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Epileptic seizures following an ischaemic hemispheric stroke

About 25% of the first occurring seizures are noted in patients over 60 ys old with steady increase of incidence at advanced age from 50/100,000 at 60 ys. to 100–150/100,000 people at the age of 80 ys. (1). Epilepsy is the third most common CNS disease in elderly after stroke and dementia. Cerebrovascular origin is an important cause of occasional epileptic fits and so-called late onset epilepsy. This factor is responsible for about 52% recognised causes, before tumorous aetiology (12.5%), CNS degenerative processes (11.5%), trauma and metabolic disturbances (2, 3). Early seizures (ES) defined as those occurring within the first week or two weeks are mostly observed during 24 h after a stroke in 2.5–5.7% of patients and they often represent the earliest symptom of brain damage (2–5). Late seizures (LS) occur within more than two weeks after a stroke. Both types may be acute sporadic symptomatic or repetitive fits. Then they represent the post-stroke epilepsy (3, 5, 6). Pathomechanisms of ES and LS in stroke-affected brain are probably different. It is not known whether ES or rather LS might be a risk factor for further epilepsy (2, 5). In this study we have analysed the relationship of the first epileptic fits and selected parameters of the clinical state in patients with the ischemic stroke in supratentorial region within the earliest phase of illness.

MATERIAL AND METHODS

Retrospective survey of 196 consecutive patients admitted to the stroke unit during 12 months with diagnosis of a first ischemic stroke and without katamnesis of previous epilepsy was performed. Pharmacological treatment was introduced according to recent standards (iv isotonic solutions till up 1500 ml/day, acetylsalicylic acid –75 mg/day, piracetam iv 12 g/day/per 3 days). Relanium 10 mg iv was only applied as a rescue medication in case of epileptic fit. Analysis included: gender, age, stroke risk factors and incidence of early (ES) and late seizures (LS) within 42 days' follow-up.. Computed tomography (CT) was performed in 82% and EEG in 23% of cases (all with seizures). We have also determined the type of seizures, initial stroke severity and localization. ES were defined as those appearing during the first 14 days after admission. In this group we have evaluated the contribution of metabolic factors: temperature, serum electrolytes, glicaemia, parameters of kidney and liver function. A control group of 14 stroke patients without seizures matched for the stroke type, age and gender was used to compare the occurrence of metabolic abnormalities. Seizures semiology was estimated according to the recommendation of the International League Against Epilepsy. The type of stroke was classified in 4 clinical categories according to the Oxfordshire Community Stroke Project (OCSP). The chi-square test was used in statistical comparisons.

RESULTS

The average age of 196 ischaemic stroke patients (n – 102 =52% men, n – 94= 48% women) was 63.3 ys (SE±13.9; range: 42–79 ys). Twenty-three (12%) stroke patients presented epileptic seizures: n – 14 (7%) ES and n – 9 (5%) LS. There were no significant age and sex differences among groups with ES, LS and patients without seizures (Table 1). The main risk factors for stroke were: hypertension (83%), diabetes mellitus t. II (73%), hypercholesterolemia (34%) and atrial fibrillation (24%). According to the Oxfordshire Stroke Community Classification, 11 out of 14 ES patients presented symptoms typical of PACI category, two were classified as TACI and one as POCI. CT imaging revealed the frontal lobe localisation of infarct in five cases, temporal in three, parietal in three and occipital in one patient. In two patients a multi-lobar infarction in a forebrain region was detected. In all cases CT confirmed the cortical involvement of lesion (Table 2). The majority (12 of 14) of ES occurred within the first 24 hours. Both early and delayed seizures manifested as focal motor fits contralaterally to the involved hemisphere. A half of ES evolved to complex partial or secondarily generalised fits. In the ES group metabolic abnormalities were found significanly more frequently: hyperglycemia in 71% of cases ($p<0.01$) and fever in 86% ($p<0.001$) (Table 3). There was a higher total incidence of metabolic abnormalities in patients with ES (n – 42) than in reference group (n – 22) (Table 4).

