CLINICAL STUDIES / ETUDES CLINIQUES

ETIOLOGY AND ELECTROCLINICAL PATTERN OF LATE ONSET EPILEPSY IN IBADAN, SOUTHWESTERN NIGERIA.

ÉTIOLOGIE ET MOTIF DE L'EPILEPSIE ELECTROCLINIQUES D'APPARITION TARDIVE A IBADAN, AU SUD OUEST DU NIGERIA

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ABSTRACT

Background
Late onset epilepsy (LOE) is a common neurological problem throughout the world. It is an area that has not been fully explored in the developing countries like Nigeria. The aim of the present study is to determine the pattern of presentation of late onset epilepsy with the view to identifying the etiologic as well as describe their electro-clinical pattern.

Methods
120 consecutive patients presenting at the University College Hospital with LOE were recruited. A detailed history was obtained in every case, and complete neurological examination was performed. EEGs were done in all patients. Contrast CT Scans and MRI were performed.

Result
One hundred and twenty subjects comprising 71 (59.2%) males and 49 (40.8%) females were studied. The ages of the patients ranged between 25 and 85 years with a mean of 53years (sd =14.6). The ages at onset of epilepsy ranged between 25 and 84 years with a mean of 52 (sd=14.8). All the subjects had classifiable seizure types, 31 (25.8%) had generalized seizure. The most common type of seizure was partial seizure diagnosed in 89 (74.2%) subjects. Fifty two (43.3%) of the subjects had abnormal neurological findings. Twenty one (30.9%) had cerebral infarcts and 20 (29.4%) had cerebral tumor. Those with symptomatic epilepsy were more likely to have neurologic deficit, simple partial seizure, secondarily generalized seizure, focal epileptiform discharges and focal slow waves.

Conclusion
The most common abnormalities in LOE were cerebral infarct and brain tumor. A careful history, neurological examination and an EEG are adequate in the initial work-up of patients with LOE.

INTRODUCTION

Epilepsy is a common neurological problem throughout the world. It constitutes a grave problem and occurs more often in the developing countries of Africa and South America than in the developed countries of Europe and North America. (1) Late onset epilepsy is described as epilepsy beginning in adult life, (2) about 20-25% of patients with epilepsy will have their first seizure after the age of 25 years. (2) In Nigeria, the prevalence of epilepsy varies widely in different communities. In a community based study among Nigerian Africans, Osuntokun et al reported a prevalence of 5.3 per 1000 among Igbo-Ora inhabitants in Western Nigeria. (3,4) In another study in mid-western Nigeria a prevalence of 6.2 per 1000 among was reported.(5) In this region, it's been documented that onset of epilepsy in 68% of patients was in the first and second decades of life.(6,7) However, epilepsy with onset of seizures in adult life is not a rare phenomenon in this environment. It is an area that has not been fully explored in the developing countries like Nigeria. Late onset epilepsy has received disproportionate emphasis due to a belief that 'tumour' is the commonest cause, and that every patient with adult onset epilepsy is a tumour suspect. With the availability of neuroimmaging and electroencephalography, the investigation of patients has become a lot easier. However, in a developing country like Nigeria, CT Brain scan and EEG are expensive and scarce tools of investigation, hence, the need to describe pattern of late onset epilepsy in this environment.

The aim of the study was to determine the pattern of presentation of late onset epilepsy with the view to identifying the etiologic factors and ascertaining the frequency of different etiologic factors as well as classifying and describing the pattern of epileptic seizure occurring in these patients.

MATERIAL AND METHODS

Late-onset epilepsy was defined as the occurrence of one or more seizures starting after the age of 25 years. (8,9) A total of 120 consecutive patients presenting in University College Hospital (UCH) with epilepsy after age of 25 years were recruited from the general and medical outpatient clinics of the tertiary institution over a two and a half year period (June 2003-Jan 2006).The diagnosis of epilepsy was accepted in the presence of at least 2 stereotyped episodes of transient period neurologic dysfunction characterized by focal or generalized convulsion, loss of consciousness or period of altered awareness associated with special sensory, somatosensory, psychic automatic symptoms and/or automatism. The attacks must have been witnessed by another person who corroborated the history. Patients above 25 years of age, with informed consents and who had EEG, presenting with seizures for the first time were included in the study whereas those with single seizure and patients who had convulsions during the course of an acute illness like meningitis, encephalitis and head injury were not included in the study.

