ORIGINAL ARTICLE

Brain astrocytomas in South-East Nigeria: a 3-centre experience

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ABSTRACT

Background: Although astrocytomas are the most common primary brain tumours worldwide, they are still poorly reported in our environment.

Methodology: We retrospectively studied adult patients with astrocytic tumours treated over a 5-year period in 3 tertiary hospitals within South-East Nigeria. Patients' clinical data as well as radiology and histology reports were analyzed. Follow-up interval was 3months to 4.5 years. Data analysis was performed using *SPSS version 16* with evaluation of confidence limits at the 95% level of significance.

Results: A total of 231 patients with computed tomography / magnetic resonance imaging diagnoses of brain tumours were seen, 61 patients had features of brain astrocytoma and were studied, while 46 had histological confirmation. Age range was 16-77 years with a mean of 43.4±1.7 years (95% CI). The mean age for those with low grade tumours was 35.3±0.9years (95%CI) and 49.6±0.4years for high grade tumours (95%CI), and the male:female ratio was 1.5:1. Major complaints were headache and seizures in 70.5% (43 patients) and 58.3% (35 patients), respectively, while duration of symptoms was 2 to 17months, with a mean of 9.6±1.7 (95%CI) months. The tumours in 41 cases were supratentorial, 17 cases were infratentorial, while 3 cases were transtentorial. Of the cases that had operative treatment, 33patients had microsurgical resections, 11 had biopsy only, while 31 had cerebrospinal fluid diversion. Histologically, 13 patients had low grade tumours (WHO grades I and II), while 36 patients had high grade (WHO grades III and IV). Survival rates after 1year and 3years follow-up were 77% and 61% for low grade tumours and 27% and 8.3% for high grade tumours.

Conclusion: There is a need to establish a national brain tumour registry to properly evaluate the profile of brain tumours including astrocytomas.

***Keywords**: Brain tumours, computed tomography, histology, magnetic resonance imaging, survival*

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INTRODUCTION

In the past, intracranial tumours were thought to be rare among negroes in general.[1] An initial published study on intracranial tumours in Nigeria utilised data from necrospy and, hence, provided limited information on the clinical profile of brain tumours.[2] However, studies on intracranial tumours in the Nigerian population by Odeku who established the first specialist neurological surgery service in West Africa, at the University College Hospital Ibadan Nigeria, did not only disprove the earlier claims, they also elucidated the patterns of presentation and profiles of treatment of intracranial tumours among Nigerian negroes.[3,4]

It should be noted, however, that Odeku's studies on intracranial tumours and subsequent works by some other authors had focused on intracranial tumour patterns in general, and some of these studies actually suggested a high occurrence of astrocytomas.[3,4,5,6,7,8] In a previous study by Ohaegbulam, from our sub-region more than 3 decades ago, gliomas were reported as the most common intracranial tumours.[9]

Astrocytoma has been recognized as the most common primary intracranial tumour worldwide. In our recent study on intracranial tumours in children, we also found a high occurrence of astrocytomas.[10] Therefore, we have in this current work, focused on astrocytomas amongst adult patients with primary brain tumours who received neurosurgical treatment in three tertiary hospitals in South-East Nigeria with established specialist neurosurgical practice.

To the best of our knowledge, this is the first paper from our sub-region evaluating the sub-population of adult primary brain tumour patients with astrocytoma.

METHODOLOGY

This is a 5-year institution-based, retrospective cohort study of adult patients with astrocytoma, treated by the authors in three tertiary hospitals within South-East zone of Nigeria from October 2009 to September 2014. The patients' clinical records and laboratory results, including radiology and histology reports, as well as follow-up data, were analyzed using the Statistical Package for Social Sciences (SPSS) version 16, and the Confidence Limit was evaluated for inferential statistics and results set at the 95% level of significance.

All patients with high grade tumours were treated with radiotherapy, while some of them received chemotherapy (temozolomide), as well. Low grade tumours were treated with surgery only, whereas, all diencephalic and brain stem tumours received radiotherapy only.

