Neurology Asia 2013; 18(1) : 23 – 27

Epilepsy profile in adult Nigerians with late onset epilepsy secondary to brain tumor

[1]LF Owolabi, [2]RO Akinyemi, [3]MO Owolabi MO, [1]UM Sani, [3]A Ogunniyi

[1]Aminu Kano Teaching Hospital, Kano; [2]Federal Medical Centre, Abeokuta; [3]University College Hospital, Ibadan, Nigeria

Abstract

Background: Occurrence of epileptic seizure in patients with brain tumors is not uncommon. In spite of the huge data from the developed world on epilepsy caused by brain tumor, there is paucity of data emanating from Nigeria, hence, this study. *Methods:* The cases were recruited from a total of 302 consecutive patients with late onset epilepsy, with first episode of seizure after 25 years of age, from three tertiary centres in northern and southern Nigeria. Information was collected on the demography, seizure characteristics, and additional neurological, cognitive or behavioral symptoms. All the patients had EEG and neuroimaging. *Results:* Sixty six patients, comprising 48 males (73%) and 18 females (27%) had symptomatic seizure from brain tumor which constituted 21.9 % of patients. Seizure was the only symptom in 27.3% and the first symptom in 36.4% of the patients. Forty five (68.2%) patients had focal seizure. The most common histological type was low grade astrocytoma. Common EEG findings were epileptiform discharges (54.5%) and focal slowing (24.2%). EEG was normal in 10.6% of the patients.
Conclusion: Seizure as the initial symptom was common among Nigerian patients with brain tumor presenting as late onset epilepsy. Gliomas were the most common brain tumor. There is need to investigate for tumor in Nigerian patients presenting with late onset epilepsy.

INTRODUCTION

Occurrence of epileptic seizure as presenting feature in patients with brain tumors is not uncommon and many studies have been conducted in this respect.[1-4] Studies have suggested that 30–70% of patients with supratentorial tumors will develop seizures during the course of their disease.[5-7] Seizure could also be an established forerunner of a brain tumor in 15 to 100% of patients.[7-9] Approximately 20–40% of adults with brain tumors suffer a seizure before the tumor is diagnosed and an additional 20–45% will develop seizures during the course of tumor treatment and follow-up.[9-10] Even among children, studies have shown that seizures were the presenting clinical symptom in 12% of children with a primary brain tumor.[11]

In spite of the huge data from the developed world on epilepsy caused by brain tumor, there is scarcity of information regarding seizure characteristic, electroencephalographic and neuroimmaging findings among Nigerian adult patients with brain tumors.[12-18] The purpose of this study was to review the detailed seizure characteristics of a population of adult subjects with brain tumors from multiple centres in Nigeria.

METHODS

The study design was prospective. Subjects were recruited from a total of 302 consecutive patients, presenting at University College Hospital (UCH) Ibadan (southern Nigeria), Aminu Kano Teaching Hospital (AKTH), Kano (Northern Nigeria) and Murtala Muhammad Specialist Hospital (Northern Nigeria), with epilepsy of late onset (i.e seizure onset at ≥ 25 years of age)[19,20] from June 2003 to June 2008. Eligibility criteria included at least one unequivocal witnessed seizures and a clinically and radiologically diagnosed brain tumor, from the general and medical outpatient clinics of the health facilities. Seizure and epilepsy were defined according to the International League Against Epilepsy classification in 2005.[21] The documentation included: sex, age at onset of seizures, age at diagnosis of brain tumor, seizure type, neurological, cognitive and/or behavioural symptoms. Electroencephalography (EEG) was done in all cases during the interictal period using a 16-channel SLE EEG machine with 10-20 system electrode placements. The results of the EEG, computerized tomography (CT) of the brain, magnetic resonance imaging (MRI), tumor histology and treatment of the epilepsy were also

Address correspondence to: Dr Owolabi Lukman Femi, Neurology unit, Department of Medicine, Aminu Kano Teaching Hospital, Bayero University, PMB 3452 Kano, Nigeria. E-mail: drlukmanowolabi@yahoo.com

Table 1: Demography and tumor types of the study patients

Age group in years	Tumor				Total
	Primary		Secondary		
	Male	Female	Male	Female	
30-39	1	1	1	1	4
40-49	7	2	0	0	9
50-59	10	1	2	2	15
60-69	17	2	1	1	21
70-79	7	4	1	1	13
80-89	1	3	0	0	4
Total	43	13	5	5	66

documented.

Analysis of data was done using a statistical software package SPSS version16. Descriptive statistics were depicted using absolute numbers, simple percentages, range, and measures of central tendency (mean, median) as appropriate. The chi-square test was used to test the significance of associations between categorical groups. Statistical significance was fixed at probability level of 0.05 or less.

