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A Case Report of A Female Adolescent with Arteriovenous Malformation and Traumatic Brain Injury

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ABSTRACT

This is the case of a 13-year-old female with a history of Traumatic Brain Injury (TBI) 8 years ago. TBI resulted to acute bleed of the right frontotemporal lobe with residual motor deficit. Patient now presented with unprovoked focal seizures. She was managed as a case of epilepsy and started antiseizure medications. On further work up, she was noted to have Arteriovenous Malformation (AVM) on the right temporal lobe. She successfully underwent embolization of the AVM. Patient tolerated the procedure and the seizures have been controlled since then.

Keywords: Arteriovenous malformation; Seizure; Embolization

INTRODUCTION

Seizures are defined as a transient occurrence of signs and symptoms as a result of abnormal, excessive, or synchronous neuronal activity in the brain characterized by abrupt and involuntary skeletal muscle activity.[1]Epilepsy is the most common neurological brain disorder seen in children.[2] One-third of cases of epilepsy are caused by acquired injuries while the remaining cases are believed to be due to genetic factors. The diagnosis of epilepsy can be challenging since many epilepsy imitators have to be considered hence neuroimaging and electroencephalography seem to be critical in determining the etiology of the condition.[2]

CASE DESCRIPTION

KM, a 13 year old female, from, Davao City, Philippines came in due to seizures. The history was first noted 8 years PTA (2014) when she had a history of fall while playing associated with loss of consciousness, vomiting, blurring of vison, slurring of speech and paralysis of the left upper extremity. This prompted consult at a local hospital where

cranial CT scan was done and showed hemorrhage at the right fronto-temporal lobe. Patient was admitted for 18 days and managed medically and eventually discharged with residual left upper extremity weakness. Physical therapy was done for a short duration. Focal deficit persisted.

Eight years PTA, with persistence of the left sided weakness, the patient was noted to have changes in behavior, manifested as easy irritability. Repeat cranial CT scan was done which showed malacic changes in the right frontal lobe. No intervention was done. In the interim, patient underwent physical therapy for the left sided weakness. No significant improvement was noted but otherwise the patient lived a normal life.

Nine (9) months prior to admission, patient complained of numbness of the face with onset of left sided hemifacial twitching. Patient had 2 episodes per month lasting about 5 seconds each. Consult was done with a pediatric neurologist and managed as a case of epilepsy. She was given Levetiracetam as maintenance medication. Electroencephalogram (EEG) was done which showed spikes and slow waves at the right frontotemporal and frontocentral areas. Cranial CT scan was requested but was not done due to the pandemic.

Six (6) months prior to admission, seizure episodes increased in frequency, now occurring 3 times a day. Follow up was done and dosage of levetiracetam was increased. Cranial CT scan was done which revealed AVM, right frontal, and hence was advised consult with a neurosurgeon. (See Appendix A)

Five (5) months PTA, patient was seen by neurosurgeon who gave them 3 options to address the AVM; 1) Surgery; 2) Embolization 3) Radiosurgery. Family opted for embolization and was referred to our institution.

Patient was seen by Interventional Radiology the following month and cranial CT 4 vessel angiogram was done which showed tuft of tortuous dilated vessels at right temporal lobe confirming a diagnosis of AVM and an old infarct in the right frontal lobe. Embolization was not done immediately due to financial constraints.

Two (2) months PTA, seizure episodes worsened with increasing episodes about 2-4 times per day, lasting for 20-30 seconds. Thus, she was given Valproic Acid and advised to continue Levetiracetam. No noted recurrence of seizure with the additional medication.

One (1) month prior to admission, patient complained of headache with a pain scale of 8/10. It was localized on the frontal area, non-radiating, relieved by paracetamol and sleep. Headache episode also recurred 3 weeks PTA. Patient also had breakthrough seizure 1 week prior to admission. With the presence of headache and seizure episode, embolization was immediately scheduled hence admitted.

The patient had history of allergic rhinitis but no previous surgeries. Her mother and aunt had migraine headaches while her cousin had acute cerebral bleed.

Physical Examination showed stable vital signs and growth parameters appropriate for age. She was conscious, coherent, cooperative, not in distress. Other physical examination findings are essentially normal. Pertinent neurologic examination showed the following results: Motor: 5/5 in right upper and lower extremities, 4/5 in left upper and 5/5 left lower extremities. She had spastic fingers on the left with limitation on extension after flexion for a few seconds. No sensory deficits and deep tendon reflexes are normal with 2+ in all extremities.

