Clinical Neurophysiology Practice 4 (2019) 164–167

Contents lists available at ScienceDirect

Clinical Neurophysiology Practice

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

Case report

Multinodular and vacuolating neuronal tumor (MVNT): A presumably incidental and asymptomatic case in an intractable epilepsy patient

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ARTICLE INFO

Article history:
Received 20 March 2019
Received in revised form 18 April 2019
Accepted 13 May 2019
Available online 16 July 2019

Keywords:
Post-encephalitis epilepsy
Brain tumor
Long-term video electroencephalogram
Magnetic resonance imaging (MRI)

ABSTRACT

Introduction: Multinodular and vacuolating neuronal tumor (MVNT) had been initially described as an epilepsy-related brain tumor, but recent studies demonstrated it could be found incidentally in non-epilepsy patients.

Case report: A 33-year-old woman with intractable post-encephalitis epilepsy presented a cluster of multinodular T2 hyperintensity in the left temporal lobe, which was very similar to the characteristics of MVNT. Long-term video electroencephalogram demonstrated that the habitual seizures were originated from bilateral temporal area and the interictal epileptic discharges were seen multifocally, although the lesions with MVNT appearance were localized in the left temporal lobe. It was presumed that the epilepsy in this patient was due to encephalitis in the past, and the link between the lesions and the epilepsy in this patient seemed weak.

Conclusion: Although MVNT had been considered as an epilepsy-related brain tumor, we suggest it is not necessarily preferable to perform surgical resection of MVNT even on patients with epilepsy, unless epileptic foci are highly related to MVNT.

1. Introduction

Multinodular and vacuolating neuronal tumor (MVNT) is a newly defined benign brain tumor first described in 2013, and now included in the most recent *World Health Organization Classification of Neoplasms of Central Nervous Systems* (Huse et al., 2013; Louis et al., 2016). Although the tumor was initially associated with epileptic disorders (Bodi et al., 2014; Fukushima et al., 2015, Huse et al., 2013), recent case studies demonstrated MVNT could often be found incidentally in non-epilepsy patients and therefore invasive examination or treatment should be carefully considered (Nunes et al., 2017).

We present a case of MVNT suspected in a refractory epilepsy patient whose long-term electroencephalogram suggested epileptogenicity outside the MVNT lesions.

2. Case report

A 33-year-old woman with intractable epilepsy was referred to our epilepsy center for clinical evaluation. At age 31, she experienced status epilepticus subsequent to a febrile episode and following prolonged coma that continued several weeks. She had no prior history of epilepsy or seizure-related disorders. Initial diagnosis was limbic encephalitis, based on inflammatory findings of cerebrospinal fluid. She was treated with intravenous steroid administration and plasma exchange at another hospital. Although she gradually recovered from comatose state and discharged home in two months without any disability for daily living, symptomatic epilepsy with frequent seizures with impaired awareness persisted. She described that her seizure started with strange odor or déjà vu sensation, and then she felt dizziness or lightheadedness. It sometimes accompanied jerky movements of the right side

Abbreviations: MVNT, multinodular and vacuolating neuronal tumor; MRI, magnetic resonance imaging; T2WI, T2-weighted image; FLAIR, fluid-attenuated inversion recovery; FDG-PET, 18 fluoro-2-deoxyglucose positron emission tomography; vEEG, long-term video electroencephalogram; EEG, electroencephalogram; DNET, dysembryoplastic neuroepithelial tumor.

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https://doi.org/10.1016/j.cnp.2019.05.003
2467-981X/

of her face and arm, and eventually led to impaired awareness. Although she was taking levetiracetam 1000 mg and lamotrigine 400 mg, she usually had 1–2 seizures a day. She had previously taken carbamazepine, lacosamide, perampanel and topiramate which did not lead to improvement.

Her latest brain magnetic resonance imaging (MRI) revealed a cluster of variably sized multiple nodular high intensity lesions on T2-weighted image (T2WI) and fluid-attenuated inversion recovery (FLAIR) in white matter of the left temporal lobe along with the border of inner cortex (Fig. 1A). The lesions did not show any mass effect or enhancement with gadolinium. Similar findings were also observed in the past MRI when the patient had encephalitis two years before, and the size of the lesions were not different from the latest one. The characteristics of MRI findings were consistent with those of MVNT. 18 fluoro-2-deoxyglucose positron emission tomography (FDG-PET) of brain demonstrated moderate decrease of uptake in the lesion area (Fig. 1B). Laboratory findings of her blood and cerebrospinal fluid did not reveal any other causes of epilepsy.

