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Epilepsy in middle-aged and elderly people: a three-year observation

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ABSTRACT – An analysis of the medical documentation and investigation of 130 cases of epilepsy diagnosed in a group of people over 50 years of age (average: 65.4 years) revealed that the most common type of seizure in the group studied was partial (66.2%), followed by seizures with secondary generalization (33.8%). Epilepsy was caused by cerebrovascular disease (50.8%) considerably more often in patients over 74 years of age, craniocerebral trauma in patients addicted to alcohol (13.1%), especially those under 65 years of age, primary or metastatic neoplastic disease (10.7%), and others. The authors wish to draw attention to the leukoaraiosis factor, which might be the proepileptogenic cause of epilepsy recognized in the group of patients over 74 years of age (56.5%) and is much more frequent in this group than in the group of patients under 65 years of age (1.6%). Moreover, some drugs, such as L-dopa and Baclofen, might have been related to the epileptic seizures. In 29 patients (22.3%) the definite cause of late-onset epilepsy was unknown. The authors suggest in such cases, both follow – up tomographic examination and careful clinical examinations. In the study group of patients with initially unknown seizure etiology, some diseases, such as cerebral tumor or colon and pancreatic neoplasm, were diagnosed during follow-up examination. These processes were revealed several months after the first epileptic seizure.

Key words: late-onset epilepsy, etiology, type of seizure, diagnostic, elderly

Epilepsy is the third most common chronic neurological disease among the elderly as regards incidence, the two more common being cerebrovascular disease and dementia (Wallace *et al.* 1998, Van Cott 2002). Nowadays, there are over 70 million people in the World over 80 years old. According to demographic forecasts, the number of people in this age group will increase 5-fold in the next 50 years. The number of people who are older than 65 is estimated to be about 170 million in developed countries and 248 million in developing ones (The World Health Report 1998, The World Health Report 2001). In Poland the figure is now 4,250,000, and accepting the WHO demographic forecast for the year 2030, the number will be around 8 million. So we can expect that the incidence of diseases typical of the elderly will also increase.

Research on the Rochester, Minnesota, population (collected between 1935 and 1984) showed that epilepsy in patients older than 70 occurred two to three times more often than in children (Hauser *et al.* 1993). Taking the prevalence of epilepsy into consideration, we find that in the whole population it is 4-10/1000 and that this increases with age (Olafsson and Hauser 1999, Bell and Sander 2001, Jallon

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2002). Consequently, among people older than 60 it is 10.9/1000, and in those over 80, 13.1/1000 (Craig and Tallis 1991, MacDonald *et al.* 2000). The incidence of epilepsy is 40-70/100,000 a year, and this also increases with age. Among those older than 60, it ranges from 76/100,000/year to 159/100,000/year (MacDonald *et al.* 2000, Sirven 2001).

It can be very difficult to establish a diagnosis of late-onset epilepsy, especially in cases of complex partial seizures, because of other, accompanying, somatic diseases. What is more, the presentation of epilepsy in elderly people can be misleading and might resemble TIA (transient ischemic attacks), TGA (transient global amnesia), hyper- or hypoglycemia, or numerous cardiac arrhythmias (Godfrey 1989, Rovan 1998).

The aim of our clinical analysis was to define the types and causes of epileptic seizures in patients with diagnosed epilepsy who were older than 50 years and who were hospitalized for the first time.

Materials and methods

On the basis of documentation available at the Department of Neurology of the Wroclaw Medical University, a retrospective analysis of all patients over 50 years of age who were hospitalized with diagnosed epilepsy between Jan. 1, 2000, and Dec. 31, 2002, was performed.

We included those patients who had had at least two epileptic seizures over four weeks and who were older than 50. We excluded from our analysis patients with seizures in their medical history (occurring before the age of 50), with inborn brain injury, or those who were taking anticonvulsant medications prescribed because of seizures accompanied by loss of consciousness.

