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First seizure in adults: a prospective study from the emergency department

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A prospective study of 98 consecutive adults with a first seizure to determine the most important etiological factors and the optimum diagnostics. 27 were thought to have cryptogenic seizures. Main causes of symptomatic seizures were: cerebral infarction, alcohol-withdrawal, CNS infections, tumors, vascular malformations, traumatism and miscellanea. Eight were infected by human immunodeficiency virus (HIV-1) representing 8.2% of all the patients with a first seizure and 20% of the 15–45-year age group. CT disclosed structural lesions in 33 cases. MRI in those with normal CT and no other explanation of seizure revealed additional lesions in 22.2%, but did not change management in any. We conclude that CT is essential in evaluation of adults with first seizure. MRI may be useful in selected cases. The HIV-infected now represent an important group with a first seizure.

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About 5% of the population may expect to have a seizure (1), and many will be referred to an Emergency Department. However, there have been few studies of adult seizures in the emergency ward (2–5). The only prospective study (2) was not specifically focused on new-onset seizures. It included 24 first-time seizures (children and adults) and no clear conclusions could be drawn from this small group.

Diagnosis of epileptic seizure is subject to interobserver variability (6). Few studies have mentioned diagnostic criteria; to minimize the interobserver variability, we used diagnostic criteria suggested by van Donselaar et al. (6). This study was designed to determine the most important etiological factors of new-onset seizures in emergency and their optimum diagnostics.

Material and methods

The study began in February, 1990 and ended 10 months later. The Emergency Department of this hospital serves an urban population of 700 000. A full-time neurologist is available in Emergency. Every possible first seizure was evaluated by the consultant neurologist, from a complete neurological examination and relevant items of medical history, including: alcoholism, medication, illicit drug use and risk factors for HIV-1.

Criteria for inclusion were: 15 years dd or older and a first seizure; diagnostic criteria (6), seizure classification (7). Patients with known brain tumors were excluded.

Diagnosis was based on: a) general medical examination by an internist, b) thorough neurological examination by the neurologist, c) 12-lead electrocardiogram, d) haematological and biochemical screening tests which included blood cell counts, glucose, creatinine and electrolytes, e) unenhanced CT scan; if this was normal, CT scan was repeated after intravenous administration of iodinated contrast medium. Sometimes depending on clinical criteria only a contrast-enhanced CT scan was performed. All CT scans were read by a neuroradiologist and by the neurologist attending.

If no etiology could be found, a MR scan was performed at 0.5 T within a month of seizure. Serology for HIV-1 was done in patients at the risk group (drug abusers, previous transfusions, homosexuals, persons with a great number of sexual partners). Whenever possible, a 16-channel electroencephalogram (EEG) was performed in the Epilepsy Unit of the Neurology Department, and interpreted by a qualified electroencephalographer.

Neuroimaging criteria (CT and MR scan) were used for diagnosing cerebral infarction, tumor, vascular malformation, subdural hematoma, and cerebral malformation. The cause was assumed to be trauma if there was a history of head injury with loss of consciousness. Standard criteria were used to diagnose meningitis, encephalitis, toxoplasmic abcess

in HIV-infected patients, alcohol-withdrawal, uremia, hyponatremia and drug toxicity.

Results

In the course of the study 98 patients were diagnosed in Emergency as having a first seizure, 70 (71%) were men and 28 (29%) were women. During this time, there was a total of 40 000 referrals to Emergency. The mean age was 49.2 years (15–87). Age distribution is shown in Fig. 1.

Causes. 27 patients were thought to have cryptogenic seizures (27.6%). Of symptomatic seizures, the main causes were: cerebral infarction (23); alcohol-withdrawal (11); CNS infections (9); tumors (8) including 1 meningioma, 2 gliomas and 5 metastases; vascular malformations (6) including 3 arteriovenous malformations, 2 cavernomas and 1 venous malformation; 4 were attributed to trauma; drug toxicity accounted for 3, 2 were due to the theophylline toxicity and one to cyclosporine toxicity; there were 2 subdural hematomas and 2 cases of hyperglycemia (hyperosmolar state). Uremia, hyponatremia (115 mEq/L) due to psychogenic water drinking, and cerebral malformation accounted for one case each. There was pathological confirmation of the diagnosis in 8 patients (five neoplasias, two subdural hematomas and one vascular malformation) (Table 1).

Only 11 of those with cerebral infarction (47.8%) had a past history of cerebrovascular disease. Three of the five patients with metastases had previously diagnosed tumors. The other two were metastases from lung cancer in male heavy smokers.