A detailed history, including eyewitness corroboration was obtained in every case, and complete neurological examination was performed. EEGs were done in all patients. Contrast CT Scans and MRI were performed whenever clinically indicated.

A structured proforma was completed per eligible subject.All the subjects completed the questionnaires designed to obtain demographic information on the age, sex, level of education, marital status, occupation, age at onset of seizures frequency of seizures, duration of seizures and drugs among other variables. The questionnaires were completed under the supervision of the investigator.

RESULTS

One hundred and twenty subjects comprising seventy one (59.2%) males and forty nine (40.8%) females were studied. The male to female ratio was 3:2.The ages of the patients ranged between 25 and 85 years with a mean of 53years (standard deviation =14.6). The ages at onset of epilepsy ranged between 25 and 84 years with a mean of 52 (standard deviation=14.8). The peak age frequency at onset of epilepsy was in the fifth decade. One hundred and fourteen of the patients (95 %) were above the age of 30 years at onset. The age and sex distribution is shown in table 1. All the subjects had classifiable seizure types, thirty one (25.8%) had generalized seizure. Of the generalized seizure, thirty (25%) subjects had generalized tonic-clonic seizure and one subject had myoclonic seizure. The commonest type of seizure was partial seizure diagnosed in eighty nine (74.2%) subjects; forty one subjects (34.2%) were simple partial, twenty six (21.7%) were complex partial and twenty two (18.3%) were secondarily generalized. Table 1 showed distribution of seizure type by age group.

All the subjects (41) with simple partial seizure had simple motor type. There was associated Todd's paralysis in four (9.8%) subjects and three (7.3%) of these subjects had a versive episode. Twenty six (21.7%) subjects had complex partial seizure out of whom, nineteen (73%) had aura. The commonest form of aura encountered was sensory as it was present in 47.4% of the subjects with aura. Twenty one subjects had automatism and the commonest type of automatism seen was oroalimentary which was present in fifteen (71.4%) subjects. The other forms of automatism encountered were one (4.8%) case of mimicry and five

(23.8%) subjects with ambulatory type. Fifty two (43.3%) of the subjects had abnormal neurological findings. Comparing partial and generalized seizure types, fifty (56.2%) out of the eighty nine patients with partial seizures had abnormal neurological examination as compared with only two (6.5%) out of thirty one patients with primarily generalized seizures. The difference was statistically significant P <0.05.

The commonest etiologies were cerebral infarcts and tumors, twenty one (30.9%) of the patients with abnormality had cerebral infarcts, twenty (29.4%) of them had cerebral tumor, the cerebral infarcts occurred most commonly within age bracket of 60-69. Seventeen (25%) subjects had cerebral atrophy only, ten out of the seventeen patients (60%) with cerebral atrophy had past history of head injury, cerebral arteriovenous malformation was found in three (4.4%) subjects, cerebral toxoplasmosis abscess in three (4.4%) subjects, cerebral abscess (pyogenic) in two (2.9%) subjects, one subject (1.5%) had an intracerebral haemorhage and one (1.5%) patient had a cyst in the brain (table 2).The most common type of seizure in patients with cerebral infarcts and cerebral tumors was simple partial seizure seen in 16 and 14 patients respectively (table 3), Out of the twenty two patients with post-stroke epilepsy, first seizure ever occurred in only three (13.6%) at the onset of stroke. Out of the patients with cerebral infarcts fourteen (66.7%) involved the cerebral cortex while the remaining seven (33%) were subcortical.

Out of the twenty patients with cerebral tumor, histologic diagnosis (after surgery) was obtained in seven; 2 meningioma, 4 low grade astrocytoma and 1 glioblastoma multiforme.

All the patients had electroencephalography, and the records of eighty five (70.8%) of them were abnormal, Sixty six (77.6%) subjects had epileptiform (spikes, sharp waves, spikes and wave, polyspikes) pattern, sixteen (18.8%) had slowing in the delta and theta range while nonspecific abnormalities, including focal slow activity, regional or generalized bisynchronous slow activity, focal attenuation and generalized suppression, were found in three (3.5%) subjects. When EEG findings were related to the seizure type , seventeen out of the thirty one patients had generalized spike and wave pattern, two of them had no specific generalized abnormality, EEG was normal in twelve of these patients. Out of the eighty nine subjects with partial seizures sixty six had focal epileptiform discharges while EEG was normal in twenty three of the subjects. Table 4 showed correlation between focal seizures, unilateral clinical signs and focal EEG abnormalities in different etiological groups of the patients.