We did the retrospective analysis of 130 patients who were between 50 and 88 years old (average age was 65.4 +/- 9.4 years), which included 69 women aged 50-86 (average: 65.9 +/- 9.5 years) and 61 men aged 50-88 (average: 64.8 +/- 9.4 years). The whole group was divided according to age into four standard subgroups (Garrard *et al.* 2000): subgroup A (aged 50-64), subgroup B (aged 65-74), subgroup C (aged 75-84) and subgroup D (older than 85 years of age). There were 62 patients in subgroup A (30 women and 32 men, average age: 56.4 +/- 4.3 years), 45 patients in subgroup B (26 women and 19 men, average age: 68.7 +/- 2.8 years), 20 patients in subgroup C (12 women and 8 men, average age: 78.3 +/- 2.7 years), and 3 patients in subgroup D (1 woman aged 86 and 2 men aged 87 and 88; average age: 87.0 years) *(table 1)*.

The analysis of the medical documentation included the results of subjective and objective examination, medical history and previous pharmacological treatment that might have reflected the epileptogenesis, and objective family history for epilepsy and seizures. We evaluated, from among the laboratory investigations, blood morphology, electrolytes, glucose, urea and creatinine levels, electrocardiography (ECG), routine electroencephalography (EEG), and in 7 cases, also sleep deprivation EEG and CT and/or MRI imaging results. We classified the types of seizure with the help of the International Classification of Epileptic Seizures (Bancaud *et al.* 1981).

Patients, whose etiology of epileptic seizure after their first hospitalization was not defined, were summoned again to our Department of Neurology after 12 months in order to obtain information about any pharmacological treatment (including antiepileptic drugs), the frequency and type of seizures, and diagnostic examinations during that time.

Results

Routine EEG recordings in 20 patients (15.4%) showed no abnormalities. In 32 (24.6%) patients with epileptic seizures we found focal epileptiform discharges (mainly theta and delta slow waves). Bilateral or generalized discharges on the EEG occurred in 64 (49.2%) patients. EEG recording was not performed in 14 (10.8%) patients because of the unequivocal character of seizures, numerous cerebrovascular and neoplastic lesions in the CT examination, or the very poor state of health of the patient.

In 44 (33.8%) patients, medical history, morphology of seizures, and EEG results suggested the diagnosis of primary generalized tonic-clonic seizures; in the remaining 86 (66.2%) patients they suggested the presence of complex partial seizures with or without secondary generali-

Table 1. Types of epileptic seizures in the groups investigated.

Investigated groups of patients	Subgroups				
	All	A	B	C	D
Number of patients	130	62	45	20	3
Sex F/M	69/61	30/32	26/19	12/8	1/2
Age x (SD)	65.4 +/- 9.4	56.4 +/-4.3	68.7 +/-2.8	78.3 +/-2.7	87.0
Primary generalized seizures	44 (33.8%)	23 (37.1%)	14 (31.1%)	5 (25.0%)	2 (66.7%)
Complex partial seizures	78 (60.0%)	35 (56.4%)	29 (64.4%)	13 (65.0%)	1 (33.3%)
Simple partial seizures	8 (6.2%)	4 (6.4%)	2 (4.4%)	2 (10.0%)	0 (0%)

zation (this included 78 patients with complex partial and 8 patients with simple partial seizures). Secondary generalized seizures occurred in 26 patients with complex partial seizures *(table 1)*.

In subgroup A, we diagnosed primary generalized seizures in 23/62 (37.1%) patients, complex partial in 35/62 (56.4%) patients, and simple kinetic in 4 (6.4%) patients. Among the patients with partial seizures, secondary generalized seizures occurred in 10 (25.6%) cases.

In subgroup B, we accepted a diagnosis of primary generalized in 14/45 (31.1%) patients, complex partial seizures occurred in 29/45 (64.4%) patients, and simple kinetic seizures in 2 cases (4.4%). In 12 (38.7%) patients with partial seizures, the diagnosis was secondary generalized seizures.