Long-term video electroencephalogram (vEEG) was performed for 72 h and three habitual seizures were recorded: Two of them started with déjà vu and strange odor sensation followed by nodding movement of the head and subsequent fluttering of right hand and foot. Her consciousness was partially impaired during the seizure. vEEG showed rhythmic wave that started from the left middle temporal area and spread to the ipsilateral frontal region, and then to the contralateral hemisphere (Fig. 2A); The other started with lightheadedness and vEEG showed similar rhythmic waves that started from the right anterior temporal area (Fig. 2B). Interictal EEG showed frequent multifocal spikes and sharp waves in the bilateral anterior to middle temporal area.

Based on the EEG findings that demonstrated the multiple independent seizure onsets in both hemispheres, the patient was considered to have bilateral multifocal epileptic foci, whereas the lesions with MVNT appearance on MRI were localized in the left temporal lobe. Although MVNT had been described as an epilepsy-related brain tumor, we refrained from resection surgery because it was not certain that the lesions were epileptogenic in this patient. She has been followed up with multiple antiepileptic drugs.

3. Discussion

We found nodular T2 hyperintensity lesions in brain MRI of a patient with intractable post-encephalitis epilepsy. Although the lesions were localized to the left temporal lobe, her epileptic foci were found to be bilateral and multifocal. We argue that the cause of her epilepsy was a previous encephalitis rather than the apparent lesions on MRI.

We suspected that the lesions were MVNT, originally described as an epilepsy-related brain tumor. MVNT was first identified in

