Clinical Neurology and Neurosurgery 159 (2017) 39–41

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

The association of arachnoid cysts and focal epilepsy: Hospital based case control study

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ARTICLE INFO

Keywords:
Focal epilepsy
Arachnoid cysts
Video-EEG
Case control study

ABSTRACT

Objective: Arachnoid cysts (ACs) are common findings in brain MRI. Our aim was to examine frequency and distribution of ACs in patients with focal epilepsy, compared to healthy control subjects, and to investigate the association of AC and electro-clinical features of focal epilepsy.
Patients and methods: We performed a retrospective case-control study, using data from 180 patients that underwent video-EEG monitoring between 2009 and 2012, and of 114 healthy controlled subjects. Analysis of electro-clinical data and structural MRI images was conducted.
Results: A significantly higher proportion of ACs in the focal epilepsy group (19/180; 10.5%) compared to healthy control subjects (3/114; 2.6%) ($p = 0.012$) was identified. Significant congruence of semiological features or interictal and ictal EEG with AC localization was identified in only one MRI nonlesional patient with temporal cyst localization.
Conclusion: ACs are seen more often in patients with focal epilepsy. Explicit association between focal epilepsy and AC is possible but exceptional. More likely, focal epilepsy and AC share a common etiological ancestor but represent distant and distinct entities.

1. Introduction

Intracranial cysts are heterogeneous lesions and common findings in brain Magnetic Resonance Imaging (MRI), with a broad hystopathological spectrum [1]. Two studies discovered that individuals in the general population present with a variety of abnormalities on neuroimaging: Katzman et al. (1999) reported that 18% of healthy asymptomatic subjects demonstrated incidental abnormal findings, including very rare cysts ie. nasopharygeal cysts (0.1%), choroid and pineal cysts (0.2%), and arachnoid cysts (0.3%) [2], and Vernooij et al. (2007) found a slightly higher proportion of arachnoid cysts among 2000 healthy participants in the Rotterdam study (1.1%) [3].

Except for neurocysticercosis, the relationship of all other cystic lesions and epilepsy is inconsistently reported [4,5]. Studies about association of epilepsy and arachnoid cysts (AC) provided significant uncertainties in data [6]. Our aim was to examine frequency and distribution of ACs in focal epilepsy patients compared to healthy control subjects. In addition, we investigated the association of ACs and electro-clinical features of focal epilepsy.

2. Patients and methods

2.1. Patients and healthy controls

Patients were selected from the database of the Epilepsy Center video-EEG Monitoring Unit from August 2009 till May 2012. We used 64-channel acquisition system with 10–20 electrode placement with anterior temporal electrodes added. Antiepileptic drugs (AEDs) were reduced/discontinued in the absence of patient-specific contraindications in all patients. Focal epilepsy was diagnosed in 245/310 patients (79%). Focal interictal discharges but no focal seizures were recorded in 65 patients (20.9%). We studied 180/310 patients (58.04%) who underwent long-term vEEG monitoring in whom focal epileptic seizures were recorded. Electro-clinical data of the patients were collected, as

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http://dx.doi.org/10.1016/j.clineuro.2017.05.014
Received 23 January 2017; Received in revised form 16 April 2017; Accepted 9 May 2017
Available online 12 May 2017
0303-8467/

Table 1
Clinical, EEG and neuroradiological data (n = 180).

Positive risk factors for epilepsy (78/180; 43.3%)[a]	Febrile convulsions 51 (28,3%); Traumatic brain injury 14 (7.8%); Perinatal trauma 13 (7.2%); Encephalitis 7 (3.9%); Brain surgery 6 (3.3%);
Epileptogenic lesion (124/180; 68.9%)[b]	Hippocampal sclerosis (HS) 58 (32.2%)[c]; Focal cortical dysplasia (FCD) 26 (14.4%); Dysembryoplastic neuroepithelial tumor 8 (4.4%); Remote infarct 6 (3.3%); Cavernoma 4 (2.2%); Glioma 3 (1.7%); Gliosis 3 (1.7%); Ganglioglioma 1 (0.6%); Nodular heterotopia 1 (0.6%); Hamartoma 1 (0.6%); Dermoid cyst 1 (0.6%); FCD and cavernoma 1 (0.6%); Dual pathology (HS and FCD, polymicrogyria, remote infarct or gliosis) 11 (6.1%); Multiple plaques of demyelination (at least two juxtacortical) 2 (1.1%); Normal brain MRI 54 (30%)
Total number of focal seizures recorded on vEEG monitoring	1712 (median 5 per patient/range 1–384)[d]
Interictal EEG findings (spikes or sharp waves in regional distribution)[e]	Interictal EEG discharges was not recorded in 12 patients (6.7%); Single type of interictal discharges 109 (60.6%), Two independent types of interictal discharges 47 (26.1%), Three independent types of interictal discharges 12 (6.7%)
Ictal EEG region	Temporal 65 (36.1%); Fronto-temporal 60 (33.3%); Frontal 22 (12.2%); Temporo-posterior 11 (6.1%); Parietal 4 (2.2%); Fronto-central 4 (2.2%); Hemispheric 4 (2.2%); Temporo-central 2 (1.1%); Vertex 2 (1.1%); Nonlocalized 6 (3.3%)
WAIS-III[f]	IQ total 90.4 ± 14.4 (59–133); IQ verbal 91 ± 14.9 (60–135); IQ manipulative 90.1 ± 15.4 (59–132)

[a] Multiple positive risk factors for epilepsy were identified in 8 patients.
[b] Multiple plaques of multiple sclerosis were identified in 2 patients.
[c] Bilateral HS was identified in 5 patients.
[d] Focal seizure with secondary generalization was recorded in 74 patients (41.1%); median 2 (range 1–10).
[e] Tho most prevalent interictal discharges correlated with epileptogenic lesion if present in all cases with two or three independent discharges.
[f] 23 patients were not testable.

well as wide set of neuropsychological tests including WAIS-III which was used for further analysis (Table 1).

