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Case Report
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A Rare Cause of Recurrent Refractory Status Epilepticus; Familial Cerebral Cavernomatosis

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Abstract

Introduction: Cerebral cavernomas are congenital malformations characterized by abnormal sinusoid-like capillaries in brain. Most of cavernous malformations are asymptomatic and are discovered incidentally through neuroimaging. Clinical symptoms of cavernomas depend on mass effect and irritation of recurrent hemorrhage caused by lesion itself.

Case Report: A 25 years-old male patient was seen in the emergency service with an unconscious state. Before his admission to ER, he had been unconscious for nearly 4 hours and presented convulsions for every 15 minutes. In CT images, multiple hyperdense lesions were detected in both hemispheres and brain stem. There was also a hyperdense lesion located in the septum pellucidum. His EEG which was performed in the clinic showed continuous generalized spike and wave activity. Following two doses of intra-venous diazepam, loading dose of fenitoin was administered. Despite administering multi-drug therapy, his seizures lasted 4 days and required ICU care.

Conclusion: Cerebral cavernomas can be the cause of refractory status epilepticus as presented in our study. It is essential to rapid diagnosis and aggressive treatment.

Keywords: Cerebral Carcinomatosis; Magnetic Resonance Imaging; Status Epilepticus

Introduction

Cerebral cavernomas (CC), also known as cavernous angiomas, are congenital malformations characterized by abnormal sinusoid-like capillaries adjacent to one another with little or no interposed cerebral parenchyma [1]. The overall incidence of intracranial CC is approximately 0.4% to 0.5% in the general population, accounting for approximately 10% to 20% of all cerebral vascular abnormalities [2]. Cerebral CCs are classified into two forms namely sporadic and familial forms. Sporadic form represents with single lesion and has no hereditary association whereas familial form is very uncommon and autosomal dominant inherited in which patients have multiple lesions [3,4]. Most of cavernous malformations are asymptomatic and are discovered incidentally through neuroimaging. Computed tomography (CT) and magnetic resonance imaging (MRI) are used in the diagnosis of CC but MRI is more effective imaging tool for detecting cavernous malformation [5]. Clinical symptoms of CC depend on mass effect and irritation of recurrent hemorrhage caused by lesion itself. These lesion characteristics, especially hemorrhagic transformation, are associated with focal neurologic deficits and seizures. Behold the result, treatment of CC is greatly depended the lesion growth, number and hemorrhagic transformation. However, an established therapy is still under debate [6]. In this paper we present a case with multiple CCs represented with status epilepticus. Seizure control was challenging and established by ICU admission and multiple anti-epileptic drug administration.

Case Presentation

A 25 years-old male patient was seen in the emergency service with an unconscious state. He had a history of seizures for nearly 10 years and he was on medication of levetiracetam with a dose of 2000mg/day. Before his admission to ER, he had been unconscious for nearly 4 hours and presented convulsions for every 15 minutes. At the time of neurologic examination, he had tonic spasms in both upper and lower extremities and torso along with urinary incontinence. A few minutes later, his seizure progressed into the clonic phase. Further neurologic examination showed bilateral positive sign of Babinski and lack of bilateral pupillary reflex. He had a body

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Table 1: Reports of cerebral cavernomas associated with status epilepticus.

Authors	Type of study	No of subjects	Features	Presentation	Outcome/Treatment	Emphasis
Kamada et al. 1994	Case Report	1	Single lesion with unknown family history	Frequent systemic tonic-clonic convulsions	Surgical excision of cavernoma along with resection of additional focus detected with intraoperativeelectrocorticography	A remote epileptic focus can be present and removal of angioma only may not resolve the seizures.
Equchi et al. 1996	Case Report	1	Single lesion with unknown family history	Complex partial seizures with unconscious state	Resolved in one hour with i.v. diazepam	Rarity of the entity. Importance of imaging.
Garcia-Moreno et al. 1998	Case Report	1	Familial form	Status epilepticus	Not mentioned	Association with cutaneous angiomas
Aladdin and Gross. 2008	Case report	1	Pregnancy and single lesion with no family history	Frequent seizures followed by post ictal confusion	Fenitoin, Lorezepam, ICU transfer Carbamazepine, General anesthesia Propofol. Termination of pregnancy	Hormonal factors precipitate the clinical course of cavernoma and trigger the status.

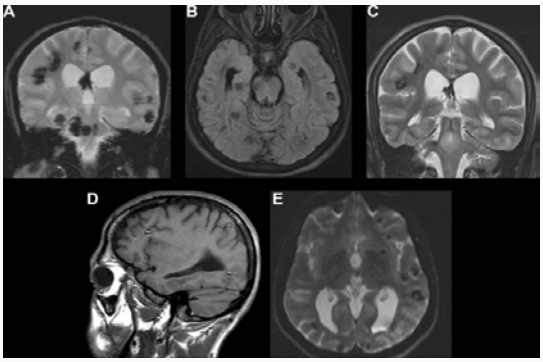

Figure 1: A: Coronal T2 Gradient Echo; B: Axial Flair; C: Coronal T2 weighted; D: Sagittal T1 weighted; E: Diffusion weighted, images of the patient shows extensive lesions consistent with multiple cerebral cavernomatosis.

