

# Dysembryoplastic neuroepithelial tumor and temporal arachnoid cyst on a child with epilepsy. Which one to operate? Case report and literature review

*Tumor neuroepitelial disemбриoplásico y quiste temporal aracnoideo en un niño con epilepsia. ¿Cuál operar? Reporte de un caso y revisión de la literatura*

Ariam A. Martínez-Luna<sup>1</sup>, Gustavo Aguado-Carrillo<sup>1\*</sup>, Francisco Velasco-Campos<sup>1</sup>, Ana L. Velasco-Monroy<sup>1</sup>, and Erick Gómez-Apo<sup>2</sup>

<sup>1</sup>Department of Functional and Stereotactic Neurosurgery, Hospital General de México, Mexico City, Mexico; <sup>2</sup>Department of Neuropathology, Hospital General de México. Mexico City, Mexico

## Abstract

A 6 year-old male, with seizures characterized by abnormal epigastric sensation, behavioral arrest, upper extremities search automatisms and secondary tonic-clonic generalization. Magnetic resonance imaging showed a hypointense cystic extra-axial image with an increase in the thickness of the convolutions in the first and second gyri of the right frontal lobe. It was decided to resect the frontal lesion with transoperative motor mapping. Morphological and immunohistochemical findings corresponded to dysembryoplastic neuroepithelial tumor with focal cortical dysplasia. Adequate semiology, analysis of the electroencephalogram, and imaging studies allowed treating adequately the cortical dysplasia. At present, the patient is seizure-free without medication (Engel IA).

**Key words:** Arachnoid cyst. Cortical dysplasia. Cortical mapping. Dysembryoplastic neuroepithelial tumor. Focal epilepsy.

## Resumen

Niño de 6 años con crisis caracterizadas por sensación epigástrica, arresto conductual, automatismos de búsqueda y generalización tónico-clónica secundaria. La resonancia magnética mostró una imagen extraaxial quística y un aumento del grosor de las circunvoluciones del primer y segundo giros del lóbulo frontal derecho. Se decidió resear primero la lesión frontal con guía por mapeo transcortical intraoperatorio. Los hallazgos morfológicos e inmunohistoquímicos mostraron un tumor neuroepitelial disemбриoplásico con displasia cortical focal. La semiología, el análisis del electroencefalograma y la imagen permitieron orientar el tratamiento. Actualmente el paciente está libre de crisis y sin medicamentos (Engel IA).

**Palabras clave:** Quiste aracnoideo. Displasia cortical. Mapeo cortical. Tumor neuroepitelial disemбриoplásico. Epilepsia focal.

## Correspondence:

\*Gustavo Aguado-Carrillo

Dr. Balmis, 148

Doctores

C.P. 06720, Ciudad de México, México

E-mail: gustavoaguado@hotmail.com

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## Introduction

Neuroepithelial dysembryoplastic tumor is a benign neoplasm, grade I of the WHO, characterized by cortical dislamination, lesions in cytoarchitecture where glioneuronal elements such as oligodendroglia, astrocytes, and poorly differentiated neurons called “floating neurons” are observed, and abnormalities of the white matter. Based on this, it is classified in its different forms: simple, complex, non-specific, and diffuse, of which the complex and non-specific form is frequently associated with focal cortical dysplasia<sup>1,2</sup>. They can be located anywhere in the supratentorial cortex but have a special predilection for temporal lobe<sup>3,4</sup>. Although exceptionally they can be found in other sites such as septum pellucidum, caudate nucleus, medulla, and cerebellum.

They typically present with focal epilepsy resistant to treatment in children and young adults. An incidence is reported in all cases with temporal lobe epilepsy, where 8.6% are due to neuroepithelial dysembryoplastic tumors<sup>1,5</sup>. Amplification of the inotropic glutamate receptor and peritumoral neuronal migration disorders may be the underlying cause of seizures. It is important to remember that 80% is associated with focal cortical dysplasia, which seems to have its own epileptogenicity<sup>3,6</sup>. Other symptoms that can be found are dysarthria, facial asymmetry, focal weakness or visual weakness, and obstructive hydrocephalus in cases where it is found in septum pellucidum<sup>7,8</sup>.