On relating pattern of EEG abnormality to abnormal CT findings, eighteen out of nineteen subjects with cerebral infarcts and eighteen out of nineteen subjects with cerebral tumour had focal abnormalities on EEG (table 5). Further analysis on the sixty eight subjects with abnormal CT Brain showed that epileptiform activity was associated with infarct in thirteen (19.1%) of the subjects, with tumor in ten (14.7%) of the subjects, with atrophy in five (7.4%) subjects. Ten (14.7%) subjects with normal CT had epileptiform activity on EEG record. Comparing symptomatic with idiopathic epilepsy, symptomatic epilepsy was more likely to have neurologic deficit, simple partial seizure, secondarily generalized seizure, focal epileptiform discharges and focal slow waves (Table 6).

DISCUSSION

Seizures and epilepsy of late onset are important and are increasingly common clinical problems.The subjects included in this study were seen in a tertiary care centre thereby introducing an element of referral bias. (10) In spite of this constraint however, the findings provide some important information which may be useful in the understanding and management of late onset epilepsy.

The male preponderance in this study is similar to the findings in other studies amongst Africans and Caucasians. This male preponderance has been attributed to the pattern of hospital attendance in this environment.(6,11) and this may also be due to occupational and social exposure to epileptogenic insults, like head injury. In this study, the frequency of epilepsy after the 25yrs of age increased as the age increased reaching a peak in the 5th and 6th decade of life. This finding is in conformity with the report of CDC of current trends in prevalence of self reported epilepsy in The United State (1986-1990).(12) This pattern may reflect increased incidence of some of the risk factors particularly cerebrovascular accident and neoplasm in this age group. It could also be partly due to reduced seizure threshold that is said to occur at the extremes of life.

The study showed a higher frequency of partial seizure than primarily generalized, this finding is consistent with the findings of some workers in this environment and amongst Caucasians.(13,14,15) However, Ogunniyi et al in their study on the use of computerized neuroimaging in the evaluation of Nigerian epileptics found a higher frequency of generalized seizure than partial seizures. The disparity may be partly accounted for by the inclusion of less than 25years of age patients in whom epilepsies are more likely to be idiopathic hence generalized and partly because the study was carried out on selected subjects who could afford computerized tomography. The findings are also in contrast with predominance of generalized seizure in early onset epilepsy. The high frequency of simple partial seizure as opposed to partial seizure with complex symptomatology may not be unconnected with the modal age group (> 50years) during which idiopathic or genetically based epilepsy become less common.

The higher proportion of neurologic deficit in symptomatic epilepsy of late onset as compared to idiopathic epilepsy in this study could be due to higher incidence of structural lesion in the former which incidentally constitute a discrete epileptic focus as well as responsible for the neurologic deficit. This finding emphasizes the importance and relevance of the presence of neurological deficit as a finding that should increase one's suspicion of an underlying structural lesion in the brain particularly when found in conjunction with partial epileptic seizure type in an adult. Nevertheless, the absence of neurological deficit no matter how subtle it is does not necessarily exclude, as seen in this study, structural brain lesion.

Over ninety three percent of the subjects had brain CT. Majority of those that did not have CT Brain were those below 30yrs of age and those with complex partial seizure. This may be a reflection of the general belief that the younger the patient the less the likelihood of finding an underlying cerebral structural abnormality and may also be partly ascribed to the awareness of the fact that structural abnormalities identifiable by computerized tomography are not usually present in patients with complex partial seizure and primarily generalized seizure . A high proportion (56.7%) of the subjects had abnormal CT, this finding is comparable to that of Ogunniyi et al.(16) However, this finding is higher than the proportion obtained in various European studies with their figure varying between 34 and 51%.(17,18) This difference is conceivably due to the cut off age of 25yrs used in this study as the subjects with late onset epilepsy have a higher probability of associated cerebral lesions.(19,20) The findings of Daras and others in their hospital based study of adult onset seizure (62.6%) agrees with the findings in this study(19) The financial implication of getting CT scan done is seemingly the most important factor in this environment. In circumstances where CT was normal, physical signs were absent in a large proportion of the cases. Therefore physical signs may be useful in predicting what CT may show as evident by the agreement between these parameters. However, the absence of physical findings should not be used solely to exclude the presence of a structural lesion, as space occupying lesion may be missed in some cases.(21)

