Surgically treated intracranial supratentorial calcifying pseudoneoplasms of the neuraxis (CAPNON) with drug-resistant left temporal lobe epilepsy: A case report and review of the literature

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Abstract

Calcifying pseudoneoplasms of the neuraxis (CAPNON) are rare pathological lesions that can present anywhere in the central nervous system. Symptoms vary depending on the location, though they often include seizures, especially in intracranial and supratentorial lesions. A case of intracranial supratentorial CAPNON presenting with drug-resistant left temporal lobe epilepsy is reported. The patient had a history of drug-resistant focal seizures for over 36 years. The lesion was located in the left mesial temporal lobe, but hippocampal sclerosis and hippocampal invasion were not apparent. The lesion was removed without hippocampectomy, and the patient has been seizure-free for one year.

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Keywords:
- Calcifying pseudoneoplasms of the neuraxis (CAPNON)
- Drug-resistant epilepsy
- Supratentorial
- Surgical treatment
- Temporal lobe epilepsy

1. Introduction

Calcifying pseudoneoplasms of the neuraxis (CAPNONs) are very rare lesions; only 90 cases including 54 (60%) intracranial cases and 36 (40%) spinal cases have been reported [1–59]. These lesions are benign and slow growing, and can present anywhere in the central nervous system, both intracranially and involving the spine. The symptoms depend on the location of the lesion: for example, intracranial lesions can cause headache, seizure, motor paralysis, cranial nerve deficits, or cognitive dysfunction, while spinal lesions can cause back pain, radiculopathy, or myelopathy. Patients with intracranial and supratentorial lesions often present with seizures [55]. Up to now, there have been few reports with detailed descriptions of drug-resistant epilepsy caused by CAPNON [24,28,32,55,58].

A case of CAPNON that presented with a long history of drug-resistant left temporal lobe epilepsy and was treated successfully with surgical removal is presented.

2. Case presentation

2.1. History and examination

A 52-year-old right-handed man had a history of drug-resistant seizure for over 36 years. When he was 16 years old, he had his first episode of focal impaired awareness seizure (FIAS). He took some anti-seizure drugs for several years and stopped thereafter. His frequency of seizures was once per several months, but he had not taken any anti-seizure drugs afterwards. At the age of 47 years, he had a generalized tonic–clonic seizure while at work. He then again started taking anti-seizure drugs. However, his seizures were not well controlled by any kinds of anti-seizure drugs for over five years and increased in frequency to several times per day. Finally, he was referred to our hospital taking carbamazepine 200 mg and lamotrigine 150 mg daily. Computed tomography showed a mass lesion (14 × 18 × 12 mm³) with massive calcification at the mesial side of the left temporal lobe (Fig. 1). Magnetic resonance imaging (MRI) showed a mixed low-intensity mass without edematous change surrounding the lesion on T1 and T2-weighted imaging, and it showed markedly low intensity on susceptibility-weighted imaging (Fig. 2A–C). There were no features of hippocampal sclerosis.
apparent on FLAIR imaging (Fig. 2D). Fluorodeoxyglucose-positron emission tomography showed prominent hypo-metabolism in the lesion and relatively low accumulation at both mesial and lateral parts of the left temporal lobe compared with the right side (Fig. 3). Electroencephalography showed frequent spikes and waves at F7, T3, and T5 (Fig. 4). Magnetoencephalography showed dipoles clustering with upper direction at the frontal base, not at the hippocampus (Fig. 5). We performed video-EEG monitoring for three days, however, could not capture his seizure at that time. We did not pursue repeat video-EEG evaluations because other preoperative evaluations strongly

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**Fig. 1.** Computed tomography showing a high-density lesion (14 × 18 × 12 mm³) at the left mesial temporal lobe. (A): soft tissue density image (B): bone density image.