Magnetic resonance imaging can be classified as type 1: cystic/polycystic well defined, hypointense in T1, nodular type 2, with heterogeneous signal, and type 3 iso/hypointense T1, poorly delimited. Focal cortical dysplasia is mainly associated with type 3<sup>9</sup>. Frequently, it is composed of one or several cysts and contains microcalcifications. Spectroscopy may show a low peak of N-acetylaspartate with no elevation of choline<sup>2,7</sup>. Immunohistochemistry shows reactivity for Neu-N and Olig-2. The proliferation index Ki-67 is low, 0-1.6%.

Differentiating diagnoses should include oligodendrogiomas, gangliogliomas, neurocytomas, pilomyxoid astrocytomas, and pilocytic astrocytomas.

The dysembryoplastic tumor reported here, was accompanied by cortical focal dysplasia, which is a group of epileptogenic brain abnormalities, produced by alteration on neural migration. Classified by the International League Against Epilepsy (2011) in three types, distinguishing isolated forms I and II, and type

III associated with some other injury. That in turn is subdivided into four categories Digestion Fractional Crystallization IIIa associated with hippocampal sclerosis, IIIb associated with tumors, IIIc associated with vascular malformations, and IIId associated with any other type of congenital lesion<sup>10,11</sup>.

On the other hand, arachnoid cysts are benign extra-axial collections formed by cerebrospinal fluid. About their etiology, the hypothesis with greater acceptance establishes that cysts are produced by dysgenesis in the embryological development of the subarachnoid space<sup>12</sup>.

At our best knowledge, this is the first case reported in Mexico, and in the international literature, there is just one similar case informed<sup>13</sup>. Therefore, information related to these entities and how they interact is sparse and more detailed description of future cases is needed, to wide or improve our comprehension in the matter.

## Case report

A 6 years old child without perinatal complications and with an adequate psychomotor development according to his age. He began his condition at 3 years of age by presenting an episode characterized by loss of awake status of approximately 5 min and recovery ad integrum, 8 months later he presented a seizure characterized by abnormal epigastric sensation followed by behavioral arrest and search automatisms with the upper extremities and secondary tonic-clonic generalization, short postictal period. At 4 years of age, he presents an episode that begins with tonic movement in the left hand, expression of fear, followed by behavioral arrest, the automatism of laughter, and finally generalized hypertonia, quick postictal recovery. These episodes appear with nocturnal predominance, reaching 4-5 seizures per day. In the physical and neurological examination, there are no pathological data to be highlighted. The treatment was with levetiracetam 1 g every 12 h, topiramate 50 mg every 12 h, oxcarbazepine 300 mg in the morning and 600 mg at night having a poor control of seizures despite this drugs so he was considered to have a refractory epilepsy, and therefore candidate for epilepsy surgery.

The surface electroencephalogram (EEG) shows slow-wave tip complexes in frontocentral regions. Ripples are observed in phase opposition in the right temporal region. During EEG clinical event occurs, while he was asleep, he awakens, rubs his face with his right hand, raises right thoracic limb, and adopts

a dystonic left-hand posture, generalized increase in muscle tone, left cephalic version and stare, no postictal period.