Patient was admitted under the service of interventional radiology and comanaged with Pediatric Neurology. Bleeding parameters and electrolytes were within normal. Embolization of the arteriovenous malformation at the right temporal area was successfully done however with note of aneurysmal rupture from the AVM nidus. Embolization was rapidly performed using liquid Onyx until vascular stasis and absence of contrast extravasation was achieved.

DISCUSSION

The International League Against Epilepsy (ILAE) Task Force defined epilepsy as any of the following conditions: 1) At least two unprovoked (or reflex) seizures occurring >24 h apart; 2) One unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; 3) Diagnosis of an epilepsy syndrome.[3]

Epilepsy is the most common neurological brain disorder seen in children.[2] One-third of cases of epilepsy are caused by acquired injuries while the remaining cases are believed to be due to genetic factors. The diagnosis of epilepsy can be challenging since many epilepsy imitators have to be considered hence neuroimaging and electroencephalography seem to be critical in determining the etiology of the condition.[2] Adequate anti-seizure medications usually result in satisfactory seizure control, and enable persons with epilepsy to lead a normal life.

The International Classification of Epileptic Seizures divides epileptic seizures into 2 large categories: focal (formerly known as partial) seizures, the first clinical and electroencephalographic (EEG) changes suggest initial activation of a system of neurons limited to part of 1 cerebral hemisphere. The term simple partial seizures is an outdated classification that refers to focal seizures with no alteration in consciousness whereas complex partial seizures, currently also referred to as focal dyscognitive, denote focal seizures with altered awareness of the surroundings. In generalized seizures, the first clinical and EEG changes indicate synchronous involvement of all of both hemispheres.[4] In seizures where the beginning is missed or obscured, the onset is classified as unknown.[5] For this case, we would be limiting our discussion to focal seizures.

Partial (now referred to as focal) seizures account for approximately 40% of seizures in children and can be divided into simple partial seizures (currently referred to in the most recent ILAE classification as focal seizures without impairment of consciousness), in which consciousness is not impaired, and complex partial seizures (currently referred to as focal seizures with impairment of consciousness, also called focal dyscognitive seizures), in which consciousness is affected. Simple and complex partial seizures can each occur in isolation, one can temporally lead

to the other (usually simple to complex), and/or each can progress into secondary generalized seizures (tonic, clonic, atonic, or most often tonic–clonic).[4]

Focal seizures without impairment of consciousness can take the form of sensory seizures (auras) or brief motor seizures, the specific nature of which gives clues as to the location of the seizure focus. Brief motor seizures are the most common and include focal tonic, clonic, or atonic seizures. Often there is a motor (Jacksonian) march from face to arm to leg, adversive head and eye movements to the contralateral side, or postictal (Todd) paralysis that can last minutes or hours, and sometimes longer. Unlike tics, motor seizures are not under partial voluntary control; seizures are more often stereotyped and less likely than tics to manifest different types in a given patient.[4]

Etiology of the seizure in general can be structural, genetic, infectious, metabolic, immune, or unknown.[5] Of particular interest in this case is the structural etiology of seizures. Structural lesions that are commonly resected for the treatment of focal epilepsy can be divided into six main disease categories: hippocampal sclerosis, brain tumors, malformations of cortical development, vascular malformations, glial scarring (including stroke and traumatic brain injury) and brain inflammation.[6] Hippocampal sclerosis characterized by neuronal cell loss in anatomically defined sectors of the hippocampal formation. The hippocampus becomes atrophic, which is visible as volume loss on MRI T1-weighted sequences and hyperintense signal on T2/fluid attenuated inversion recovery (FLAIR)-weighted sequences.

The etiology of hippocampal sclerosis is likely a complex interplay between genetic background/causes and environmental insults, including prolonged febrile seizures, traumatic brain injury, and infective cause A frequent cause of focal-onset seizures are brain tumors, accounting for 10% to 15% of all adult-onset and 0.2% to 6% of all child-onset epilepsies. Brain tumors with a glioneuronal composition are of particular interest in epilepsy, as they often present with seizures in childhood, are usually of low malignancy (Grade I), and occur mostly in the temporal lobe. Typical examples are gangliolioma and dysembryoplastic neuroepithelial tumors. Most malformations of cortical development present with drug-resistant seizures in early childhood. Focal cortical dysplasia (FCD) is the commonest epilepsy-associated brain malformation and occurs most often in the frontal lobe. Malformations of cortical development are divided into those that result from: abnormalities of neuronal proliferation/apoptosis (such as microcephaly, type II FCD, cortical tubers in patients with tuberous sclerosis complex and hypothalamic hamartomas); abnormal neuronal migration (such as lissencephaly, grey matter heterotopia, double cortex and cobblestone cortex); and abnormal post-migration cortical development (such as polymicrogyria and schizencephaly).