Inclusion Criteria. Patients aged 16years and above, with histologically proven astrocytoma or brain imaging – computed tomography (CT) or magnetic resonance imaging (MRI) - diagnosed cases of diencephalic and brain stem glioma. Intra-axial masses other than astrocytoma, such as brain abscess and extra-axial tumours, were excluded. Follow-up period varied from 3months to 4.5years.

RESULTS

Of the 231 patients with CT/MRI diagnosis of brain tumours seen, 61 patients had features suggestive of brain astrocytoma and were studied, while 49 patients had histological confirmation. Age range was 16-77years with a mean of 43.4 ±1.7years (95% CI), *see Table 1.*

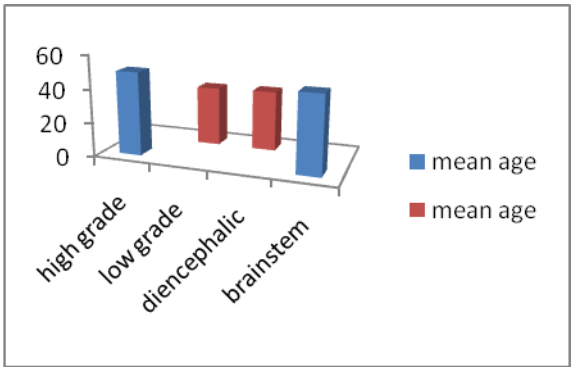
The mean age for those with low grade tumours was 35.3±0.9years (95%CI), while the mean age for high grade tumour patients was 49.6±0.4years (95%CI). For patients with

brainstem tumours, the mean age was 45.8±1.2years (95%CI), while for those of them with diencephalic astrocytoma, the mean age was 38.3±0.5years (95%CI), *see Figure 1.*

Table 1: Age distribution

Age	No.
16-30	13
31-45	21
46-60	19
61-70	7
71-85	1
Total(N)	61
Mean=43.4±1.7yrs(95%CI)	

Figure 1: Relationship between mean age and tumour grade or location



There were 37 males and 24 females with an M:F ratio of 1.5:1. Major complaints were headache and seizures in 70.5% (43 patients) and 58.3% (35 patients), respectively. Other symptoms were vomiting 50% (31 patients), altered mental status 32% (20 patients), visual disturbances 32% (20 patients) and cognitive impairment 25% (16 patients). Duration of symptoms was 2-17months with a mean of 9.6+/-1.7months (95%CI). Of these, 41 cases were supratentorial, 17 were infratentorial, while 3 transtentorial. At surgery, 38 patients had microsurgical resections, 11 had biopsy only, while 31 had CSF diversion. Histologically, 13 patients had low grade tumours (WHO Grades I and II), while 36 patients were high grade (WHO Grades III and IV), *see Table 2 and Figure 2.*

The 13 patients with low grade tumours were treated with surgical resection alone, while 48 patients with high grade, diencephalic or brainstem tumours received either adjuvant radiotherapy (for high grade cases and 3 diencephalic astrocytoma patients biopsied endoscopically) or radiotherapy, as primary treatment (for 8 non-biopsied diencephalic cases and all 5 brainstem tumours). Chemoradiation was given to 3 patients, using temozolomide with radiotherapy, *see Table 3.*

Table 2: Histological distribution and anatomical location

	Supra tentorial	Infra tentorial	n
A. Histology:			
Low grade	10	3	13
High grade	22	14	36
B. Other locations:			
Brainstem			5
Diencephalic			11
Transtentorial			3

Figure 2: Tumour grade / location

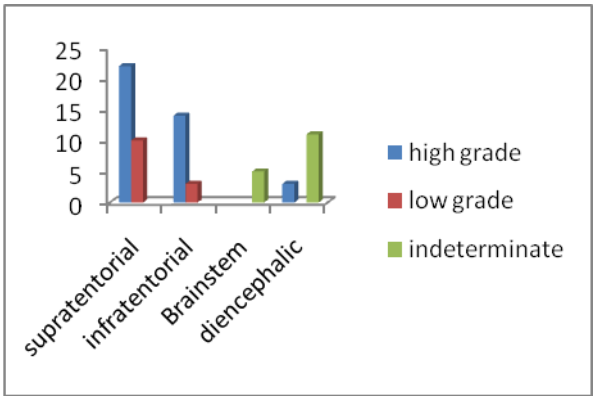


Table 3: Treatment modalities

Modality	No.
Surgery	
Microsurgical Resection	38
Biopsy	11
VP Shunt	28
ETV	3
Radiotherapy	13
Chemotherapy	3