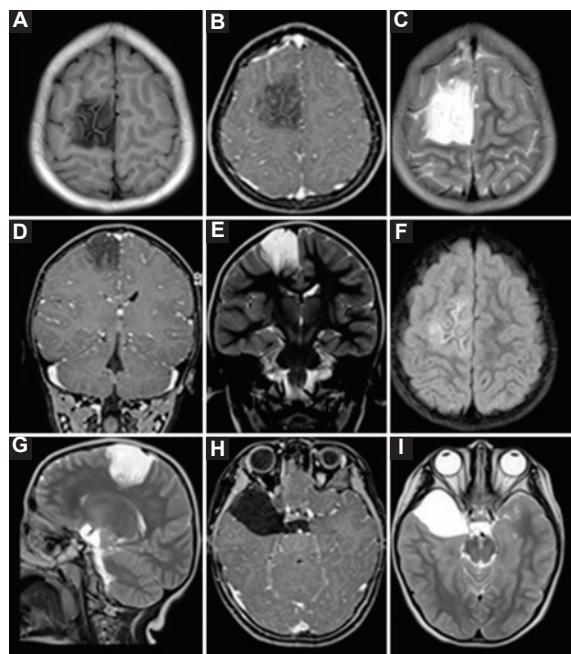
Neuropsychological assessment reports a global cognitive index within the range and the mean for chronological age, mild to moderate difficulties in fine motor skills, difficulty in the visuospatial and constructive area at the material, and graphic level. There was a poor performance on some items like attention, manipulation and organization of information. It concludes alterations associated with the right frontal region.

Cranial magnetic resonance imaging showed a hypointense cystic extra-axial image in T1, fluid-attenuated inversion recovery (FLAIR), and hyperintense in T2 without abnormal reinforcement to the application of the gadolinium, with dimensions of  $4.8 \times 4.3 \times 4.4$  cm, in relation to an arachnoid cyst. In the most dorsal region of the first and second gyri of the right frontal lobe, an increase in the thickness of the convolutions is observed. Being hypointense in T1, with enhancement with gadolinium, and hyperintense in T2 and FLAIR and its dimensions  $4.4 \times 3.3$  cm (Fig. 1).

It was decided to resect the frontal lesion with transoperative motor mapping having negative responses to cortical stimulation in the region of interest, reaching amplitude of 10V with a frequency of 5 Hz and a pulse width of 100 ms. A total macroscopically resection was performed with favorable immediate postoperative evolution. Clinically, the patient is neurologically intact and seizure-free (Engel IA) since surgery without medication.

### Pathological anatomy

In the histological sections examined, low-grade malignancy, intra-axial neoplasm, characterized by non-infiltrating growth, microcystic pattern, characterized by the presence of acellular mucin lakes that are surrounded by cells of small to medium size, with oval nuclei, chromatin dense and homogeneous, with dense and uniform cytoplasm, and with well-defined cell membrane; focally, some larger cells with an evident nucleolus are identified. Immunohistochemistry was performed with a positive expression for vimentin, positive for CD56 as a neuronal marker, and focal positive for glial fibrillary acidic protein; and with a negative expression for a cocktail of cytokeratins and for synaptophysin. In the adjacent cerebral parenchyma, a cerebral cortex with a dysplastic appearance can be seen due to the loss of the hexalaminated architecture, the neuronal cells are disordered, formed



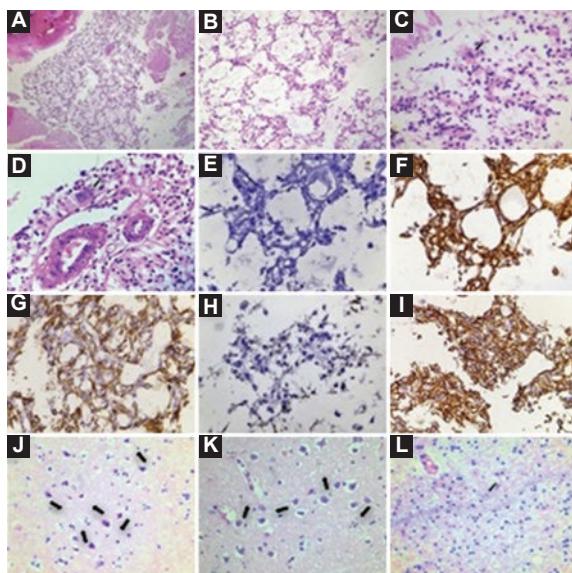
**Figure 1.** Magnetic resonance imaging showing an intra-axial lesion in the most dorsal region of the first and second gyri of the right frontal lobe. **A:** T1 axial. **B:** T1 axial with gadolinium. **C:** T2 axial. **D:** T1 coronal with gadolinium. **E:** T2 coronal. **F:** Fluid-attenuated inversion recovery axial. **G:** T2 sagittal. **H:** T1 axial with gadolinium showing the right temporal arachnoid cyst. **I:** T2 axial image of the temporal arachnoid cyst.