Vascular malformations associated with seizures include cortically-located cavernous hemangiomas (cavernoma) and arteriovenous malformations. The vast majority of such lesions are not associated with epilepsy, and secondary phenomena, such as intracranial hemorrhage and/or hemosiderin deposition, in surrounding cortex are necessary to generate seizures. Seizure onset is, therefore, usually later compared to other disease categories.

Glial scarring is another common disease category in focal epilepsies and results from an exogenous brain insult, often traumatic brain injury (usually presenting as glio-mesodermal scar). In patients with early-onset focal onset

epilepsy, ischemic or hemorrhagic stroke are the most common causes for glial scarring (e.g. encephalomalacia after perinatal injury). The epileptogenic mechanisms of gliosis are not yet fully understood. Molecular alterations of astrocytic ion channel composition or increased adenosine kinase production may play a role. Interestingly, glial scars resulting from neurosurgical interventions rarely produce a seizure disorder.

In this case, post traumatic epilepsy is considered since patient had a history of TBI and seizures with previous imaging of malacic changes. Tumor is also considered since seizure is one of the most common symptoms of pediatric brain tumors. Pediatric tumors usually present as generalized seizure owing to their usual infratentorial origin. However some focal seizure secondary to tumor can also be found in glioma and meningioma.

AVMs are usually silent disease and asymptomatic until rupture. Some usual presentation includes hemorrhage, recurrent headache and seizures. Seizure is the second most common presentation of AVM, which occur in 20%–45% of patients.[7] The mechanism of seizure in AVM is multifold, and includes those seizures directly due to hemorrhage and hemosiderosis, as well as seizures secondary to vascular steal, perinidal edema, and nidus size and location.[7] In those who present with seizure, at least 50% of patients with AVM will experience seizure recurrence within 5 years of a first-ever seizure event.[7]

AVMs are unusual focal aggregations of dilated arteries and veins in the brain parenchyma where the absence of a normal vascular structure and capillary bed leads to direct connections between arteries and veins.[8] The prevalence of AVMs is estimated to be between 0.06 and 0.11% from on autopsy-based review.[9] Locally, the prevalence has been estimated at 0.2% to 0.8% of the general population,[10] however this data is sorely outdated. Currently there is no recently published local data on the incidence for AVM.

With untreated AVMs, the annual risk of rupture in children is 4.4%–5.5%, and that risk is significantly reduced after treatment.[11] Reviewing this patient's history, the first symptom of this patient was cerebral hemorrhage which happened 8 years PTA. It was attributed though to the head trauma.

Arteriovenous malformations (AVMs) were traditionally thought to represent congenital lesions resulting from disordered embryogenesis however other studies have supported the notion that they can also develop postnatally.[12] Altered flow dynamics, structural vascular abnormalities, and underlying molecular mechanisms all play a role in the development of AVMs.[13] Feeding artery pressures may predispose to rupture, possibly due to increased vessel wall stress.[14] Abnormal venous architecture and venous hypertension also contribute in the development and rupture of AVMs.[14]

Diagnostics: Digital subtraction angiography (DSA) is the reference standard for the evaluation and characterization of brain AVMs. Its unsurpassed spatial and temporal resolution allow it to readily delineate the arterial supply, nidus, and venous drainage of an AVM and to depict hemodynamic factors, such as the degree of arteriovenous shunting, which are largely inapparent on noninvasive imaging. One of the important angiographic features is the visualization of the AVM during the arterial phase of an early draining vein since this feature confirms the presence of an arteriovenous shunt. Intraventricular hemorrhage as a result of AVM rupture is secondary to the apex of the nidus (seen as a wedge-shaped arrangement of tangled vessels on cerebral angiography) projecting toward the ventricular surface. Furthermore, in the presence of hemorrhage, mass effect can be appreciated on an angiography. It is important to note that a thrombosed AVM may not be detected on a cerebral angiography.[15]

Other imaging modalities which are often the initial studies used to evaluate symptoms that are not specific to AVMs include CT, CT angiography, MRI, and magnetic resonance angiography. However, these imaging techniques are limited in their sensitivity and ability to provide detailed imaging of AVM architecture. Each imaging technique provides its own unique strength: CT angiography provides better vascular detail of AVMs. MRI and magnetic resonance angiography provide greater visualization of surrounding structures adjacent to the nidus. Furthermore, MRI can detect thrombosed vessels as hyperintense signals and show any associated hemorrhage at various stages of evolution. T2-weighted and GRE sequences are the most sensitive to breakdown products. MRI can be important for preoperative planning because it allows for an appropriate surgical approach while demonstrating the relationship of the AVM and important parenchymal structures.[15]