RESULTS

Out of 302 patients with late onset epilepsy seen during the study period, 66 (21.9%) patients comprising 48 (73%) males and 18 (27%) females had brain tumor. Their age ranged between 34 and 85 years with a mean of 59.18 ± 12.1 years. Of the 66 patients with tumor, 56 (82.4%) patients had primary central nervous system (CNS) tumors while the remaining 10 (17.6%) patients had metastases (Table 1). The primary CNS neoplasm group included 43 men and 13 women with a mean age of 67.6 ± 9 years. Metastatic group consisted of 5 men and 5 women with a mean age of 43.1 ± 6.8 years.

Seizure was the only symptom in (27.3%) and the first symptom in 36.4% of the patients. The other presenting symptoms were headache (72.7%), vomiting (36.4%), blurring of vision (36.4%), altered level of consciousness (18.2%) and behavioral and/or personality changes (7%). Seven (10.6%) patients had past history of head injury.

Fifty four (82%) patients had neurologic deficit on examination, when compared with 2 (1.5%) of 129 patients with idiopathic generalized epilepsy. Presence of neurologic deficit was predictive of brain tumor ($p<0.05$). Neurologic deficit on examination was also predictive of abnormal EEG in these patients ($p<0.05$)

Partial seizure, found in 45 (68.2%) patients, was the most common seizure type out of which 33 (73%) were simple motor, 5 (11.1%) were sensory, 2 (4.4%) were psychic and one (2.2%) visual. Eighteen patients (27.3%) had secondarily generalized seizure type. Three (4.5%) patients had generalized seizures (Table 2). There was associated Todd's paralysis in 10 (15.2%) patients and 10 (15.2%) other patients had versive seizures. The duration of seizure attack was less than 2 minutes in majority (72.7%) and seizure frequency was once to several attacks per day in 21.2%.

More patients with CNS metastasis (60%) compared with primary CNS tumors (55.6%) had seizure as the first symptom. However, the difference was not statistically significant ($p = 0.796$).

Table 2: Distribution of seizure types of the study patients

Epileptic seizure type	Frequency	Percent (%)
Partial	45	68.2
Secondarily generalized	18	27.3
Generalized	3	4.5
Total	66	100

Table 3: Distribution of histological types of the brain tumors

Tumor	Frequency
Primary*	
Low grade astrocytoma	9
Meningioma	7
Glioblastoma multiforme	2
Oligodendroglioma	2
Metastatic	
Lungs	3
Breast	2
Liver	2
Prostate	1
Cervical	1
Melanoma	1

*Histology was only available in 20 patients with primary CNS tumor.

Of the 56 patients with primary CNS tumors, histological diagnosis was available in 20 patients, with low grade astrocytoma being the most common (9), followed by meningioma (7), glioblastoma multiforme (2) and oligodendroglioma (2). Based on neuroimaging, most primary CNS tumor involved more than one lobe. The tumor involved parietal lobe in 58%, frontal (56%), temporal (33%) and occipital (33%). The origin of the metastatic brain tumors are as outlined in Table 3.

As for EEG of the 66 patients, the most common abnormality was epileptiform discharges (54.5%) followed by focal slowing (24.2%). Normal record was seen in 10.6%. The EEG abnormalities correlated with the anatomical location of the tumor in two thirds (72.7%) of the patients (Table 4).

Three antiepileptic drugs, carbamazepine (33), phenytoin (12), and valproate (8) were used. They were mainly used as monotherapy. Two patients required combination of carbamazepine and valproate and 2 had phenytoin and valproate to achieve seizure control. All the patients were referred for neurosurgical intervention, 36 of the patients were followed up for a minimum of 4 months, 3 patients died, and 28 patients were seizure free on monotherapy at 4- month post-surgery. .

DISCUSSION

In this study, we examined the profile of epileptic seizure as the presenting symptom leading to the diagnosis of brain tumors. Approximately 22% of our patients with late onset epilepsy had brain tumors as the etiological factor. This finding is consistent with reports from similar studies elsewhere.[22,23] The figure was, however, lower for children.[6] This difference could be partly explained by the incidence of tumors increases with age because of cumulative errors of metabolism and DNA damage.[24]

Higher proportion of male was recorded in our study. This finding was similar to the findings in other studies amongst Africans and Caucasians. Male preponderance in this study could be partly attributed to the pattern of hospital attendance in our setting as women often require the consent of their husbands for hospital attendance.[25]

Table 4: Distribution of EEG findings

Predominant EEG abnormality	Frequency	Percent
Focal epileptiform discharges	36	54.5
Generalized epileptiform discharges	4	6.1
Focal slow waves	16	24.2
Non specific	3	4.5
Normal	7	10.6
Total	66	100

