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Epileptic Seizures Following Ischaemic Cerebral Infarction

Clinical Picture, CT Findings and Prognosis

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Summary. Clinical, CT and EEG findings of 100 consecutive patients suffering from epileptic seizures following hemispheric cerebral infarction were evaluated retrospectively. All patients were followed up for an average of 49 months. Twelve patients suffered from cardiogenic brain embolism, 20 had an occlusive disease of the internal cerebral artery. Forty-seven patients had a single middle cerebral artery infarct, 6 each a posterior cerebral artery or watershed infarct. CT showed lacunes in only 6 cases, 8 had multiple larger infarcts and 27 were normal. Seventy-six patients suffered from generalized seizures, 54 from partial fits, predominantly focal motor seizures. Seventy-one patients had their first seizure within the 1st year after stroke, 30 within 2 weeks after the infarct. The interval between stroke and the first epileptic fit exceeded 1 year in the remaining 29 cases. If the first fit occurred in the acute phase after stroke, the risk of further ones was significantly lower than when the first fit occurred in the chronic stage. The frequency of fits mainly depended on the occurrence of epileptic potentials in the EEG and the interval between stroke and the first seizure. During follow-up 27 patients suffered a recurrent stroke, and 52 patients died. Cardiac failure was the predominant cause of death; only 4 patients died as a consequence of an epileptic fit.

Key words: Cerebral infarction – Epilepsy – Computed tomography

Introduction

Epilepsy associated with cerebrovascular disease is not uncommon. Seizure may precede, accompany or follow stroke after days or even years [3]. Frequency of epilepsy in connection with ischemic cerebrovascular disorders has been estimated to be between 4.0% and 28% in the literature [3, 5, 6, 8, 10, 14–17, 19–21, 23]. Nevertheless, no report has dealt with this topic in relation to the findings of computed tomography (CT). Further, knowledge of factors which influence prognosis of epilepsy following ischaemic stroke is fragmentary.

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Patients and Methods

Medical records, CT scans, electroencephalograms and cerebral angiograms of 100 consecutive patients suffering from epileptic seizures following hemispheric ischaemic cerebral infarction were evaluated retrospectively. Diagnosis of cerebral infarction was either proven by CT or assumed because of a persisting neurological deficit after a stroke in cases with normal CT findings. None of the patients had seizures before stroke or evidence for other causes of epilepsy. CT and EEG were performed in every case, 35 patients had angiography, and 83 Doppler sonography of the cerebral vessels. Only EEGs conducted about 24 h before or after a seizure were considered. Patients were followed up for an average of 49 months, 80 for over 6 months. The mean age of the patients was 65 years; 49 were 70 years or older. Sixty-five patients were male, 35 female. Arteriosclerosis was assumed to be the aetiology of the infarct in cases with an appropriate angiographic finding, demonstration of an occlusion or a stenosis of the neck arteries by Doppler sonography, or the presence of vascular risk factors without a potential cardiac source of brain embolism. Cardiogenic embolism was diagnosed as the cause of stroke according to the criteria of the Cerebral Embolism Task Force [4]. Ninety-three patients were treated with anticonvulsants (phenytoin: 82 patients, carbamazepine: 9; others: 2). Compliance of 65% of the treated patients was good.

Results

The Infarcts

The aetiology of the cerebral infarcts of 59 patients was arterioslcerosis without significant stenosis of the cerebral vessels. In a further 20 patients arteriosclerosis had caused an occlusion of the internal carotid artery or a stenosis exceeding 50% ipsilateral to the infarct. Cardiogenic embolism was assumed to be the aetiology of the infarct in 12 patients, most of whom suffered from non-

Table 1. CT findings in 100 patients with epileptic seizures following ischaemic stroke

CT findings	No. of patients
Normal	27
Single MCA infarct	47
Single PCA infarct	6
Watershed infarct	6
Multiple non-lacunar infarcts	8
Lacunes	6

rheumatic atrial fibrillation. The aetiology of the stroke in 9 patients remained undefined.