Treatment: Multimodality therapies for AVMs are currently available including open vascular resection, radiosurgery, and/or endovascular embolization[7]:

1. Craniotomy for surgical resection of an arteriovenous malformation was first reported in the 1920s, but the surgical procedure has been refined with the use of the operating microscope, stereotactic guidance, and modern instrumentation. Microsurgical cauterization of feeding arteries and of draining veins allows for complete removal of the arteriovenous malformation as a single specimen but necessarily poses some risk to contiguous brain tissue, since the dissection plane is outside the boundary of the malformation. The clinical implications of any damage to the surrounding tissue depend on the functional significance of the brain regions contained in the margins of the proposed surgical resection, and these implications have to be considered during the process of treatment selection and preoperative evaluation.
2. Stereotactic radiosurgery is a well-studied treatment for cerebral arteriovenous malformations. Equivalent technologies, such as a gamma knife, cyber knife, and proton beam, deliver focused, high-dose radiation to the arteriovenous malformation, which induces gradual sclerosis of the blood vessels and thrombosis of the lesion. Successful obliteration of the arteriovenous malformation is predicted on the basis of the size of the lesion and the dose of radiation delivered to the margins of the malformation (the “marginal dose”). Lesions that respond most favorably to stereotactic radiosurgery are very small, VRAS grade 1 or 2 malformations (<4 cm3), which are treated with a radiation dose of 18 Gy or more. With this treatment, the rate of lesion obliteration, assessed by means of either magnetic resonance imaging (MRI) or angiography, approaches 80%. Larger lesions (grades 3, 4, or 5) are treated with lower marginal radiation doses and are cured less than half the time (48%), and treatment is associated with a considerable risk of radiation-induced necrosis of the adjacent brain (3%). One of the greatest limitations of stereotactic radiosurgery for an arteriovenous malformation is the substantial delay in the radiographic obliteration of the lesion, which takes 2 to 4 years on average. Most data suggest that the risk of bleeding during this period is only slightly lower than the risk during the period before treatment.

3. Endovascular treatment of arteriovenous malformations is achieved by microcatheter delivery of agents such as N-butyl-2-cyanoacrylate or a non-adhesive ethylene vinyl alcohol copolymer. The procedure requires super selective catheterization of arteries feeding the arteriovenous malformation, with the goal of filling the nidus and occluding feeding vessels while preserving collateral vessels to the normal adjacent brain. Most often, partial embolization has been used in preparation for definitive microsurgical resection. With larger arteriovenous malformations in particular, preliminary embolization causes a staged reduction in blood flow and ameliorates the disturbed regional vascular autoregulation, which can otherwise result in bleeding into the normal surrounding brain during and after surgical resection, a phenomenon termed "perfusion pressure breakthrough." Preoperative embolization also reduces surgical morbidity by occluding deep arterial feeding vessels, minimizing the need for extensive dissection into deep white matter pathways adjacent to the arteriovenous malformation. Nevertheless, preoperative embolization has resulted in persistent neurologic deficits in 2.5% of patients.
4. The advantage of microsurgery lies in superior AVM obliteration rates and swift seizure response. In addition, by incorporating electrophysiological monitoring during AVM resection, adjacent or even remote epileptogenic foci can be identified, leading to extended lesionectomy and improved seizure control. Radiosurgery, despite resulting in reduced AVM obliteration and prolonged time to seizure freedom, avoids the risks of surgery altogether and may provide seizure control through various antiepileptic mechanisms. Embolization continues to be used as an adjuvant for both microsurgery and radiosurgery.

In our case, patient preferred embolization since it was less invasive than open surgery. It is believed that AVM embolization provides its benefit on seizure control by rendering epileptogenic brain tissue hypoxic, although this may induce intranidal angiogenesis and thus seizure recurrence. Notwithstanding, patients treated solely with embolization who continue to experience seizures probably harbor residual gliotic plaques and perinidal gliosis, in addition to epileptic foci distal from the primary AVM site. (Figure 1 & 2)

