Case Report

Intracranial Tumour Presenting with Varying Seizure Types

Adetunji Obadeji, Benjamin O. Adegoke

Department of Psychiatry, Ekiti State University Teaching Hospital, Ado-Ekiti, Ekiti State, Nigeria

ABSTRACT

Epileptic seizures are one of the common manifestations of brain tumors. Identifying the cause of seizures remains the main challenge in most developing countries; either due to the absence of appropriate radiological equipment like the CT scan and MRI or when available, the affordability of the cost of such investigations by the patient becomes a challenge. This makes radiological evaluation a non-routine investigation for seizure management in this part of the globe. Often times, such seizures manifest as focal seizures with secondary generalization and are often refractory to antiepileptic treatment but with remarkable response to surgical intervention, particularly in benign ones. Here, we present a 22-year-old man who presented with varying seizure types following an intracranial cyst, and poor response to anti-epileptic medications. The changing presentations possibly suggest the progression or increase in the size of the cyst. An awareness of this presentation may lead to an earlier identification of the cause of such seizures.

INTRODUCTION

Epileptic seizures are one of the manifestations of brain tumors. In most developing nations like ours, identifying the cause of seizures remains a main challenge; this may be due to absence of appropriate radiological equipment like the CT scan or MRI, and when this is available, affordability of the cost of such investigations by patient maybe a challenge; thus making radiological evaluation a non-routine investigation for seizure management. Among patients with brain tumors, about 30–60% present with seizures as their initial symptom.[1,2] With slow-growing primary brain tumors, however, the seizure incidence increases to about 80–90%,[3,4] and between 60% and 100% among low-grade gliomas, while among those with glioblastomas it ranges between 40% and 60%.[5] Often times, the seizures manifest as focal seizures with secondary generalization and are often refractory to antiepileptic treatment;[6] with approximately 15%–50% of patients with low grade gliomas demonstrating pharmaco-resistance, particularly with insular or temporal tumor or the presence of simple partial seizures.[7,8] In a significant number of patients, seizures represent the first clinical sign of a brain tumor, though representing a favorable prognostic factor.[7]

The pathogenesis of tumor-related epilepsy remains poorly understood, however, two pathways of tumor-related epilepsy have been proposed[9]. First, the tumor itself may excrete molecules that could make the tumor tissue epileptogenic, or rather change the peri-tumoral micro-environment and turn this into an epileptogenic zone. Secondly, the tumor compresses the surrounding normal tissue, which eventually becomes epileptogenic following

Corresponding author:
Dr. A. Obadeji
Department of Psychiatry, Ekiti State University/Ekiti State University Teaching Hospital,
PMB 5535, Ado-Ekiti, Ekiti State, Nigeria. E-mail: doctunjioba@yahoo.com. Phone: +2348083150116

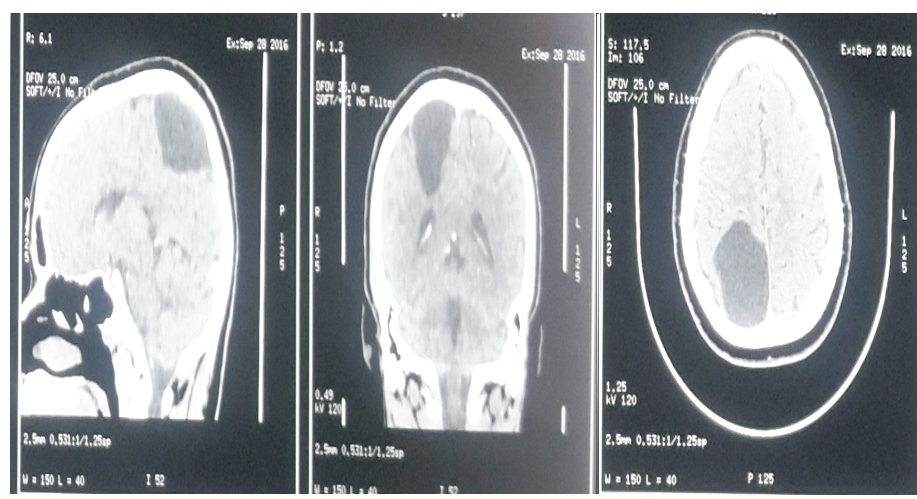
ischemia or hypoxia. These may cause secondary changes, such as alteration in the neurotransmitters and their receptors, inflammatory responses or rather metabolic changes that eventually cause seizures. However, neither of these theories can fully explain the patterns of seizure incidence. The pathogenesis of seizure development is likely to be different for brain tumors with a different histology.[9] For example, developmental tumors with well-differentiated cells release neurotransmitters and other modulators that are involved in epileptogenesis.[10] Understanding of epileptogenesis may provide guidance in the search for new strategies for surgical and medical treatments of tumor-related epilepsy.

CASE REPORT

We present a 22year old man who presented at our neuropsychiatric unit with a history of repeated sudden loss of awareness of his surroundings and loss of speech. Such episodes usually lasted for few minutes before regaining consciousness. The frequency gradually increases and at the time of presentation he experiences about five to seven episodes a week and at different settings; school, church, or in the house. At this time, there was no associated history of loss of muscle tone or jerky movement of the limbs.

Based on clinical history, a tentative diagnosis of absence seizure was made. He was commenced on Ethosuximide. At the same time, EEG and laboratory investigations such as electrolytes, urea, and creatinine were requested. The EEG revealed an epileptiform pattern in keeping with a generalized tonic-clonic seizure. The laboratory tests requested were essentially within normal limit. Based on the EEG report the medication was reviewed and changed to Carbamazepine, and gradually titrated to a dose of 1200mg a day. There was a gradual reduction in symptoms and he became symptom-free after 2months of commencement of medication.