The majority of the patients had neurologic deficit on examination and the presence of neurologic deficit was predictive of structural brain lesions especially brain tumors. Previous studies have suggested that presence of focal neurological signs may contribute to an earlier diagnosis of tumor.[22-27] Neurologic deficit on examination was also predictive of abnormal EEG. These findings complement previous studies, in both adults and children which have investigated the relationship between findings on neurological examinations, brain tumors and EEG abnormalities.[28-31]

Abnormal EEG was seen in close to 90% of our patients. The most common EEG abnormality in this study was epileptiform discharges followed by focal slowing. Focal slowing, in the delta frequency range, appeared to be the most reliable predictor of tumor in previous studies.[32] EEG was normal in 10.6%, and periodic lateralizing epileptiform discharges (PLEDS) were not recorded in this study. Overall, the pattern of EEG findings in this study further corroborates the previous findings on EEG pattern in patients with brain tumor.[33-34] The EEG abnormalities correlated anatomically with the location of the tumor in two third of the cases. The fair agreement between EEG and neuroimaging suggested that EEG has a place for screening for structural lesions in the brain in late-onset epilepsy. However, there has also been a previous study that showed that the correlation between focal EEG findings and structural lesions is neither close nor consistent.[35]

In this study, histological diagnosis (post-surgery) was available in 20 patients with primary brain tumor; low grade astrocytoma was the most common, followed by meningioma, glioblastoma multiforme and oligodendroglioma. Although the number of our patients with histology is small, this distribution is consistent with the observations from a previous study on brain tumor in eastern Nigeria over a five-year period.[18] In the study of 48 cases of intracranial tumors, glial tumors accounted for 20.8%, pituitary tumors 18.8%, meningiomas 16.7%, metastatic tumors 10.4%. In another study of 210 patients in Ibadan, southwestern Nigeria, gliomas, was the most common histological type.[16] However, in a report of hospital-based cancer registry in Zaria in northern Nigeria, brain tumor was reported to be rare.[22] Similar studies in the developed countries have also shown preponderance of gliomas.[7-10]

In our study, most of the primary CNS tumors structurally involved more than one lobe. The tumor involved parietal lobe in 58%, frontal (56%) temporal (33%) and occipital (33%). This is similar to the anatomical distribution of supratentorial glioma reported by Tandon *et al* from India.[23]

Travelling abroad for neurosurgery, referral to centres outside the study sites, intraoperative or postoperative deaths and loss to follow up were the reasons for the relatively few patients with histological diagnosis in our study. As for the affluent Nigerian seeking treatment abroad, lack of confidence in the local health care as well as high cost of care were important reasons. It further emphasizes the need to upgrade the Nigerian health system.

Preoperatively, seizures in majority of our patients were controlled using a single anticonvulsant. However, because all the patients had anticonvulsants, it is uncertain whether the relatively low incidence of post-operative seizure was solely as a result of drug use or tumor excision. Evaluation of epilepsy prophylaxis for post-operative cases in those with brain tumor did not show significant reduction in the incidence of seizures[36], On the other hand, Rasmussen reported overall reduction of seizure by 60-80% following surgery.[37]

As the patients included in this study were seen in tertiary care centres, referral bias cannot be excluded. In spite of this limitation, we belief our study adds to the knowledge on epilepsy and seizures in Nigeria, West Africa.

In conclusion, tumor accounts for a fifth of patients presenting with late onset epilepsy in Nigeria. Gliomas were the most common brain tumor presenting with epileptic seizures. There is need to investigate for tumor in Nigerian patients presenting with late onset epilepsy.

DISCLOSURE

Disclaimer: None

Source of support: Nil

REFERENCES

1. Penfield W, Ericson TC, Tarlov I. Relation of intracranial tumors and symptomatic epilepsy. *Arch Neuro Psych* 1940; 44:300-15.
2. Lund M. Epilepsy in association with intracranial tumours. *Acta Psych Neurol Scan* 1952; 81(Suppl):3-149.
3. Rasmussen T, Blundell J. Epilepsy and brain tumour. *Clin Neurosurg* 1961; 7:138-58.
4. Smith DF, Hutton JL, Sandermann D, *et al*. The prognosis of primary intracerebral tumours presenting with epilepsy: the outcome of medical and surgical management. *J Neurol Neurosurg Psychiatry* 1991; 54:915-20.