In subgroup C, the medical documentation suggested a diagnosis of primary generalized seizures in 5/20 (25.0%) patients, complex partial in 13/20 (65.0%) patients, and simple partial in 2 (10.0%). Among the patients with partial seizures, secondary generalized seizures occurred in 4 (26.6%) cases. Finally, in the 3 patients over 85 years of age (subgroup D), we diagnosed primary generalized seizures in two and complex partial in one.

In every subgroup, changes in ECG, which might have been the cause of consciousness disorders, were not registered.

Cerebrovascular disease was the most common cause of epilepsy in our study: 66/130 (50.8%) patients had a cerebrovascular focus or foci, in one case without clinical manifestation (« silent » stroke). We found this etiology in 26/62 (41.9%) patients in subgroup A, in 25/45 (55.5%) in subgroup B, and in 15/23 (65.2%) in the oldest patients (subgroup C and D) *(figure 1)*.

Craniocerebral trauma with a brain contusion focus in the course of alcoholic disease was accepted as a cause of epilepsy in 17 (13.1%) patients. It was responsible for seizures in 14/62 (22.6%) patients in subgroup A, 2/45 (4.4%) in subgroup B, and in only 1/23 (4.3%) patients in subgroups C and D. Only in one case was alcohol addiction the etiological factor, but without focal cerebral lesion.

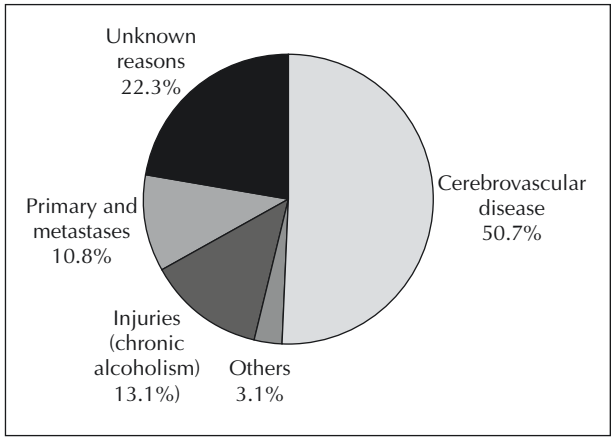

Figure 1. Causes of epileptic seizures in our study (130 patients).

In 14 (10.7%) patients, we found primary cerebral tumors or metastatic cerebral foci. This was present in 6/62 (9.7%) patients in subgroup A, in 5/45 (11.1%) in subgroup B and in 3/23 (13.0%) patients in subgroups C and D.

In the oldest subgroups (C and D), apart from focal ischemia or hemorrhagic lesions on CT examination, we found the presence of leukoaraiosis in 13/23 (56.5%) patients. In subgroup A, we found only 1/62 (1.6%) and in subgroup B – 4/45 (8.9%).

In 1 (0.8%) case we discovered a large arachnoida cyst in the frontal area with cerebral ventricle dislocation. Moreover, in one patient we observed evidence of cerebral viral inflammation. A factor favourable to seizures might have been the simultaneous use of L-dopa in 7 patients, and of Baclofen in 2 patients with spastic paresis.

In 29/130 (22.3%) of patients, we were unable to identify any possible cause of the seizures.

Twenty-three of the 29 patients with no confirmed cause of seizures returned after 12 months. Eight of them had suffered no epileptic seizures within the previous six months. Seven were still continuing with previously established anticonvulsant treatment. In 6 patients, seizures still occurred in spite of treatment. In 3 cases we performed CT or MRI examinations again, but this still did not help to establish the cause of the seizures.

Three months later we determined a primary cerebral tumor in 1 patient (55 years old) and vascular dementia in 2 patients. After a few months of hospitalization in the Neurological Department we discovered neoplastic developments on the colon and pancreas in 2 women (69 and 78 years old). Both died following surgical intervention. Two others also died, one as a result of trauma and the other of unknown reasons. We obtained information from the family and/or caregiver.

Discussion

Our results show that epileptic partial seizures with or without secondary generalization are the most common type of seizure (66.2%) in patients over 50 years of age. The second most common type of seizure, according to incidence, is primary generalized (33.8%).