Figure 3: Treatment modalities

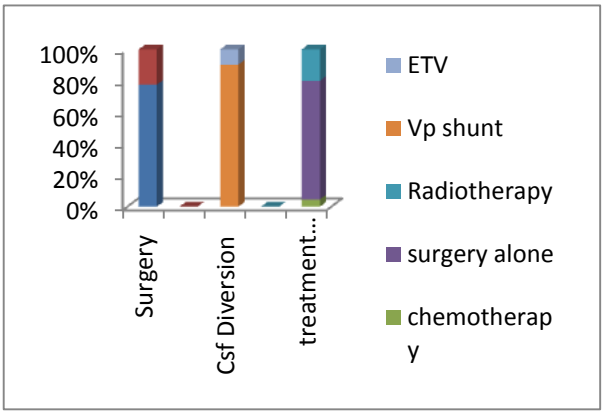
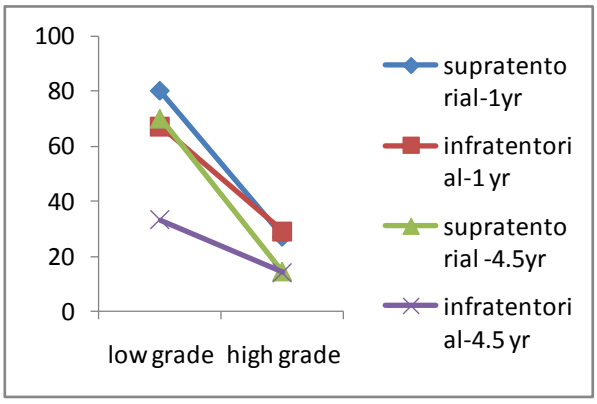


Figure 4: Relationship between tumour location, grade and survival



Survival rates (Figure 4) after 1year and 4.5years follow-up, respectively, were 77% (10 patients) and 61% (8 patients) for low grade tumours and 25% (9 patients) and 8.3% (3patients) for high grade tumours. The 1-year and 4.5-year survival rates for supratentorial tumours were 80% (8 patients), 70% (7 patients) for low grade tumours, 27% (6 patients) and 13.6% (3 patients) for high grade tumours. For infratentorial tumours, survival rates were 67% and 33% for low grade tumours, and 29% and 14.2% for high grade tumours. Survival for diencephalic tumours 27% (3 patients) at 1year and nil at 4.5years, relatedly, survival for brainstem tumours was 20% (1 patient at 1year), and 0% at 4.5years.

DISCUSSION

Astrocytomas are neoplasms of the central nervous system (CNS) in which the predominant cell type is derived from a transformed and immortalized astrocyte.[11] The male predominance found in our study has been reported previously, whereas the degree of gender predominance has also been found to vary with the degree of tumour aggressiveness.[12] Compared to a slight male preponderance in low grade giomas, a more significant male predominance has been recognized among patients with high grade gliomas, suggesting a possible protective role by female hormones.[12]

Peak age incidence has also been shown in previous studies to vary with tumour grade as we also found in our study (Figure 1). Low grade tumours occur in younger age groups, while high grade tumours are seen to occur more in the older population.[13] It is currently known that low grade tumours have a tendency to dedifferentiate into higher grades over time.[13]

Headaches and seizures were the most common symptoms in our series. These symptoms were also quite common in our previous series on children with brain tumours in Nigeria.[10]

Late presentation has been previously reported among patients with brain tumours generally in our environment and the poorer outcome associated with brain tumours has also been partly attributable to it.[3,4,5,9,10] In our series, this problem is still recognizable showing that not much has changed both in patients and care givers' awareness and prompt recognition which results from adequate education of the populace on the one hand and also, in the effectiveness of our health system's referral chain on the other, over the years.