The most common abnormality was cerebral infarct. Many studies conducted on Caucasians and Americans agree with the findings of this study. Ottonello et al in their study of late onset epilepsy showed preponderance of cerebrovascular accident, trauma and alcohol as the commonest aetiology.(22) In Jimenez et al 3yr prospective study of etiology of late onset epilepsy, the most commonly identified cause of epilepsy was cerebrovascular disease. (23) Hernandez et al, in a study to identify etiology of late onset epilepsy, showed that stroke was the commonest,(24) many other studies also agreed with this finding.(24,25) Out of the twenty two patients with post-stroke epilepsy, first seizure occurred in only three (13.6%) at the onset of stroke. This proportion is lower than that reported by Dannuka et al. (26) In their study, 77% of the thirty five subjects with post stroke epilepsy studied had seizure at the onset of the stroke. (27) In another series, out of 97 patients who had experienced seizures in the post-stroke period, seizures occurred in 55 at the onset of stroke. (28-32) The finding in this study would suggest that absence of seizure at the time of or in the immediate period of stroke event does not necessarily imply a reduced likelihood of developing seizure later in life.

Nonetheless, it is noteworthy that some of these patients never had hospital-diagnosed-stroke before they developed epilepsy and that infarct in the brain was only picked up on neuroimmaging. This largely underscores the importance of neuroimmaging in patients developing first seizure late in life. The involvement of cerebral cortex has been emphasized in the pathogenesis of epilepsy caused by stroke. (31,33) Some authors have given more stress on the size of cerebral infarction. In this study, two third of these patients had infarcts involving the cerebral cortex. This is lower than the proportion (85%) of the post infarct stroke patients found in Dannuka.et al's study. (27) However, MRI was not done in the current study, thus, the possibility that some patients with cortical involvement might have been missed cannot be ruled out.

Out of the twenty patients with cerebral tumor, histological diagnosis (post surgery) was available in seven. Six were slow growing tumors (meningioma and astrocytoma.) and one was glioblastoma multiforme.The average duration of illness before presentation in either case ranged between three months and nine months. The incidence of brain tumors occurring in patients of all ages under treatment for epilepsy was reported to vary from 0.6% to 20%.(34-37) It has been stated that primary intracerebral tumors, presenting with epilepsy, are relatively benign. The third commonest abnormality on CT in this study was cortical atrophy which was present in 25% of the patients. This finding was not in conformity with the report of Ogunniyi et al in which cortical atrophy was the commonest abnormal CT finding. (16) The proportion of cortical atrophy found in this study is also lower than the reported range of 51% and 65% in many european series, (21) It is, however, debatable whether atrophy precedes or is secondary to epilepsy. In as much as association is not synonymous with causation, one can not conclusively opine that the cortical atrophy is the cause of seizures. Nonetheless, frequent or severe episodes of seizure tend to be associated with neuronal loss and several mechanisms may be involved, (38) Convulsive seizures tend to cause massive depletion of brains energy reserves, the associated massive influx of calcium ions leads to generation of free radicals and mobilization of free fatty acids with a massive increase in arachydonic acid which ultimately inhibit or uncouple mitochondrial activity. (38) The release of glutamate causes excitotoxic cell damage with cell swelling and eventual death.(39) This association could explain Gower's aphorism that "seizure begets seizures" probably by causing neuronal damage and setting up a vicious cycle. (40) Ten out of seventeen patients with cerebral atrophy had past history of head injury. The association of atrophy with head trauma may be a reflection of

the severity of the attacks with sustenance of either cerebral contusion or concussion. Head trauma is a well known risk factor for epilepsy especially when such trauma is associated with loss of consciousness and/or post traumatic amnesia for about 24 hours and skull laceration. (41) It is however noteworthy that contrary to previous studies elsewhere, (8,42) cerebral cysticercosis was not evident in our study.

The principal concern of the clinicians is to recognize symptomatic cases from the idiopathic cases. In appraising clinical parameters between these 2 groups (Table 6), we found that the most important criteria in support of underlying structural abnormalities are the presence of neurological deficit, certain types of epilepsy and certain EEG abnormalities. These parameters could be a guide for clinicians, in resource poor countries, to select patients for neuroimmaging.