**Fig. 2.** Magnetic resonance imaging showing a mass lesion at the left mesial temporal lobe. The lesion is low intensity on the T1-weighted image (A), mixed intensity on the T2-weighted image (B), and low intensity on the susceptibility-weighted image (SWI) (C). There are no features of hippocampal sclerosis apparent on the coronal FLAIR image (D).
2.2. Operation

A frontotemporal craniotomy was performed, and the Sylvian fissure was dissected widely. A small corticotomy was made at the temporal tip to approach the lesion. The lesion was a stone-like yellow mass and was completely removed in one piece (Fig. 6). After removal, an intraoperative electrocorticogram was done to check the irritability of the surrounding brain. Although some abnormal discharges at the surrounding temporal lobe remained, additional corticectomy or hippocampectomy was not performed, as planned.

2.3. Histological findings

Histologically, the lesion consisted of amorphous lamellar calcification, with eosinophilic matrix in background. These calcifications had concentric circular structure like psammoma bodies. Epithelial cells around the mass showed spindle shapes and no atypia. There was no necrosis, microvascular proliferation, or mitotic activity. (Fig. 7A,B) On immunohistochemistry, the matrix was positive for vimentin (Fig. 7C); some calcification was positive for S-100 protein (Fig. 7D); matrix of the lesion was positive for glial fibrillary acidic protein (GFAP) (Fig. 7E), and epithelial membrane antigen (EMA) was mostly negative (Fig. 7F). Based on these histological findings, the diagnosis of CAPNON was made.

2.4. Postoperative course

A follow-up MRI demonstrated the complete removal of the lesion (Fig. 8). At the last follow-up, there were no findings of lesion recurrence. The patient has been seizure-free since the surgery for one year, despite postoperative scalp EEG showing remaining small spike-and-waves at the F7 and T3 electrode derivations. This patient will remain on anti-seizure drugs and be followed up annually by MRI.

3. Discussion

In the present case, CAPNON located in the mesial temporal lobe was a cause of drug-resistant temporal lobe epilepsy, and by removing the lesion itself, a seizure-free outcome has been achieved in the one-year follow-up period. Thirty-six years is relatively long for the duration of epilepsy, and the patient suffered from deterioration of verbal memory and delayed recall on the WMS-R, which were suspected to be due to the long-standing temporal lobe epilepsy, yet these memory deteriorations might have been prevented by earlier treatment.

In the literature, there were 54 (60%) intracranial cases [3,6,7,10,16,20,24–29,31–33,35–48,50–53,55–59] and 36 spinal cases (40.0%) [1–23] of CAPNON. Of the intracranial cases, 36 lesions were supratentorial [3,6,7,10,16,20,24,25,28,29,31–33,35,38,40–44,47,50–52,55,57–59]. Seizures were the most common symptom in supratentorial CAPNON (17/36 cases: 47.2%). Tables 1 and 2 summarized the previously reported 17 cases of surgically treated intracranial supratentorial CAPNON associated with seizures. The seizure types were generalized tonic-clonic seizure (GTCS) in 7 cases (41.1%), focal impaired awareness seizure (FIAS) in 4 cases (23.5%), focal aware seizure (FAS) in 2 cases (11.8%), and not described in 4 cases. Among them, the detailed preoperative examinations and surgical strategy were reported in only 7 cases [24,28,29,35,50,57,58] (38.9%).

We believe that the unique points of the present case are the imaging findings and the clinical course of epilepsy. Preoperatively, we initially considered the lesion as oligodendroglioma [61], ganglioglioma [61] or cavernous malformation [62]. That was because these are known to be calcified and cause seizures [63] [64]. After the surgery, it was pathologically diagnosed as CAPNON. Retrospectively reviewed, the imaging findings matched well with the previously reported characteristics of CAPNON (less mass effect to the surrounding normal brain and no invasion to the brain parenchyma). In the reported cases with CAPNON, the seizure outcomes following surgery were described in 10 cases and among them, seizure freedoms were achieved in 9 cases. On the other hand, reported seizure-free outcomes were 67% in low grade glioma [65], 80% in glioneuronal tumors [64] and 82.1% in supratentorial cavernous malformations [66]. Considering the efficacy of surgery for CAPNON