Table 1. Characteristics of stroke patients by age, gender and occurrence of seizures

Early seizures		Late seizures	Without seizures	Total population
No. of patients	14 (7%)	9 (5%)	173 (88%)	196 (100%)
Mean age, yrs	63.8	64.4	65.4	63.3
Male gender	6/14 (43%)	5/9 (56%)	91/173 (53%)	102/196 (52%)

Table 2. Characteristics of stroke in patients with early seizures (n – 14)

Stroke localization in CT (n)		Stroke type (n)	
Frontal	5	PACI	11
Temporal	3	TACI	2
Parietal	3	POCI	1
Occipital	1	LACI	0
Multi-lobar	2		
Cortical involvement	14		

Table 3. Metabolic and biochemical parameters in patients with early stroke

Parameter	Patients with seizures (N)	Patients without seizures (N)
Temperature > 37°C	12 ***	3
Glucose >120 mg/dl	10 **	2
Na < 135 mmol/l	7	3
K < 3.5 MMOL/L	6	4
Creatinine > 1.4 mg/dl	2	2
Total bilirubin > 1 mg/dl	1	1

n – number of patients; *** p< 0.001; **p<0.01

Table 4. Incidence of metabolic abnormalities in stroke patients

Abnormalities (number per patient)	Patients with seizures (N)	Patients without seizures (N)
None	-	4
1	2	4
2	2	2
3	5	2
4	4	2
5	1	-
Total incidence	42	26

DISCUSSION

The occurrence of epileptic seizures during acute stroke is a well known phenomenon but their risk factors are not fully established. In this retrospective study 23 out of 196 consecutive patients (12%) with a diagnosis of recent ischemic injury in brain supratentorial region experienced stroke-related seizures. They occurred as an acute within two weeks after stroke onset in 60% of cases or were noted later up to 42 days in other 40%. This frequency was higher than the range evaluated in some previous studies (3, 6, 7). Our analysis was restricted to a selected group of patients with the first ischemic incident and with definite confirmation of recent organic lesion on CT scans that was performed within 48 hs. Furthermore, seizures were registered during a short period of six weeks' follow-up. As in previous studies on differentiated types of stroke also in this study the majority of early seizures occurred within the first day (2, 3, 6, 7). Both early and delayed fits manifested contralaterally to the involved hemisphere as single, simple partial motor seizures. Only in a part of patients they evolved to complex partial or/and secondary generalised. The main stroke risk factors in patients with seizures were hypertension, atrial fibrillation, diabetes mellitus and hypercholesterolemia. Simultaneously, in patients with early seizures, but not in patients without

seizures transient hyperglicaemia and fever were noted. These disturbances are frequently observed in other acute symptomatic seizures. They are also accompanied by a more severe clinical state in both ischemic and haemorrhagic stroke. In numerous works these two factors were considered as prognostically unfavourable (8, 9). In the well-known Copenhagen Stroke Study in 1,197 patients with acute ischemic or haemorrhagic stroke it was established that only severity of the initial clinical state was in relation with early seizures. This observation was confirmed in newer prospective observations (5). Simultaneously, the immediate seizures were noted mostly in patients with atrial fibrillation, diabetes mellitus and in those with significantly elevated glicaemia on admission. On the other hand, these early seizures were not associated with a higher risk of mortality but with comparable or even better outcome (5). It has been thought that early seizures were more common with embolic (mainly cardioembolic) than thrombotic infarcts although not all studies supported this relationship (2, 6, 7, 10, 11). It has been also supposed that patients with early seizures are less likely to develop recurrent seizures (that means post-stroke epilepsy) than patients with late seizures. This might confirm their independent and different pathomechanisms (4, 10, 12). Embolic pathomechanism, mainly the one connected with atrial fibrillation, is well known as responsible for sudden manifestation of brain ischemia with dramatic initial symptoms. Transient hyperglycaemia is an important biochemical factor of an acute brain involvement in the early phase of the ischemic or hemorrhagic stroke and also in patients without previous diabetes mellitus. Hyperglicaemia is not strictly equivalent with the area of definite damage but it seems to correspond with the magnitude of recent and partially reversible brain dysfunction, both in the region of damage and penumbra (5, 8, 9). Also seizures are quite often observed as the first or one of the earliest symptoms of the stroke. Epileptic fits might represent the answer of brain to violent postischemic changes in its metabolism that exert an influence on neurotransmission and neuron excitablity (13).