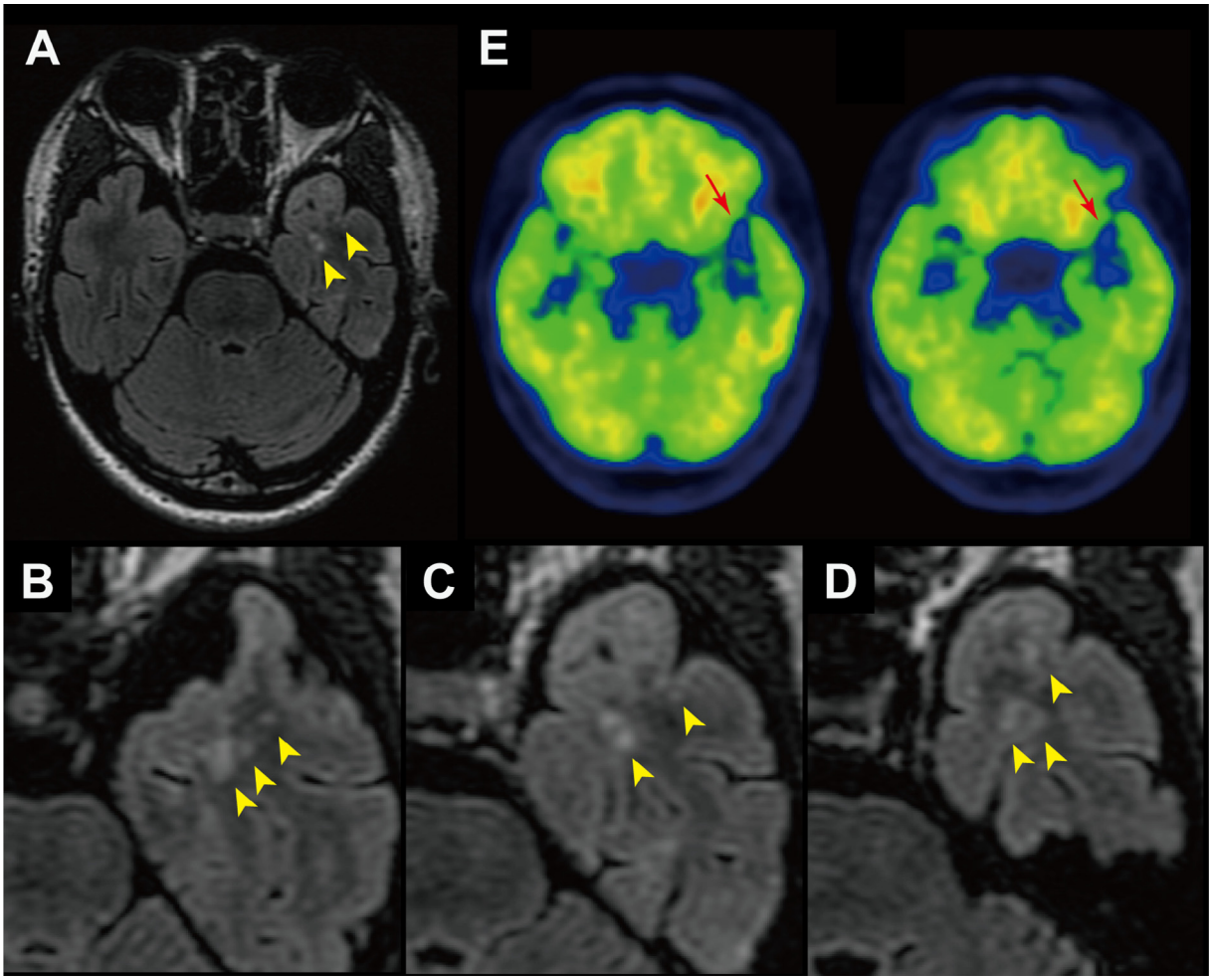

Fig. 1. (A–D) A cluster of multiple nodular high intensity lesions without mass effect *(arrowheads)*, which was compatible with multinodular and vacuolating neuronal tumor (MVNT), was shown in the white matter of the left temporal lobe in fluid-attenuated inversion recovery (FLAIR) of brain magnetic resonance imaging (MRI). (E) Moderately reduced uptake of nuclide *(arrows)* was detected in the lesion area in 18 fluoro-2-deoxyglucose positron emission tomography (FDG-PET) of brain.

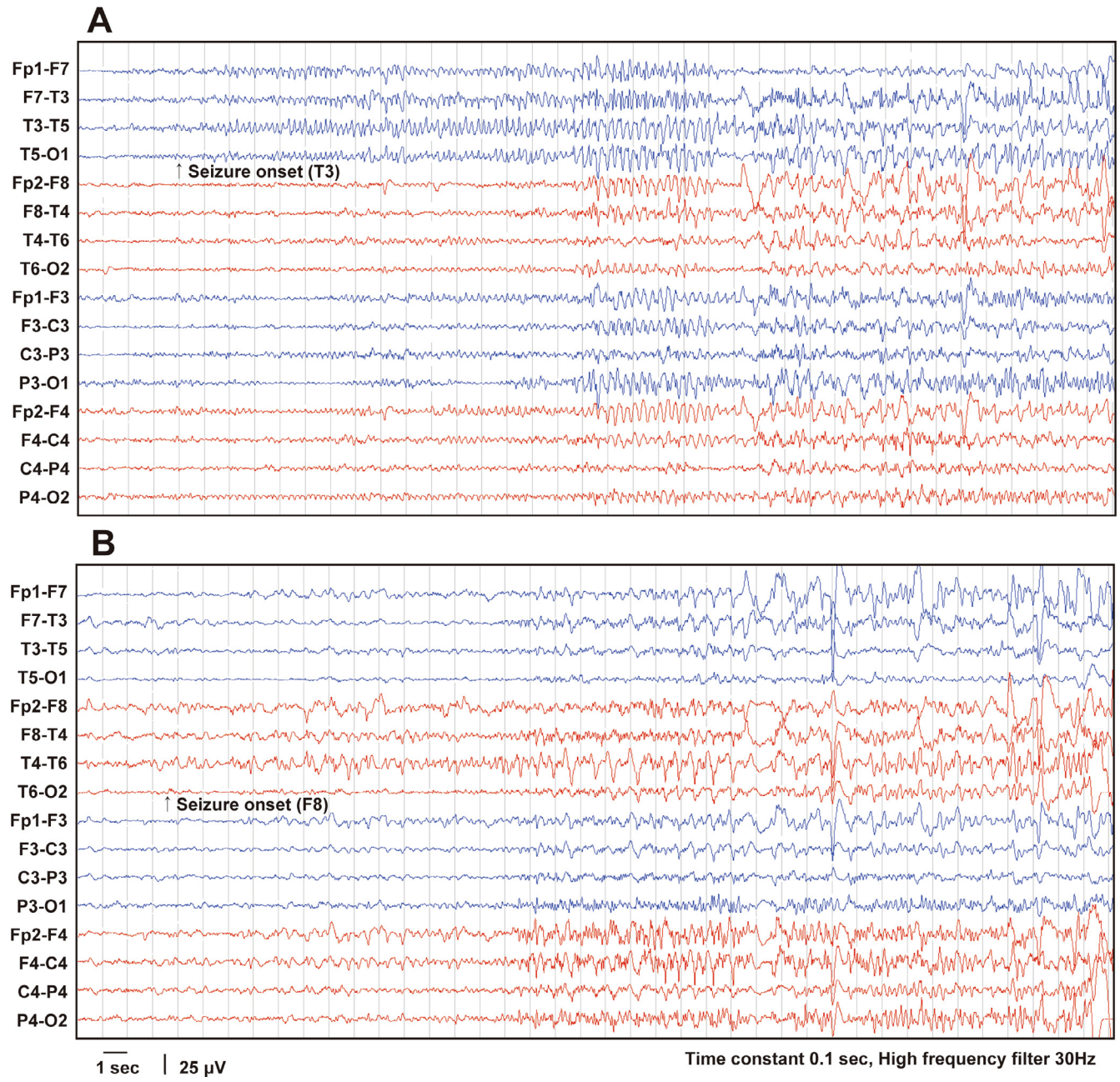

Fig. 2. Long-term video electroencephalogram demonstrated two types of seizures: (A) Rhythmic waves started from middle-temporal area (T3) and gradually increased its amplitudes and spread to ipsilateral frontal area, then to the contralateral hemisphere; (B) The similar pattern of rhythmic waves started from the right anterior-temporal area (F8).