A healthy control (HC) group (n = 114) was identified among employees of the Neurology Clinic, Clinical Center of Serbia (physicians, nurses, research associates, and administrative personnel), patient relatives, and students from the Medical School, University of Belgrade with no previous history of chronic neurological and psychiatric diseases. Neurological examination was normal in all healthy control subjects. The study was approved by the Ethical Committee at the Clinical Center of Serbia. Written informed consent for education and research was obtained from all patients and healthy volunteers participating in the study.

2.2. Brain MRI acquisition and analysis

In active and control group we acquired structural images using 1.5T Avanto Siemens, and 1.5T Achieva Philips MRI Scanners. In all patients we performed protocols for frontal, posterior or temporal epilepsy (axial and coronal planes varies accordingly) depending on electroclinical data. We applied the following sequences: 3D T1W isotropic volume image in the sagittal orientation (TR/TE = 7,1/3,2 ms, flip angle 8°, FOV 256 mm, slice thickness 1 mm with no interslice gap, 170 slices), Turbo Spin Echo (TSE) T2-weighted image in axial orientation (TR/TE = 3000/90 ms, FOV 230 mm, slice thickness 5 mm, interslice gap 1 mm, 25 slices), FLAIR in axial orientation (TR/TE = 11000/140 ms, FOV 250 mm, slice thickness 3 mm, no interslice gap, 25 slices) TSE T2 w coronal image (TR/TE = 3294/100 ms, FOV 230 mm, 3/0 mm, 32 slices), FLAIR coronal image (TR/TE = 11000/140 ms, FOV 250 mm, 3/0 mm, 32 slices), T2 w Gradient Echo/Fast Field Echo (Siemens/Philips) axial image (TR/TE = 798/23 ms, flip angle 18°, FOV 230 mm, 5/1 mm, 25 slices) and T1 w – Inversion Recovery coronal image (TR/TE = 2830/15 ms, FOV 230 mm, 5/1 mm,).

Control subjects brain MRIs were taken from ongoing projects. Axial planes were aligned with longitudinal axis of the corpus callosum. For the purposes of the present study we used 3D T1W sequences in sagittal orientation (TR/TE = 7,2/3,3 ms, FOV 256v256 mm, 1 mm/no interslice gap, 181 slices with three plane reconstruction in postprocessing acquisition), and DUAL_TSE (T2w/PD) (TR/TE = 3124,9/100, FOV 240 × 240 mm, 3 mm/no interslice gap, 89 slices).

An experienced neuroradiologist (IN) by visual analysis defined quality and location of the epileptogenic lesions and AC. The following AC features were taken into consideration: precise anatomical localization, size, number of ACs, and the compressive effect of the ICs.

2.3. Statistical analysis

Continuous variables were compared using independent sample *t* test, and Mann-Whitney *U* test. Proportions and unadjusted odds were analyzed using Pearson Chi-square test or Fisher's exact test when appropriate. All analysis were made using SPSS version 16.0 (IBM, Chicago, IL).

3. Results

Mean age of patients with focal epilepsy was 34.2 ± 10.9 (range 13–66; male/female 92/88), mean age of disease onset was 14.2 ± 10.1 years of age (range 1–48), and mean duration of disease was 19.9 ± 11.7 years (range 1–55). Mean age of healthy control subjects was 36.4 ± 8.6 (range 18–57; male/female 50/64). There was no significant difference on age and gender distribution between the active and control group.

We identified a significantly higher proportion of overall ACs in the focal epilepsy group (19/180; 10.5%) compared to healthy control subjects (3/114; 2.6%) (p = 0.012). Multiple cyst types were determined in 3 male patients with focal epilepsy (Dermoid cyst/AC; AC/Perivascular space; AC/Porencephalic cyst) and in 2 (male and female) healthy control subjects (AC/Pineal gland cyst; AC/Neuroglial cyst) (p = 0.4).

The existence of ACs was not significantly associated with positive risk factors for epilepsy, occurrence of epileptogenic lesion, type of epileptogenic lesion, patients' age, disease duration or age at disease onset, mean number of seizures recorded on vEEG monitoring, presence and number of independent interictal EEG discharges, and ictal EEG onset region. Higher total intelligence quotient (IQ) (n = 16; mean 99.4 ± 15.4) was associated with presence of AC in focal epilepsy patients compared to patients with no AC detected (n = 141; mean 89.3 ± 13.9) (p = 0.008).

Table 2 shows morphological features of analyzed ACs. We analyzed electro-clinical data in 4 patients with AC localized in temporal region. We found concordance of the electro-clinical findings (interictal discharges, ictal onset region and localization of AC) in one patient without brain MRI verified epileptogenic lesion. In 2 patients (who had brain MRI verified epileptogenic lesion localized in the same hemisphere as ACs) electro-clinical data correlated with the region where the lesion was placed. In one patient without brain MRI verified