For low grade gliomas, apart from those with brainstem tumours who received radiotherapy, microsurgical resection was performed for our patients as the definitive treatment. Radiotherapy was not given because it has not been shown to improve the progression free survival.[14,15,16] In our series, complete resection was performed when there was no suspected risk of major neurologic deficit, however, when there is involvement of the eloquent brain such as the corpus callosum, microsurgical cytoreduction was performed. We did not offer adjuvant radiotherapy to this group in line with the EORTC study.[14]

Although low grade tumours typically grow slowly, it is euphemistic to describe their biologic behaviour as benign. This is because a great majority of the patients will die within 10years of the initial diagnosis.[17] High grade astrocytomas are now well recognized as a histopathologically defined group of clinically aggressive astrocytic neoplasms with diffuse growth characteristics which confers a relentlessly incurable clinical connotation.[17,18] The roles of surgery in the patient with astrocytoma are to remove or debulk the tumour and to provide where possible tumour tissue for histological diagnosis, permitting tailoring of adjuvant therapy and assessment of prognosis.[17] Biopsy, especially stereotactic biopsy, is a safe and simple method of establishing a tissue diagnosis. However, in our environment, the lack of stereotaxy and neuronavigational facilities has limited our method of tissue sampling to microsurgical resections, and freehand biopsies for most cases using static neuroimaging films, and in a few cases, endoscopic biopsy. These methods were effective in our experience and should still be used while we expect further improvement in the neurosurgical infrastructure in our region.

Total resection of astrocytomas, especially high grade tumours, is often impossible because they often invade adjacent regions of the brain. Complete resection (>98% based on volumetric MRI) has been shown to improve median survival compared to subtotal resection (13months vs 8.8months).[16,17,18] For low grade gliomas, some data support supratotal resection (i.e. removal of tissue beyond MRI-defined abnormalities), suggesting an increase in overall survival with this strategy.[19,20] Radiotherapy enhances progression free survival in astrocytoma patients with high grade tumours who had surgical resection.[15]

Three patients with grade IV tumour (glioblastoma multiforme) in our study had adjuvant chemotherapy (temozolomide) in addition to surgery and radiotherapy. This drug has been shown to offer an independent progression free survival advantage in previous multivariate studies together with surgical resection and radiotherapy in patients with high grade astrocytoma.[15]

We could not however perform a multivariate evaluation of the independent roles of surgery, radiotherapy and chemotherapy in the outcome and survival profiles of our patients in this study. We shall be focusing on these treatment modalities in a future multicentre prospective study with a larger patient population.

Survival correlates mainly with the intrinsic biologic properties of the astrocytoma and typically, ranges from 10years from the time of diagnosis for patients with grade-1 astrocytoma to less than 1year for patients with glioblastoma.[17] Low grade gliomas had better prognosis than high grade gliomas (Figure 4) and patients with supratentorial tumours also survived better than those with infratentorial tumours, regardless of tumour grade (Figure 4). Patients with diencephalic and brainstem tumours had poor prognosis as none of them was alive up to 4.5years after treatment.

A previous study had concluded that brain stem astrocytoma had better prognosis in adults when compared to children, based on the assumption that low grade brainstem tumours occur more in adults.[21] We, however, disagree with this categorisation because the current classification of brainstem astrocytomas is based on radiologic (MRI) assessment and not histological evaluation. This makes it difficult for one to differentiate between the many possible diagnoses for proper scientific comparison. Thalamic astrocytomas are associated with poor prognosis as seen in our study with 27% survival at 1year and zero survival at 4.5years. In one previous study, the disease free survival was 28% at 2years.[22]

CONCLUSION

Astrocytomas are associated with very poor prognosis in our sub-region. Most patients (>90%) with astrocytoma die within 5years of diagnosis. Late presentation and limitation of facilities for diagnosis and treatment have combined to make the care of patients with astrocytoma a nightmare for the few neurosurgeons in our sub-region. Our recommendation is that a tumour registry be established in order to properly assess the profile of patients that present with astrocytoma.

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