5. Bromfield EB. Epilepsy in patients with brain tumors and other cancers. *Rev Neurol Dis* 2004; 1 (1):27-33.
6. Ibrahim K, Appleton R. Seizures as the presenting symptom of brain tumors in children. *Seizure* 2004; 13:108-12.
7. Villemure J, de Tribolet N. Epilepsy in patients with central nervous system tumors. *Curr Opin Neurol* 1996; 9:424-8.
8. Van Breemen MSM, Vecht CJ. Optimal seizure management in brain tumor patients. *Curr Neurol Neurosci Rep* 2005; 5:207-13.
9. Vecht CJ, Wagner GL, Wilms EB. Treating seizures in patients with brain tumors: drug interactions between antiepileptic and chemotherapeutic agents. *Semin Oncol* 2003; 30 (19):49-52.
10. Moots PL, Maciunas RJ, Eisert DR, *et al*. The course of seizure disorders in patients with malignant gliomas. *Arch Neurol* 1995; 52:717-24.
11. Forsyth PA, Weaver S, Fulton D, *et al*. Prophylactic anticonvulsants in patients with brain tumour. *Can J Neurol Sci* 2003; 30:106-12.
12. Odeku, EL, Adeloye A. Cranial meningiomas in the Nigerian African. *Afr J Med Sci* 1973; 4(2):275-87.
13. Adeloye, A. Neoplasms of the brain in the African. *Surg Neurol* 1979; 11(4):247-55.
14. Adeloye, A. Intracranial metastatic tumors in Ibadan, Nigeria. *Surg Neurol* 1982; 17(3):231-2.
15. Adeloye A, Odeku EL. Metastatic neoplasms of the brain in Nigeria. *Br J Cancer* 1969; 23(2):340-8.
16. Olasode BJ, Shokunbi MT, Aghadiuno PU, Intracranial Neoplasms in Ibadan, Nigeria. *East Afri Med* 2000; 77:4-8
17. Odeku, E L, Adeloye A. Gliomas of the brain among Nigerians. *Afr J Med Sci* 1976; 5(1):31-3.
18. Ohaegbulam SC, Saddeqi N, Ikerionwu S. Intracranial tumors in Enugu, Nigeria. *Cancer* 1980; 46(10):2322-4.
19. Buerneo JG. Aetiology of epilepsy of late onset. *Rev Neurol* 2001; 33:1099.
20. Hernandez C. Etiology of late onset epilepsy. *Rev Neurol* 2001; 32:628-30.
21. Fisher RS, van Emde Boas W, Blume W, *et al*. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). *Epilepsia* 2005; 46(4):470-2.
22. Afolayan EA. Five years of cancer registration at Zaria. *Niger Postgrad Med J* 2004; 11(3):225-9.
23. Tandon PN, Mahaptra, Khosia A. Epileptic seizures in supratentorial gliomas. *Neurol India* 2001; 49:55-9.
24. Thomas N S, Laura MS. Cancer as a metabolic disease. *Nutr Metab* 2010; 7:7
25. Osuntokun, BO, Adeuja, AO, Nottidge VA, *et al*. Prevalence of epilepsy in Nigeria Africans: a community based study. *Epilepsia* 1970; 28(3):272-9.
26. Owolabi LF, Akinyemi RO, Owolabi MO, Sani MU, Ogunniyi A. Profile of epilepsy in elderly Nigerians. *Archives of Ibadan Medicine* 2011; 11: 47-50.
27. Lynama LM, Lyons MK, Drazkowski JF, *et al*. Frequency of seizures in patients with newly diagnosed brain tumors: A retrospective review. *Clin Neurol Neurosurg* 2007; 109:634-8.
28. Liigant A, Haldre S, Õun A, *et al*. Seizure disorders in patients with brain tumors. *Eur Neurol* 2001; 45:46-51.
29. Ferris RC, Nathwani A, Kennedy CR. Presenting features of brain tumors. *Dev Med Child Neurol* 2003; 45(93): 15.
30. Kim SC, Wang KC, Cho BK. Intractable epilepsy associated with brain tumors in children: surgical modality and outcome. *Childs Nerv Syst* 2001; 17:445-53.
31. Cascino G D, Epilepsy and brain tumors. *Epilepsia* 1990; 37 (3):37-44.
32. Johannes CB. Localization of slow wave activity in patients with tumor-associated epilepsy. *Brain Topography* 2004; 16:85-93.
33. Walczak TS, Scheuer ML, Reson S, Pedley TA. Prevalence and features of epilepsy without interictal epileptiform discharges. *Neurology* 1993; 43(2):287-8.
34. Salinsky M, Kanter R, Dasheiff RM. Effectiveness of multiple EEGs in supporting the diagnosis of epilepsy: an operation curve. *Epilepsia* 1987; 28:331-4.
35. Gibbs J, Appleton R. E, Carty H, Beirne M, Acomb B. Focal electroencephalographic abnormalities and computerized tomographic findings in children with seizures. *J Neurol Neurosurg Psych*iatry 1993; 56:369-371.
36. Shaw MD. Postoperative epilepsy and the efficacy of anticonvulsant therapy .Acta Neurochirugica 1990; 50:55-7.
37. Rasmussen T. Surgery of epilepsy associated with brain tumor. Raven Press, New York.1975; 3:227-9.