On the basis of this clinical data analysis we have established that complex partial seizures occur more often in patients who are older than 74. This is compatible with the results of other authors (Hauser 1992, Van Cott 2002). The incidence of primary generalized seizures (over 65) appeared to be higher in our study than in that of Hiyoshi and Yagi (Hiyoshi and Yagi 2000).

Cerebrovascular disease is the single most common pathological factor underlying epilepsy in elderly people (Gupta *et al.* 1988, Kilipatrick *et al.* 1992, Ruggles *et al.*

2001, Roberts *et al.* 1982). Post-stroke epileptic seizures occur mostly after 3 months to 1 year. In the literature, there are some examples of epileptic seizures appearing 14 years after a cerebrovascular event (Van Cott 2002). Vascular brain damage as a consequence of ischemic or hemorrhagic stroke appeared to be of prime importance in our research, and the frequency of seizures increased with advancing age, ranging from 41.9% in people under 65 years of age (subgroup A) to 65.2% over 75 years (subgroup C and D). First epileptic seizures occurred 12 weeks to 13 years after the stroke. In one case we acknowledged « silent » stroke as a cause of seizures.
The epileptic risk factor, according to De Reuck (De Reuck *et al.* 1996), is leukoaraiosis, which induces a blood flow diminution and a decrease in oxygen consumption in different cerebral cortex areas. We proved that in our group the proportion of patients with leukoaraiosis increases with age. In the oldest subgroups (C and D) it occurred in 56.5% patients, and under 65 years of age in just 1.6%.

In our study, similarly to others, the subsequent causes of epilepsy (in patients older than 50) were a cerebral neoplastic course and craniocerebral trauma in patients addicted to alcohol (Hauser *et al.* 1993). Traumatic brain contusion considerably more often caused seizures in younger patients (22.7% in subgroup A *versus* 4.3% in subgroup B); in patients over 74 years of age there was no evidence of craniocerebral trauma. Only in one case (a 59-year-old man) was alcohol abuse established as the only etiological factor causing epileptic seizures. Neoplastic disease was most common in people over 74 years of age (13% in subgroups C and D) and rarest under 65 years (9.7% in subgroup A).

Certain medications in elderly patients could have promoted epileptic seizures (Stephen and Brodie 2000). It is not clear how the L-dopa mechanism induces seizures. It is believed that it causes dysregulation of serotoninergic activity or increases the sensitivity of catecholaminergic receptors of the brain stem (Klawans *et al.* 1975, Vardi *et al.* 1978). Baclofen is an agonist of the GABA-B receptor and it owes its convulsiogenic activity to various mechanisms. It may induce a convulsion threshold decrease by a change in GABA uptake or cell membrane permeability and disequilibrium in the synaptic stimulation and inhibition processes (Schwartzkroin 1995, Mott *et al.* 1989).

In 29 (22.3%) patients, we did not manage to establish, on the basis of the documentation, the causes of epileptic seizures; this being 21% in subgroup A, 26.7% in subgroup B, and 14.7% in subgroups C and D. Twelve months later, we performed a follow-up examination which revealed that in one patient a developing brain tumor caused seizures and in 2 patients it was vascular dementia that caused epileptic seizures. We can not exclude that in 2 further cases epileptic seizures were manifestations of developing colon and pancreatic neoplasm.

In conclusion, we should state that partial seizures caused by vascular or traumatic brain damage are the most common types of seizure in patients older than 50. Leukoaraiosis and some medications (*e.g.* L-dopa and Baclofen) may also trigger seizures. Whenever possible, we should eliminate these medications or restrict their dosage. In cases whereetiology cannot be established in patients older than 50, a thorough examination should be performed to rule out the possibility of any neoplastic focus beyond the central nervous system and a follow-up CT or MRI examination of the head.

Conclusions

1. Epileptic seizures in patients over 50 years of age are mostly partial in nature: simple or complex. They are usually the consequence of vascular brain damage.
2. Epileptic seizures with no established etiology (in elderly patients) require thorough neurological and clinical examination and CT/MRI follow-up examinations. □

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