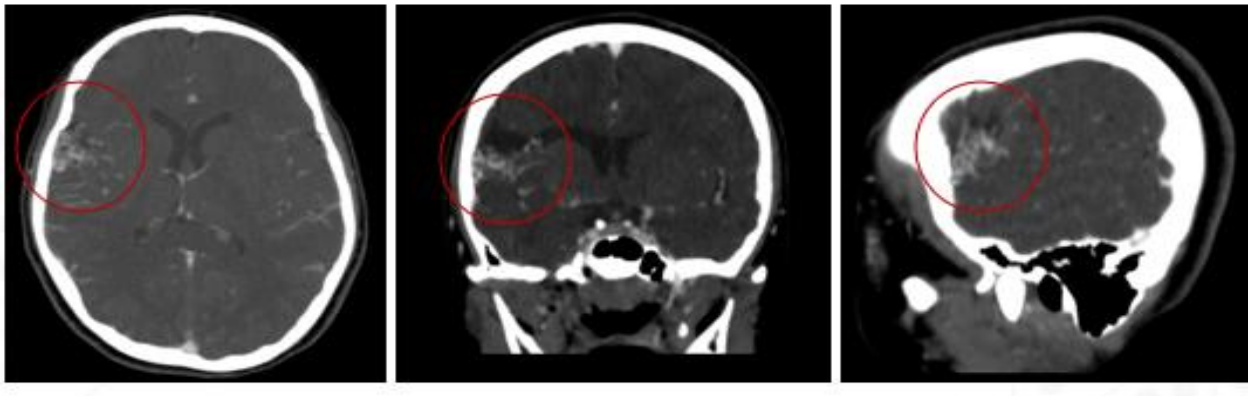
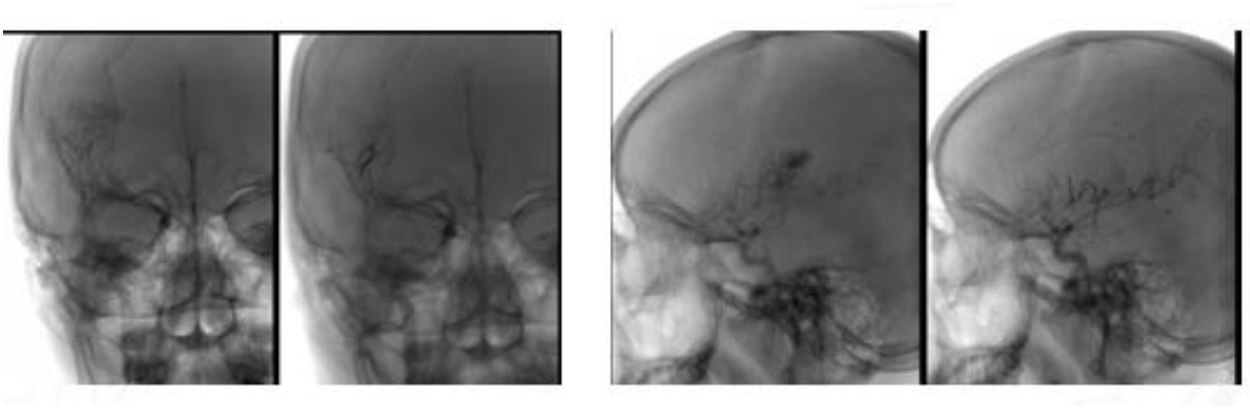


Figure 1: Contrast enhanced CT scan was requested which showed tuft of tortuous dilated vessels at right temporal lobe confirming a diagnosis of AVM. Not seen in this view is the chronic infarct at the frontal lobe



A. Pre Embolization **B. Post Embolization**

Figure 2: A. Tuft of tortuous, dilated blood vessels that is supplied by multiple branches from the insular (m2) segment of the right MCA measuring about 3.5 x 3.7 x 2.2 (APxWxH) can be seen pre-embolization. The interventional radiology service proceeded with embolization with Onyx. B. Post embolization angiography of the right ICA showed almost complete obliteration of the AVM nidus (about 90%) with significantly decreased venous drainage.

CONCLUSION

Arteriovenous malformations are lesions that are defined by the presence of arteriovenous (AV) shunting through a nidus of coiled and tortuous vascular connections that connect feeding arteries to draining veins. The most common presenting symptoms are cerebral hemorrhage and seizures as seen in this patient. Treatment can be open vascular resection or radiosurgery and or endovascular embolization. With untreated AVMs, the annual risk of rupture in children is 4.4%–5.5%, and that risk is significantly reduced after treatment. Multimodality therapies are currently available including open vascular resection, radiosurgery, and/or endovascular embolization. My patient underwent endovascular embolization using Onyx. At present she is seizure free. Antiseizure medications are continued. Physical therapy of her left upper extremity weakness is planned.

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