Eight patients were infected by HIV-1 representing 8.2% of all the patients with a first seizure, and 20% of the 15–45 year age group. The etiologies among them were: toxoplasmic abcesses (2), cryptococcal meningitis (1), herpes-zoster meningoencephalitis (1), cytomegalovirus encephalitis (1), alcohol-withdrawal (1). No cause could be found in two cases after a thorough study with enhanced CT scan and lumbar puncture (MR scan could not be done because of refusal of the patients). The seizure was the symptom that led in one patient to know that he was infected by HIV-1.

Table 1. Causes

Cause	N (%)
Idiopathic	27 (27.6)
Cerebral infarction	23 (23.5)
Alcohol withdrawal	11 (11.2)
CNS infection	9 (9.2)
Tumor	8 (8.2)
Vascular malformation	6 (6.1)
Trauma	4 (4.1)
Drug toxicity	3 (3.1)
Subdural hematoma	2 (2)
Hyperglycemia	2 (2)
Uremia	1 (1)
Hyponatremia	1 (1)
Cerebral malformation	1 (1)

The etiologies of seizures varied according to age. Table 2 compares the causes found in patients under 45 years with those found in patients over 45 years. The proportion of idiopathic seizures decreased with age; 45% in the group under 45 years and 15.5% in people over 45 years. Among symptomatic cases, the main etiologies found in the group under 45 years were: CNS infections (17.5%), alcohol-withdrawal (15%), trauma and vascular malformation (7.5% each). However, in the group over 45 years the two main etiologies were cerebral infarction (37.5%) and tumors (12%).

People over 60 years comprised 33.7% of all patients included in the study; ischemic lesions were found in 60.6%. Only 15.2% of seizures in this age-group were considered idiopathic.

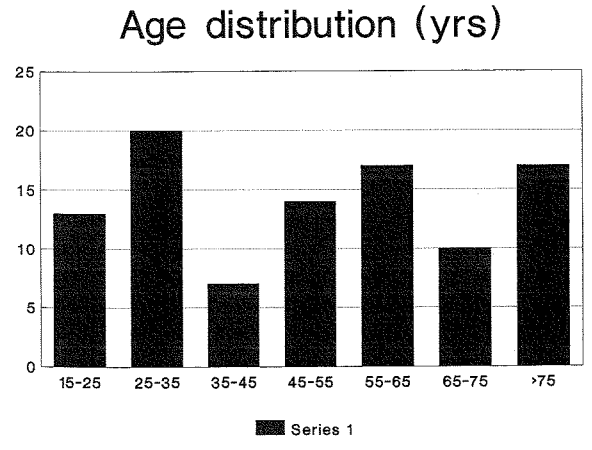

Fig. 1.

Table 2. Etiology according to age distribution (yrs)

Cause	<45 yrs	>45 yrs
Idiopathic	18 (45%)	9 (15.5%)
Cerebral infarction	1 (2.5%)	22 (37.9%)
Alcohol related	6 (15%)	5 (8.6%)
CNS infection	7 (17.5%)	2 (3.4%)
Tumor	1 (2.5%)	7 (12%)
Vascular malformation	3 (7.5%)	3 (5.2%)
Trauma	3 (7.5%)	1 (1.7%)
Drug toxicity	0 (0%)	3 (5.2%)
Subdural hematoma	0 (0%)	2 (3.4%)
Hyperglycemia	0 (0%)	2 (3.4%)
Uremia	0 (0%)	1 (1.7%)
Hyponatremia	1 (2.5%)	0 (0%)
Cerebral malformation	0 (0%)	1 (1.7%)
Total=	40	58

Type of seizure. 67 (68.4%) were tonic-clonic seizures without evidence of focal onset, 19 (19.4%) were secondarily generalised, 10 (10.2%) were simple partial, and 2 (2%) were complex partial. Fifteen cases (15.3%) presented as a status, 9 were of the generalized tonic-clonic type, 4 were focal, and 2 were complex partial status.

General medical examination. General medical examination was of little utility except for determining the presence of fever. Nine patients were febrile (temperature $>38°C$). Five of these patients had CNS infections: encephalitis (3), tuberculous meningitis (1) and toxoplasmic abcesses in a HIV-infected individual (1).

Neurologic examination. Findings were divided into two groups: focal and non-focal. Thirty-two patients were placed in the first group (32.7%) and 66 to the second (67.3%). The causes in both groups are shown in Table 3. While no cause could be found in nearly 40% of patients with non-focal findings, almost all (96.9%) of the patients in the group with focal findings had seizures that were symptomatic.