![Fig. 3. Fluorodeoxyglucose-positron emission tomography showing prominent hypometabolism in the lesion (red arrows) and relatively low metabolism at both mesial and lateral sides of the left temporal lobe compared with the right side of the hemisphere (white arrows).](image-url)
**Fig. 4.** Interictal electroencephalography showing a spike and wave pattern at F7, T3, T5, and T1 with the average (AV) reference (red arrows).

**Fig. 5.** Magnetoencephalography showing clustering dipole (red circles) accumulations with upper direction at the frontal base, not at the hippocampus.
is quite high, the lesionectomy can cure of the seizures even if the duration of the seizures are relatively long. As far as we know, the present case had the longest preoperative seizure history with a duration of over 35 years. However, we achieved a seizure-free outcome with lesionectomy alone. CAPNON is a rare lesion, and especially in the case of a single lesion, it can be ignored as a mere asymptomatic intracranial calcification. However, clinicians should keep in mind that CAPNON can be the cause of drug-resistant focal epilepsy, and also that it can be well controlled by surgical removal.

4. Conclusions

Intracranial CAPNON is a rare lesion and histologically benign, but it may cause focal epilepsy. To control epilepsy, a surgical resection can be an effective management strategy. Therefore, surgical removal should be considered if the seizures are drug-resistant.

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Ethical Statement

For clinical study: Informed consent was obtained from the subjects, and the clinical investigation was conducted in accordance with the guidelines of the human research committee or the Declaration of Helsinki.
Fig. 8. Computed tomography (A, B) and magnetic resonance images (C, D) taken after the operation showing gross total resection of the lesion and preservation of the hippocampus (D: FLAIR image).

Table 1

| No. | Report                        | Age (y) | Sex | Side | Location  | Seizure type | Time before treatment (months) | Postoperative follow-up (months) | Treatment | Tumor result | Seizure outcome |
|-----|-------------------------------|---------|-----|------|-----------|--------------|-------------------------------|----------------------------------|-----------|--------------|----------------|
| 1   | Muraki et al., 1984 [43]      | 43      | F   | R    | Temporal lobe | GTCS         | N/A                           | N/A                              | Complete resection | Recurrence-free | Seizure-free   |
| 2   | Hashimoto et al., 1986 [35]  | 29      | M   | R    | Temporal lobe | FIAS         | 216                           | N/A                              | Complete resection | Recurrence-free | N/A            |
| 3   | Bertoni et al., 1990 [10]    | 32      | M   | N/A  | Frontal lobe | GTCS         | 144                           | 360                              | Complete resection | Recurrence-free | N/A            |
| 4   | Tsugii et al., 1999 [57]     | 22      | F   | R    | Parietal lobe | GTCS         | 12                            | 96                               | Complete resection | Recurrence-free | N/A            |
| 5   | Qian et al., 1999 [6]         | 49      | F   | N/A  | Frontal lobe | GTCS         | N/A                           | 36                               | Complete resection | Recurrence-free | N/A            |
| 6   | Tatke et al., 2001 [20]      | 6       | M   | L    | Temporal lobe | GTCS         | 6                             | 6                                | Complete resection | Recurrence-free | N/A            |
| 7   | Ghosal et al., 2007 [32]     | 26      | F   | R    | Lateral ventricle | GTCS   | 120                           | 6                                | Complete resection | Recurrence-free | Seizure-free   |
| 8   | Aiken et al., 2009 [25]      | 49      | F   | L    | Hippocampus  | N/A          | N/A                           | 6                               | Complete resection | Recurrence-free | N/A            |
| 9   | Aiken et al., 2009 [25]      | 35      | M   | R    | Temporal lobe | N/A          | N/A                           | 6                               | Complete resection | Recurrence-free | N/A            |
| 10  | Mohapatra et al., 2010 [44]  | 48      | F   | R    | Temporal lobe | FIAS         | N/A                           | 6                               | Complete resection | Recurrence-free | Seizure-free   |
| 11  | Yan et al., 2011 [58]        | 34      | M   | R    | Temporal lobe | N/A          | 84                            | 48                               | Complete resection | Recurrence-free | Seizure-free   |
| 12  | Stienies et al., 2013 [53]   | 46      | M   | R    | Parietal lobe | FAS          | 144                           | 10                               | Incomplete resection | Recurrence-free | Seizure-free   |
| 13  | Lyapichev et al., 2014 [40]  | 24      | M   | R    | Temporo-parietal lobe | GTCS | 2                             | 1.5                              | Complete resection | Recurrence-free | Seizure-free   |
| 14  | Brasiliense et al., 2017 [29] | 67      | F   | Both | Frontal lobe and brain stem | FIAS | N/A                           | 4                               | Complete resection | Recurrence-free | Seizure-free   |
| 15  | Abdijaleel et al., 2017 [24] | 62      | F   | Both | Both cerebral hemispheres | FIAS | 60                            | N/A                             | Incomplete resection | N/A          | N/A            |
| 16  | Barber et al., 2018 [28]     | 14      | F   | R    | Fronto-parietal lobe | FAS | 204                           | 9                               | Complete resection | Recurrence-free | 50% reduction |
| 17  | Pasolini et al., 2018 [50]   | 17      | M   | L    | Temporo-occipital lobe | GTCS | 24                            | N/A                             | Complete resection | N/A          | N/A            |