He was seizure free for about 8months,subsequent to which he developed seizure characterized by tonic-clonic jerking of the limbs with associated loss of consciousness. Carbamazepine was titrated up but no significant reduction in frequency as well as the intensity of the seizure. This necessitates the addition of a second antiepileptic drug -sodium valproate, still without any significant improvement. Alongside with the above presentation, he also started having an episodic history of restlessness, abnormal behavior, undue aggressiveness and loss awareness of the environment. He was re-evaluated and CT was requested alongside some laboratory tests. The CTscan showed a well-circumscribed non-enhancing hypo-dense cystic lesion in the area of the right parietal lobe (Figure 1). The lesion communicates with subarachnoid space. There was associated compression of the adjacent brain parenchyma, with mild elevation of the overlying parietal bone. The basal ganglia, corpus callosum, and internal capsule appeared normal on radiological



examination. There was no feature of raised intracranial pressure. Based on these features, an assessment of right parietal lobe cyst was made.

He was referred to a Neurosurgeon, subsequently had craniotomy with the excision of the cyst. Following the surgery, there was a remarkable reduction in the intensity and frequency of the seizure. He was still maintained on carbamazepine after the surgery.

DISCUSSION

The case reported in this report represented patterns of epileptiform seizures in a 22-year man with onset at the age of 16. The seizures present in varying form and intensity. Although the initial presentation looks like absence seizure, the EEG pattern was in keeping with generalized tonic-clonic seizures which necessitate changing the medication from ethosuximide to carbamazepine. With the commencement of carbamazepine, there was a remarkable reduction in seizure frequency and severity and subsequently remission of symptoms.

After eight months of remission, he developed seizures characterized by tonic-clonic jerking of extremities with associated loss of consciousness. Initially, we thought this may be been due to poor adherence to medication due to improvement in symptoms. However, the patient claimed adherence to medications as prescribed. The dosage of carbamazepine was increased but no appreciable improvement was noticed, even with the addition of another anti-epileptic. The worsening of the seizure at this time may be due to the progression of the tumour or its effect on adjoining structures. As the tumor progresses, the tumor mechanically compresses the surrounding normal tissue, which eventually becomes epileptogenic after suffering from ischemia and hypoxia.[9,10]As noted earlier, such changes may alter neurotransmitters and their receptors activities or cause metabolic changes or inflammatory response which eventually produce epileptic seizures.[10] These tumors may also be associated with structural epileptogenic abnormalities of the cortex.

Later in the course of the illness, the patient developed seizure with predominant features of complex partial seizure despite adherence to medication. Addition of another anti-epileptic medication (Sodium valproate) did not produce significant improvement. Ideally, a combination of two drugs (polytherapy) may seem effective and possibly produce a synergistic action in cases of recurring seizures.[7,10] This necessitated the need to re-evaluate the patient; order for additional investigations including a brain CT scan. This was highly revealing as the CT scan showed a well-circumscribed non-enhancing hypo-dense cystic lesion in the area of the right parietal lobe (Figure 1). Further enlargement of the lesion or mass may have resulted in comprehension of other brain regions such as the temporal lobe thus presenting with varying seizure types we observed.

With the identification of the mass, the patient was referred to a Neurosurgeon for review and surgical intervention. With surgical intervention, there was a drastic reduction in frequency and severity of seizures over time. It has been said that each modality of tumor control (i.e., surgery, radiotherapy, and chemotherapy) contributes to seizure control. Nonetheless, about one-third of the patient with seizures secondary to brain tumours shows pharmaco-resistance to antiepileptic drugs (AEDs). Following first-line antitumor therapy, a recurrence or worsening of seizures usually heralds the progression of GBMs in approximately two-thirds of patients, although, in low-grade gliomas, this association is less evident.[11]

In seizures associated with low-grade gliomas (LGGs), molecular biology has highlighted the presence of a mutation of codons 132 and 172 of

isocitrate-dehydrogenase 1 (IDH1) and 2 (IDH2). Normally, IDH1 catalyzes the conversion of isocitrate to a-ketoglutarate as part of the citric acid cycle, but with mutation, 2-hydroxyglutarate will be formed instead.[4] This shows structural similarity to glutamate and may activate N-methyl-D-aspartate (NMDA) receptors, thus ensuing epileptogenesis.[4,12] The presence of IDH1 mutations has been shown to be associated with seizures as the initial clinical symptom, longer survival or the presence of the tumor in the frontal lobe.[4]

As highlighted by Vecht, Kerkhof & Duran-Pena, (2014),[10]tumour early identification and duration of seizure before surgery is key to improving seizure outcome. Worsening of seizures despite adherence to medications or varying seizure presentations as in this case may be an indication to re-evaluate the seizures. Identifying the seizure type and individual patient factors are keys to effective management with anti-epileptic medication.[10] The choice of medication is very important. Levetiracetam has been described as the agent of choice in the management seizures secondary to intracranial tumours, followed by valproic acid and where non of these is not effective or well tolerated, lacosamide, lamotrigine, or zonisamide are other preferable options.[10]

CONCLUSION

We've presented a 22year old man with intracranial cyst presenting with multiple seizure types, possibly resulting from the growth and extension to different brain areas. Although there was an initial response to anti-epileptic medication, there was a poor response to medication despite adherence. The case highlighted the need to re-evaluate seizures, more importantly when there is resistance to medication or change in clinical presentation.

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