Neuroimaging results. CT disclosed structural lesions in 33 cases (33.7%). The probability of a CT scan being abnormal was higher in the group with focal findings (59.3%) than in that with non-focal findings (21.2%). MR scans of the head were performed in 27 of 33 cases where no obvious cause could be discovered after a thorough evaluation which included enhanced CT scan. Four of six with cryptogenic seizures, but without MR scan, were lost to follow-up and the other two refused to undertake MRI. MR scan was abnormal on 6 occasions (22.2%). In the group with focal findings on neurologic examination, MR cranial scan was abnormal in two cases where CT scan had been normal: the case of cyclosporine toxicity where MR imaging showed white-matter abnormalities that cleared after reducing cyclosporine dosage, and a case of cytomegalovirus encephalitis.

In the group of patients with non-focal findings in the neurologic examination, MR scan was abnormal in four cases where CT scan had been normal; three cases showed small cerebral infarctions, and one case revealed a venous malformation.

Even after excluding patients who had seizures with focal features, CT and MR scans disclosed structural lesions in 10 of 51 cases (19.6%) with generalized seizures and non-focal findings in the neurologic examination.

Table 3. Etiologies of patients with non-focal findings and focal findings on neurologic examination

Cause	Nonfocal	Focal
Idiopathic	26 (39.4)	1 (3.1)
Cerebral infarction	8 (12.1)	15 (46.9)
Alcohol related	11 (16.7)	0 (0)
CNS infection	4 (6.1)	5 (15.6)
Tumor	3 (4.5)	5 (15.6)
Vascular malformation	5 (7.6)	1 (3.1)
Trauma	4 (6.1)	0 (0)
Drug toxicity	2 (3)	1 (2.9)
Subdural hematoma	0 (0)	2 (6.3)
Hyperglycemia	1 (1.5)	1 (3.1)
Uremia	0 (0)	1 (3.1)
Hyponatremia	1 (1.5)	0 (0)
Cerebral malformation	1 (1.5)	0 (0)
Total	66	32

Lumbar puncture. 24 lumbar punctures were performed and 7 of them were abnormal. Two were HIV-infected patients who were afebrile and without meningeal signs.

However, they had cryptococcal and herpes-zoster meningitis respectively. The other five were febrile immunocompetent individuals, their etiologies were: tuberculous meningitis (1), three cases of encephalitis, one of them herpetic (biopsy-proven), and one case of pleocytosis due to status epilepticus.

Electroencephalogram (EEG). An EEG was performed in 73 cases. Normal results were obtained in 32 cases (43.8%), 24 cases (32.9%) showed focal spikes or focal slowing. Other results were obtained in the remainder. CT or MR scans were abnormal in 15 of 24 cases (62.5%) with focal spikes or focal slowing. However, when EEG was normal CT or MR scans were abnormal in only 6 of 32 cases (18.8%). Three of the 6 cases were vascular malformations and the other three were cerebral infarctions.

Other investigations. Biochemical tests were useful in four cases: 2 of hyperglycemia, 1 of uremia and 1 of hyponatremia. Hyperglycemia and uremia cases were easily suspected by clinical history. However, biochemical tests were the clue that revealed serious hyponatremia in a 17-year-old girl with previously unknown psychogenic water drinking.

Discussion

The etiology of the first seizure was established in 72.4% of the patients in this series, a higher figure than that of the study of Ramirez-Lassepas et al. (48%) (22). Possible explanations for the lower incidence of idiopathic seizures in our series are that all the patients were evaluated by a neurologist within few hours after the seizure, and that a thorough examination, including CT and MR scans, was per-

formed. The proportion of symptomatic seizures increased with age, 55% in people under 45 years increasing to 85% in people over 45 years. Their etiology varied substantially between different age groups. While cerebrovascular disease and tumors were the main causes in people over 45 years, CNS infections, alcohol-withdrawal, trauma and vascular malformations accounted for almost all the symptomatic seizures in the 15–45 year age group.

First seizures in the elderly have generally been held to be rare. However, recent studies have reported high rates, 24% in the National General Practice Study of Epilepsy (8), and 35% in the study of Loiseau et al. (9). The rate of elderly seizures in this study is similar (33.7%). This findings may reflect the growing proportion of elderly people in the general population. Vascular disease is the leading etiology in this group of age. The National General Practice Study of Epilepsy obtained an estimate of 49% based on clinical and radiological criteria (8). Using neuroimaging investigations, that included CT and MR scans, we have obtained higher estimates (60%) of vascular disease as the most important etiological factor in the elderly.