2013 in a case series of 10 patients as surgically resected brain tumors exhibiting varying degree of matrix vacuolization in the neuronal cells (Huse et al., 2013). Seven out of the ten patients had epilepsy and six of them got free from seizure after the resection in the initial study, thus MVNT seemed to be associated with epilepsy. In fact, several subsequent reports showed similar clinical course which supported its epileptogenicity (Bodi et al., 2014; Fukushima et al., 2015; Yamaguchi et al., 2016). Recent report, however, described that epilepsy was found in only 8 of 33 cases of MVNT confirmed pathologically or suspected by MRI (Nunes et al., 2017). A recent case study presented a pathologically confirmed MVNT without any neurological symptoms (Shitara et al., 2018). The authors argued that MVNT may be a "leave me alone" lesion and that it does not necessarily require invasive evaluation and treatment; it is mostly asymptomatic and does not manifest enlargement during its clinical course (Nunes et al., 2017).

It is unclear whether or not the multiple nodular lesions suspected of MVNT in our case were related to her epilepsy, because MVNT has been shown to be either epileptic or asymptomatic as described above. We think that a link between her epilepsy and the left temporal lesions would be weak for three reasons. First, our patient showed bilateral seizure onsets revealed by vEEG despite the fact that the lesions were localized in the left temporal lobe. Second, multifocal epileptic discharges on EEG in this case are consistent with the characteristics of post-encephalitis epilepsy (Trinka et al., 2000), whereas previous case series reporting EEG findings in MVNT patients were mostly unremarkable or questionable spikes at most (Alsufayan et al., 2017; Cathcart et al., 2017).

No previous report on MVNT showed multifocal frequent epileptic discharges as seen in our case. Third, she had no previous episode of epilepsy or seizure-related disorders before, and her epilepsy developed only after the episode of encephalitis. Based on these, it is likely that epilepsy of this patient was due to encephalitis rather than the lesions in left temporal lobe.

One major issue in the present case is the diagnosis of the left temporal lesions. Pathological confirmation would be necessary for definite diagnosis of MVNT. However, MVNT has been reported to show well characterized MRI findings (Alsufayan et al., 2017; Nunes et al., 2017) and the imaging features alone may suffice the diagnosis of MVNT when there is no indication of biopsy or lesionectomy (Alsufayan et al., 2017). MVNT typically demonstrate a cluster of variably sized nodular hyperintensity located on the subcortical ribbon and subcortical white matter in T2WI and FLAIR without mass effect or gadolinium enhancement (Alsufayan et al., 2017; Huse et al., 2013; Nunes et al., 2017), and our case showed similar MRI findings. Non-suppression pattern on FLAIR was presumed to be associated with high protein or solid component within vacuoles (Nunes et al., 2017). Although literature regarding FDG-PET findings in MVNT is scarce, a previous report presented decreased uptake around the pathologically confirmed MVNT lesions [5], which was also similar to our findings. Decreased uptake of FDG-PET in the MVNT lesion area may represent hypometabolism in the vacuoles of the tumor cells. Several differential diagnoses should be considered such as enlarged perivascular spaces, dysembryoplastic neuroepithelial tumor (DNET) and ganglioglioma. However, the lesions in our case showed hyperintensity in FLAIR while enlarged perivascular spaces usually are suppressed in the same sequence. The lack of cortical involvement and mass effect was distinct from DNET and ganglioglioma (Alsufayan et al., 2017; Nunes et al., 2017). The imaging findings of our case were very similar to those reported in pathologically determined MVNT.

Another issue is that we cannot exclude the possibility that the patient had the dual pathology of epilepsy; both post-encephalitis state and MVNT could be the cause of epilepsy at the same time. Along this line, it is impossible to exclude that the epileptic focus in the right temporal area of this patient was secondary epileptogenesis induced by MVNT in the left temporal lobe as the primary focus. It seems important to continue a careful follow-up and consider re-evaluation of epileptogenicity of MVNT whenever needed in the future.

4. Conclusion

We reported an intractable epilepsy case with a history of encephalitis and with left temporal lesions suspected of MVNT. We conclude that it is less likely that left temporal legions were related to her epilepsy. MVNT, initially described as an epilepsy-related brain tumor, could exist as asymptomatic lesions even in epilepsy patients. Our case suggested it is not necessarily preferable to select surgical resection of MVNT even if the patients have epilepsy, unless epileptic foci are highly related to MVNT.

Ethical statement

The patient provided written consent for publication.

Declaration of Competing Interest

The authors declare there is no conflict of interest regarding this research.

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