M: male, F: female, R: right, L: left, N/A: not applicable, GTCS: generalized tonic-clonic seizure, FIAS: focal impaired awareness seizure, FAS: focal ware seizure.
| Sex        | Male | Female |
|------------|------|--------|
| Age (y) mean ± SD | 35.5 ± 16.3 | 10 (58.8%) |
| Right      | 4 (23.5%) |        |
| Left       | 1 (5.9%)  |        |
| N/A        | 2 (11.8%) |        |

| Location             | Frontal + midbrain | Temporal | Parietal | Lateral ventricle | Higocampus | Temporo-parietal | Fronto-parietal | Temporo-occipital | Multiple lesions in both cerebral hemispheres |
|----------------------|--------------------|----------|----------|------------------|------------|------------------|----------------|------------------|---------------------------------------------|
|                      | 1 (5.9%)           | 6 (35.3%)| 2 (11.8%)| 1 (5.9%)         | 1 (5.9%)   | 1 (5.9%)         | 1 (5.9%)       | 1 (5.9%)         | 1 (5.9%)                                    |

| Seizure type | GTCS | FAS  | FAS  | N/A | 2 (11.8%) |
|--------------|------|------|------|-----|-----------|

| Time before treatment (months) | Median 84 ranging from 2 to 216 |
|--------------------------------|---------------------------------|

| Postoperative follow-up (months) | Median 9 ranging from 1.5 to 360 |
|---------------------------------|---------------------------------|

| Surgery | Complete resection | Incomplete resection | Seizure-free | Seizure remaining | N/A |
|---------|--------------------|----------------------|--------------|-------------------|-----|
|         | 14 (82.4%)         | 3 (17.6%)            | 9 (53.5%)    | 1 (5.9%)          | 7 (41.1%) |

| Seizure outcome | Seizure-free | Seizure remaining | N/A |
|-----------------|--------------|-------------------|-----|
|                 | 9 (53.5%)    | 1 (5.9%)          | 7 (41.1%) |

| Total | 17 |

N/A: not applicable, GTCS: generalized tonic–clonic seizure, FAS: focal impaired awareness seizure, FAS: focal aware seizure.

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