptogenicity.

Commentary

Encephaloceles are protrusions of cerebral tissue through congenital or acquired skull defects,¹ seen typically but not exclusively in the middle cranial fossa. Albeit frequently asymptomatic,² their clinical significance has long been appreciated in the otorhinolaryngological literature due to their association with cerebrospinal fluid (CSF) leak and recurrent meningitis. In Neurology, they have been mostly discussed as an indirect sign of increased intracranial hypertension (IIH) in individuals with increased body mass index (BMI).³ Their association with seizures has gained substantial visibility in the last decade. It is still controversial, however, when they constitute incidental radiological findings versus sources of epileptogenesis.

In this manuscript (Tsalouchidou PE et al, 2021), Tsalouchidou et al⁴ attempt to elucidate this controversy. By utilizing a group of patients classified by their presurgical evaluation as having temporal lobe (TLE) versus extratemporal lobe epilepsy (ETLE), and comparing them with a group of healthy controls (HCs), the authors assessed retrospectively the prevalence and imaging characteristics of temporal encephaloceles (TEs) who were deemed to be probably epileptogenic versus asymptomatic. TEs were categorized as probably epileptogenic if they occurred ipsilateral to the presumed epileptogenic zone of the patients with TLE, without an alternative radiological explanation. Conversely, TEs were categorized as asymptomatic if they occurred in the healthy controls, in the

ETLE patients and in the TLE patients with a contralateral epileptogenic zone or with an ipsilateral epileptogenic zone attributed to another structural lesion. The emphasis of the comparison between the two categories of TEs was placed on their size, as retrospectively adjudicated by expert review.

The study population comprised of 157 patients with TLE, 150 patients with ETLE and 151 HCs. TEs were identified in 23/458 (5%) patients, retrospectively in all but one of them. Amongst them, TEs were identified in 9.6% of TLE patients, 3% of ETLE patients and 2% of HCs; a statistically significant preponderance in the TLE group. In the TLE group, TEs were unilateral in 80% of the cases and they were deemed to be probably epileptogenic 80% of the time. Comparing the asymptomatic with the probably epileptogenic cases in the whole cohort, it was concluded that small TEs (<6.25 mm diameter) were more likely to be asymptomatic, while larger TA were more likely to be epileptogenic, presumably due to increased risk of mechanical irritation of the brain parenchyma or the potential of increased association with other brain abnormalities. Only 6/23 (26%) of the TEs patients underwent selective or more extensive surgical resection, with available follow up data in 5 of them. From those, only 1 patient had isolated TE resection and became seizure free, while others had more radical mesial temporal lobe or extratemporal resections, with and without inclusion of the encephalocele, with variable seizure outcomes.

The advantage of this study is the inclusion of HCs for comparisons, a rarity in the extant literature.⁵ While data on






their BMI are not available, akin to the TLE and ETLE groups, it allows for comparison with the frequency of TEs in the epilepsy population. Even though no standardized imaging protocol was used to evaluate TEs in the TLE and ETLE groups and no interrater agreement on the radiological interpretation was provided, the results suggest an increased frequency of TEs in the TLE population that is typically undiagnosed in the first pass. The referral bias notwithstanding, this is in line with prior literature^{3,6,7} and delivers an important message to the epilepsy community. Additionally, this investigation commendably attempts to differentiate between asymptomatic versus epileptogenic encephalocles, focusing mostly on the size as a potential discriminator. Yet, it lacks robust characterization of the epileptogenic zone with stereo-EEG (sEEG) evaluation, not only to confirm its postulated from the remaining presurgical workup temporal versus extratemporal localization, but also to electrophysiologically characterize the participation of the identified TEs in the epileptic network. Without that information in hand, one can safely draw conclusions about their etiological role only with concrete postoperative data, starting ideally from those patients with limited lesionectomies to eliminate the inevitable “noise” of larger resections. With a few notable exceptions, that information is also limited in this cohort.

Such limitations are not selective to this study. In fact, most of the literature on encephalocles and epilepsy is derived by case reports, case series or small, retrospective and commonly uncontrolled studies. In a recent review,⁸ Ramos-Fresnedo et al amalgamated 267 published cases. Their ascertainment was performed using variable diagnostic criteria (e.g., brain contour abnormality, surrounding CSF signal, and associated parenchymal gliosis)^{3,6} and heterogeneous imaging protocols ranging from skull based computed tomography (CT) to combined higher resolution 3 Tesla Magnetic Resonance Imaging (MRI) with specialized sequences facilitating their identification.⁶ While most papers provided details on location and number, most lacked important characteristics such as size, typical appearance (i.e., meninges and brain as opposed to just arachnoid pits) and additional radiological stigmata of IIH. Their association with epilepsy was mostly identified in hindsight based on clinical semiology and geographic linkage with scalp EEG, with intracranial monitoring being the exception rather than the rule in the published series. Clinical information on related risk factors such as family history, history of trauma, prior surgery, tumor, infection or inflammation that could predispose to skull defects without or with seizures, frequently presenting earlier in life, as well as information on BMI or IIH symptoms that are frequently associated with TEs without or with (typically later onset) epilepsy³ was frequently absent. When surgical data were available, the majority of patients still underwent generous temporal resections, with lesionectomies or more restricted temporal lobectomies being a less popular course of action. From those who underwent any surgical intervention 61% were seizure free postoperatively, ranging from 44% in the temporal lobectomy cases to 87% in the lesionectomy cases,⁸ factoring in the selection and publication bias that this message entails. Histopathological characteristics of the surgical specimens were

provided in a minority of cases, ranging from benign brain parenchyma to gliosis, underlying meningioma or meningiomas, abnormal neuronal lamination and association with cortical dysplasia locally, versus more extensive, possibly related, developmental abnormalities, such as dysembryoplastic neuroepithelial tumors.^{3,8} Aside for limited literature on neuropsychological outcomes⁷ describing a more “benign” temporal lobe neuropsychological profile on TLE patients due to TEs, most studies lack pre- and post-operative data on that end. The limited available data suggest no significant change in the preoperative profiles with surgical intervention in the qualified cases and positive social repercussions subjectively.³ Successful lesionectomies seem to portend to fewer neuropsychological deficits, although preoperative anxiety and postoperative adjustment to “normalcy” is shared between all types of interventions.³

So, does size matter after all in epileptogenicity of TEs? The jury is not out yet. What really matters is that we now have heightened awareness, advanced radiological techniques, familiarity with sEEG investigations and minimally invasive techniques such as radiofrequency or laser ablation⁹ that could selectively address surgical targets in a step-wise approach. In other words, we have all the tools needed to prospectively and comprehensively explore the clinical, pathophysiological, radiological, electrophysiological, histopathological and postoperative characteristics that can help us differentiate asymptomatic from epileptogenic temporal and extratemporal encephalocles.

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