CONCLUSION

In Ibadan, Southwestern Nigeria, the most common abnormalities in late onset epilepsy were cerebral infarct and brain tumour and that a careful history, neurological examination and an EEG are adequate in the initial work-up of patients with late onset epilepsy. Only those patients who show abnormality on neurological examination and/or EEG abnormality need be subjected to further investigation.

Table 1 Distribution of types of epileptic seizure across age groups

AGE GROUP	**SEIZURE TYPE**					***Total***
	Generalized Tonic-Clonic	Myoclonic	Simple Partial	Complex Partial	Secondarily Generalized	
20-29	1	-	-	1	1	3
30-39	10	1	3	8	3	25
40-49	4	-	9	3	3	19
50-59	5	-	8	8	5	26
60-69	5	-	11	5	5	26
70-79	4	-	9	1	5	19
80-89	1	-	1	-	-	2
Total	30	1	41	26	22	120

Table 2. Distribution of etiological factors across age group.

Age group	***Etiological factors***										***Total***
	Unknown	Infarct	Hemorhage	Tumour	Cyst	Atrophy	Abscess	Toxoplasmosis	AVM	Subdural haemorh	
20-29	2	-	-	-	-	-	1	-	-	-	3
30-39	16	1	-	4	-	2	-	-	2	-	25
40-49	8	2	-	3	1	2	1	2	-	-	19
50-59	14	3	-	5	-	2	-	1	1	-	26
60-69	9	9	-	4	-	2	-	-	-	2	26
70-79	3	6	1	3	-	4	-	-	-	2	19
80-89	-	-	-	1	-	1	-	-	-	-	2
Total	52	21	1	20	1	13	2	3	3	4	120

Table 3. Distribution seizure type by etiology

Etiology	*Seizure type*					*Total*
	Generalized Tonic-clonic	Myoclonic	Simple Partial	Complex partial	Secondarily Generalized	
Unknown	21	1	2	23	5	52
Infarct	1	-	16	-	4	21
Intracerebral haemorhage	-	-	1	-	-	1
Tumour	1	-	14	-	5	20
Cyst	-	-	1	-	-	1
Atrophy	5	-	3	3	2	13
Cerebral Abscess	-	-	1	-	1	2
Cerebral Toxoplasmosis	-	-	2	-	1	3
AVM	-	-	1	-	2	3
Subdural haemorhage	2	-	-	-	2	4
Total	30	1	41	26	22	120

Table 4. Correlation between focal seizures, unilateral clinical Signs and focal EEG abnormalities in different etiological groups of patients with late-onset epilepsy

Etiology	*No of patients*	*Focal seizures +unilateral signs + focal EEG abnormalities*
Infarct	21	6
Intracerebral haemorhage	1	1
Tumour	20	15
Cyst	1	-
Atrophy	13	-
Abscess	2	1
Toxoplasmosis	3	1
AVM	3	1
Subdural haemorhage	4	1
Total	68	26

Table 5. Relating abnormal EEG pattern to CT abnormalities

CT Brain Abnormalities	*EEG Abnormality*		*Total*
	Generalized	Focal	
Infarct	1	18	19
Haemorhage	-	1	1
Tumour	1	18	19
Cyst	-	1	1
Atrophy	4	8	12
Cerebral Abscess	-	2	2
Cerebral Toxoplasmosis	-	3	3
AVM	-	3	3
Subdural hematoma	2	2	4
Total	8	56	64

Table 6. Clinical and EEG variable in symptomatic and idiopathic group*

Clinical and EEG variables	*Symptomatic (n=68)*	*Idiopathic (n=52)*	*Odds ratio*	*P value*
Todd's paralysis	2	2	0.76	0.580**
Neurological deficit	39	19	4.48	0.000
Types of epilepsy				
Generalized	9	21	0.23	0.001
Simple partial	39	2	31.45	0.000
Complex partial	3	23	0.06	0.000
Secondarily generalized	17	5	3.13	0.031
EEG abnormalities/discharges				
Focal epileptiform	35	11	3.95	0.001
Generalized epileptiform	7	14	0.31	0.018
Focal slow waves	10	6	1.27	0.659**
Normal	11	17	0.40	0.035

* As defined by brain neuroimaging
**Not statistically significant

Conflit d'intérêt	Aucun

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