Disorders of the central nervous system are a major source of morbidity and mortality in HIV-infected patients (10, 11). Seizures are common manifestations of CNS disease in HIV infection (12–14). A large series of patients with new-onset seizures associated with HIV infection has been published (15). However, there has been no report about the incidence of HIV-infection in new-onset seizures in unselected groups of population. Our study has found an 8.2% incidence of HIV-infection in an unselected group of people with a first seizure attending the Emergency ward of a general hospital. As HIV-infection mainly affects young people, this figure rose to 20% in the 15–45 years age group. Real numbers may be even higher since serology for HIV-infection was not done in all but high-risk patients. CNS infections are the most common cause of seizures in HIV-infected patients (15). The large number of young adult patients with a first seizure due to CNS infections in this study reflects the incidence of HIV infection in this group. Five of eight patients with HIV-infection and new-onset seizures had treatable CNS infections even in afebrile patients with normal neurological examinations. Since the absence of fever and normal neurological examinations does not exclude treatable causes in HIV-infected patients, appropriate evaluation should include enhanced cranial CT scans (or MR imaging if available). Lumbar puncture should be performed if neuroimaging results are normal and there is no contraindication to it. If serology for HIV is unknown and the patient belongs to the risk group it may be wise to manage him as HIV-infected while waiting for serology results. Even negative, serology should be repeated because acute encephalopathy with seizures can occur coincident with seroconversion to HIV-1 (16).

Previous studies have indicated that hematological and biochemical screening tests are of minimal (22) or no value (2) in the evaluation of patients with seizures. The results obtained in this study agree with the low yield of biochemical tests. However, biochemical tests were the clue that uncovered serious psychogenic water drinking in a 17-year-old girl. Laboratory tests are also helpful in identifying heavy alcohol drinkers (23). The combination of abnormal gamma glutamyltransferase (GGT) and mean corpuscular volume (MCV) identified 91% of alcoholics in a general medical population (24).

EEG remains an important diagnostic tool in evaluating patients with epileptic seizures (17). However, a normal EEG does not preclude the existence of structural lesions (18). We found structural lesions in 18.8% patients with normal EEGs.

Several papers have analyzed the role of CT scan in evaluating adults after their first seizure (19–22). AC Young et al. (19) reported 16.4% of abnormal scans (excluding atrophy) though all the patients with treatable lesions had clinical or EEG features that suggested them. However, only 31 of their patients had a single seizure. Russo et al. (20) discovered structural lesions in 25.8% of adult patients with a first seizure (excluding atrophy), but in only 5.9% of patients with non-focal findings in the neurologic examination. In the series of Ramirez-Lassepas et al. (21), CT scan identified structural lesions in 37% of patients. In the group of patients with nonfocal findings 15% had structural lesions in CT scans. CT scans showed structural lesions in only 5.7% of the patients in the series of Hopkins et al. (22). However, there are several points of the last study important enough to be mentioned. First, not all the patients underwent CT scanning. Second, older people were under-represented, perhaps leading to a lower rate of symptomatic seizures. Lastly, people with recurrent seizures before referral were excluded. As patients with structural lesions are more likely to have recurrent seizures, excluding patients with early recurrent seizures may have excluded patients with structural lesions as well. In our series, CT scan disclosed structural lesions in 33.7% of cases. Even in the group of patients with nonfocal findings in the neurologic examination, there was a 21.2% incidence of abnormal CT scans, including several cases of tumors and vascular malformations.

MRI has proved to be more sensitive than CT in detecting cerebral lesions related to epilepsy (25), specially gliomas (26) and cavernous malformations (27). However, in our study no case of glioma or cavernous malformation was detected in 27 cases of

first seizure with normal CT scan who underwent MRI. MR scans revealed additional lesions in 22.2% of cases but they did not change management in any of them. MRI is more expensive and time-demanding than CT. Though all patients with refractory seizures should have a MR scan (17), it has not yet been proved to be cost-effective to perform it in all patients with a first seizure.

In summary, our findings show that a thorough evaluation of adults after their first seizure produces a high yield of identified cause. CT is essential in this evaluation, MRI may be useful in selected cases when CT scan has been normal. HIV-infected people represent nowadays an important group among patients with a first seizure attending Emergency.

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