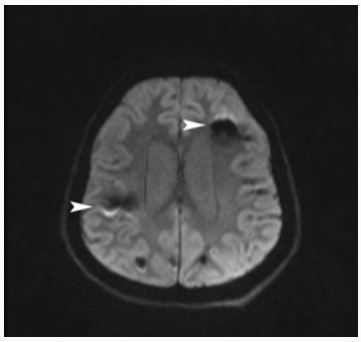

Figure 2: Diffusion weighted MR image acquired with a b value of 1000 s/mm^2 shows magnetic susceptibility artifact at the lesion-parenchyma interface (arrowheads).

temperature of 36.8°C, blood pressure of 130/80 mmHg and heart rate of 80 beats per minute. Laboratory test results were in the normal range by means of blood cell count and biochemical tests. Neuroimaging studies were performed to investigate the possible intracranial cause. CT examination of the brain was performed with 4-row multi detector computed tomography scanner. In CT images, multiple hyperdense lesions were detected in both hemispheres and brain stem. There was also a hyperdense lesion located in the septum pellucidum. The cranial MRI showed a number of lesions showing the typical imaging features of cavernous angiomas at same locations as defined by CT imaging (Figure 1). Magnetic susceptibility artifact at the interface of brain parenchyma and hemosiderin ring was seen on diffusion-weighted images (Figure 2). Intra-venous diazepam with a dose of 10mg was administered in the ER and patient was

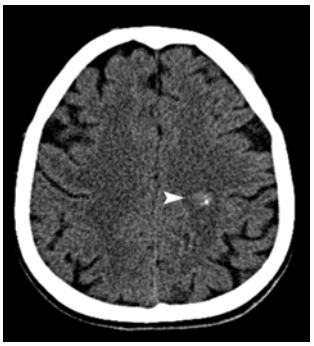

Figure 3: Axial CT image without contrast administration shows single cavernoma with a calcified focus (arrowhead).

admitted to the neurology clinic. His EEG which was performed in the clinic showed continuous generalized spike and wave activity. At this time seizures were occurring once per hour. Following two doses of intravenous diazepam, the loading dose of phenytoin (20mg/kg) was administered. He still had seizures even though he had the loading dose of phenytoin so he was transferred to ICU unit. At this time, seizures were occurring once per two hours. Seizures showed no regression and loading dose of midazolam (0.2mg/kg) administered. Midazolam dose continued as 2mg/kg/h (total 120mg/kg). On his second day, seizures were occurring but with a lower frequency. Phenobarbital was introduced with a loading dose (5mg/kg) and continued as 5mg/kg/h (total 300mg/h). Finally, on the fourth day of admission, seizures were stopped. Phenobarbital infusion continued for further 72 hours and ceased gradually. The patient became conscious. Control EEG was performed and showed periodic theta activity. The patient had no seizures following two weeks. Valproic acid medication was started with the dose of 750mg BID and patients were discharged. He had only one sister as a living relative. She was investigated and brain CT showed single hyperdense parietal lesion (Figure 3).

Discussion

We presented a case of familial cerebral cavernomatosis who had refractory status epilecticus. Patient had multiple cavernomas with hemorrhagic transformation detected on MR imaging. Treatment of status was challenging due to the presence of widespread and atypical presence of lesions.

Magnetic resonance imaging is the technique of choice for detecting CCs [5]. Zabramski et al. classified CCs into four groups according to imaging features in T1 and T2 weighted spin echo

(SE) sequences. Classification aims to classify lesions based on their hemorrhagic nature such as subacute, chronic or both. Authors also introduced gradient echo (GRE) sequence for detecting telangiectasia [7]. Furthermore, GRE sequence has higher sensitivity than SE sequence in imaging of CCs due to its ability to better detect susceptibility effect which is generated by deoxyhemoglobin or hemosiderin in CCs [3]. Subacute hemorrhagic transformation of CCs is characterized by increased intensity in T1 weighted SE images. At this stage, lesion on T2 SE weighted SE images may both be hyper or hypointense. Brunereau et al. found that symptomatic patients have significantly higher lesion counts of type 1 (subacute hemorrhage) and type 2 (mixed) CCs compared with asymptomatic ones whereas there was no significant differences observed between symptomatic and asymptomatic patients regarding the presence of type 3 (chronic hemorrhage) and type 4 (telangiectasias) lesions [3]. These results support the conclusion of Zabramski et al. [7].

Epilepsy and status epilepticus is a commonly encountered entity in the presence of brain tumors. Ten to thirty percent of patients with brain tumors suffer from seizures whereas 7% of all status epilepticus in adults are caused by brain tumors [8,9]. Tumor related status epilepticus has a comparable long term morbidity rate to those which occurred due to other causes [10]. Furthermore, tumor related SE last significantly shorter compared to non-tumor related status epilepticus [11]. However, status epilepticus should be treated aggressively especially when presented as a generalized convulsive status [12]. CC is one the benign tumors thatrelated status epilepticus. Compared with the single CC, multiple CCs are predisposed to develop hemorrhage, seizure, and neurological deficits [13]. The surrounding hemosiderin ring and gliotic tissue may also be responsible for the seizure episode [14].

There are four cases of cerebral cavernoma with status reported in the literature so far (Table 1). In these studies striking features of cavernomas described in addition to classical clinical or imaging findings. Some additional and important conclusions can be derived from these studies: (i) cavernomas could alter structural changes in the brain so that remote epileptic foci may occur. This is important because solely removal of angioma may not be an effective strategy [15]; (ii) status epilepticus can be triggered by single cavernoma [16]; (iii) cerebral cavernomas can be associated with cutaneous angiomas. It is beneficial for the clinician when a patient presented with status and cutaneous angiomas [17]; (iv) status can be triggered by extra-cranial conditions such as pregnancy in a patient with cavernoma. Hormonal factors may alter the clinical course of cerebral cavernomas [18].

Cerebral cavernomas can be the cause of refractory status epilepticus. It is essential to rapid diagnosis and aggressive treatment. MRI should be included in imaging whereas multi-drug approach should be considered. The clinician should be aware that characteristics of lesions, as well as extra-cranial manifestations, could affect the final outcome.

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