In this study hyperglycaemia and hypertermia were noted exclusively in patients with early but not with late seizures. Urgent and enlarged brain involvement might generate deeper metabolic dysregulation. These in turn, might predispose for acute seizure manifestation. The initial clinical symptoms of stroke severity might reflect these disturbances. Earlier observations indicated a relationship of early seizures with a stroke type, size and localization. Cortical infarct in carotid region seemed to be particularly important for seizure manifestation.(4, 5, 14) In our observation early seizures occurred exclusively in patients with localisation in frontal, temporal or parietal one-lobe or multilobe infarcts and only in cases with cortical involvement. This localisation was also stressed in some previous works. Some of them have found early seizures in connection with deeper lesions (5, 11, 14). This is not a discrepancy in the light of contemporary neuroimaging investigations. MRI or SPECT performed in cases of subcortical infarcts has shown that corresponding cortex was also involved in pathological process. Heuts-van Raak et al. analysed 16% from 322 patients with the occurrence of epileptic seizures after a first symptomatic and CT confirmed brain infarct of cardioembolic origin and cortex involvement. Early seizures were connected with a restricted lesion in temporo-parietal area, while larger area around the lateral sulcus created a greater risk for late seizures (14). Giroud et al. confirmed that in patients with early seizures and subcortical infarcts in lenticulostriatal region but without involvement of apparent cortex on CT, simultaneous MRI or SPECT imaging revealed cortical fronto-temporal ischemic lesion or decreased blood flow in frontal lobe, respectively (15). These analyses point out selected areas in brain cortex as more susceptible to ischemia that might develop as epileptogenic. In our study main location of lesion in forebrain region infuenced high incidence of early seizures with typical clinical semiology for this region.

CONCLUSIONS

1. Seven per cent risk of early epileptic seizures was observed in patients with acute ischemic stroke in the forebrain regions with cortex involvement.

2. Contralateral partial motor fits indicative for lesion location were the most common ones.

3. Incidence of seizures was related with hyperglycemia and fever, as factors of time-rate and size of ischaemic lesion.

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SUMMARY

The relationship between epileptic seizures and clinical manifestation of early stroke was analysed in a retrospective study of 196 patients with ischemic stroke admitted to the stroke unit during one year. Analysis included: gender, age, stroke risk factors, its type and localization, incidence and semiology of early (ES) and late seizures (LS). ES were classified if they appeared within the first 14 days. A contribution of metabolic factors: body temperature, serum electrolytes, glicaemia, parameters of kidney and liver function was evaluated. The age of patients was 63.3 years. Main stroke risk factors were hypertension, atrial fibrillation, diabetes mellitus and hypercholesterolemia. Ischaemic lesions were mainly located in frontal, parietal or temporal lobe with cortical involvement in each case. As much as 12% of stroke patients presented ES (60%) or LS (40%). In the majority early seizures appeared during the first 48 hs. Hyperglycemia and fever were significantly associated with early seizures.

Napady padaczkowe w przebiegu niedokrwiennego udaru mózgu

Analizowano występowanie napadów padaczkowych u 196 pacjentów z niedokrwiennym udarem mózgu. Stwierdzono je u 12% chorych jako wczesne (60%) do 48 godz. lub późne po 14 dniach (40%) w trakcie 42 dni obserwacji. Semiologia napadów odpowiadała częściowym prostym ruchowym zgodnie z lateralizacją uszkodzenia, u części chorych z ich wtórnym uogólnieniem. Czynniki ryzyka udaru u chorych z napadami to nadciśnienie tętnicze, migotanie przedsionków, cukrzyca II t. i hipercholesterolemia. W przypadkach z napadami padaczkowymi obszar niedokrwienia w płacie czołowym, skroniowym lub ciemieniowym obejmował korę mózgu. U chorych z wczesnymi napadami istotnie częściej stwierdzano zaburzenia metaboliczne, przede wszystkim podwyższoną ciepłotę ciała i hiperglikemię. Wczesne napady padaczkowe i zmiany standardowych parametrów metabolicznych są wskaźnikami tempa rozwoju oraz stopnia zaburzenia czynności mózgu w początkowej fazie udaru niedokrwiennego.