small irregular groups and with loss of the polarity of their cytoplasmic prolongations; in addition, in the deep white substance, some heterotopic neuronal somas are identified (Fig. 2). The morphological and immunohistochemical findings correspond to a dysembryoplastic neuroepithelial tumor with focal cortical dysplasia IIIb (adjacent focal cortical dysplasia adjacent to the tumor)<sup>10,14</sup>.

### Discussion

The case presented here has the peculiarity of having two intracranial lesions (arachnoid cyst and dysembryoplastic neuroepithelial with cortical dysplasia) due to the limited information about this rare association and how its causative physiopathology mechanisms interact, we are unable to establish the precise mechanisms behind to our findings.

Both lesions can perform as the epileptogenic focus, this is why it is really important to have a structure protocol for the approach of these cases. At our center, there is a multidisciplinary team who runs a well-established protocol. First, the most fundamental



**Figure 2.** A: hematoxylin and eosin (HE) ( $\times 40$ ), panoramic aspect of the lesion, which contrasts with the transition with the cerebral parenchyma. B: HE ( $\times 100$ ), detail of the lesion, formed by microcystic pattern due to the production of mucins. C-D: HE ( $\times 400$ ), microscopic detail of the neoplastic cells with evidence of mature neoplastic neurons (arrow). E: immunohistochemistry with CKAE1AE3. F: immunohistochemistry with vimentin. G: immunohistochemistry with PAGF. H: immunohistochemistry with synaptophysin. I: immunohistochemistry with CD-56. J-K: HE ( $\times 100$ ), panoramic aspect of the adjacent cerebral cortex, with evidence of dysplastic neurons, characterized by cytoplasmic prolongations in different directions (arrows). L: HE ( $\times 100$ ), panoramic aspect of white matter adjacent to the neoplasm, with heterotopic neurons.

part of the diagnostic is the semiology of the crisis, in our case, the characteristics of the crisis show a frontotemporal pattern, and there are two lesions within these structures, so we perform a surface EEG, the patient showed slow-wave tip complexes in frontocentral regions. The third one comprise is neuropsychological assessment, the report in our case concludes frontal region alterations. For previous considerations, criteria must include magnetic resonance imaging findings. By discussing these findings in a multidisciplinary manner, we determine to operate the frontal lesion with transoperative motor mapping having negative responses to cortical stimulation in the region of interest.

In selected cases, it is considered intracranial video-EEG recordings as the gold standard for the location of the epileptogenic focus and thus determines the best surgical strategy to optimize the control of seizures, but in cases with lesional epilepsy, it is more reliable to perform an adequate semiology of crisis to determine which lesion is responsible of epilepsy.

The predominant and most effective treatment is a total tumor resection that will lead patients to be seizure-free for more than 80% for at least 1 year<sup>6,7</sup>.

## Conclusions

The total resection of benign epileptogenic lesions such as cortical dysplasias associated or not with low-grade tumors offers the possibility of total control of epileptic seizures in those who suffer them; it is, therefore, important to have a complete and detailed study protocol that allows us to identify the precise anatomical location of the lesion responsible for seizures to plan an adequate surgical approach, together with the use of transoperative tools such as cortical stimulation for functional transoperative mapping to avoid neurological sequelae in the treated subjects.

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## Conflicts of interest

The authors declare have not conflicts of interest.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that they have followed the protocols of their work center on the publication of patient data.

**Right to privacy and informed consent.** The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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