At the time of the first epileptic seizure 46 patients had a moderate neurological deficit but were able to perform most of their daily activities without help. Thirty-four patients suffered from severe neurological disturbances necessitating regular assistance in personal matters. The neurological findings of 20 patients were normal despite areas of infarction shown by CT. No infarction area was visible in the CT scans of 27 patients in spite of a persisting neurological deficit. Forty-seven patients had single infarcts in the middle cerebral artery territory, 6 each in the posterior cerebral artery territory and in border zones. Eight CT scans revealed multiple non-lacunar infarcts. Six patients, finally, had one or more lacunes on CT exclusively (Table 1). Altogether 62 of 73 patients with an infarction area on CT had a cortical ischaemic lesion.

The Seizures

Forty-six patients suffered from grand mal only, 24 from partial seizures and the remaining 30 from grand mal and partial seizures in combination. Altogether 76 patients had generalized seizures, 40 focal motor seizures, 10 had epilepsia partialis continua, 8 partial seizures with adverse features, 2 psychomotor seizures, and 1 focal sensory seizure (Fig. 1).

Six patients were admitted to hospital because of a series of generalized seizures, a further 3 because of grand mal status. These 9 patients did not show any peculiarity concerning the aetiology or localization of the infarct, the interval from stroke to the manifestation of the epilepsy, or age.

Nineteen patients suffered a deterioration of a preexisting neurological deficit after a seizure, which was reversible in every case. Patients with an internal carotid stenosis or occlusion were threatened by a postictal deterioration more than twice as often as patients without (40% of 20 patients vs 14% of 80 patients, $P < 0.01$, chi-square test).

The EEG of 74 patients showed a slow focus. In 52 cases epileptic potentials were seen, which were exclusively focal in 48 cases. The EEG of patients with a slow focus revealed focal epileptic potentials significantly more often than those without slow focus (59% vs 16%, $P < 0.001$, chi-square test). Furthermore, epileptic potentials were included predominantly in the slow focus. On the other hand, the frequency of focal epileptic potentials was similar for patients with and without non-lacunar infarcts visible on CT (45% of 67 patients vs 47% of 33 patients).

The Relationship Between Seizures and Infarcts

Thirty patients had their first seizure within 2 weeks after stroke, half of them between minutes and 24 h after manifestation of the neurological deficit. Forty-one patients suffered from their first epileptic fit after 2 weeks but within the 1st year and 29 up to 5 years later. Sixty-five percent of the latter 29 patients had partial seizures. Patients with a short (≤ 14 days) or long (> 14 days) latency until first occurrence of seizures after stroke were comparable as regards demonstration of infarcts by CT and their localization, frequency of postical deterioration, grand mal status, internal carotid stenosis or occlusion or cardiogenic embolism as the aetiology of stroke. The risk of further seizures was three times higher, if the first seizure occurred later than 2 weeks after stroke (Table 2).

In cases with partial seizures with simple focal or sensory symptoms, infarcts in CT were always localized contralaterally to the epileptic sensations. However,

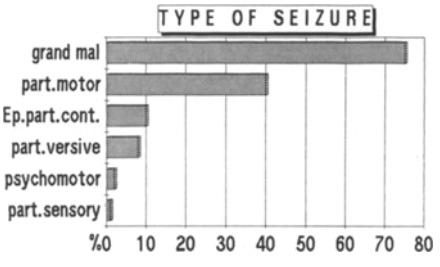

Fig. 1. Frequency of different types of epileptic seizures

Table 2. Comparison of patients with a first epileptic seizure in the acute (14 days) or in the chronic stage after stroke who were followed up for about 6 months

		First seizure in	
		Acute state	Chronic state
No. of patients		24	56
Aetiology:	Cardiogenic embolism	21%	11%
	ICA stenosis/occlusion	17%	21%
Seizures:	generalized	63%	78%
	partial	67%	54%
Postictal deterioration		21%	18%
Grand mal status/series		4%	4%
Recurrent seizures		14%	57%[a]
EEG:	slow focus	79%	77%
	epileptic potentials	54%	59%
Non-lacunar infarct in CT		54%	77%

[a] $P < 0.002$, chi-square test

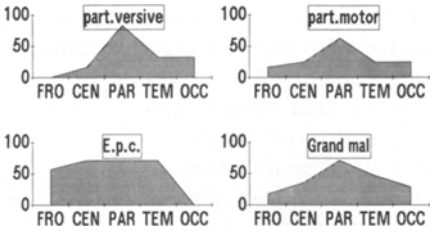

Fig. 2. Frequency of involvement of different brain regions by the infarcts depending on the type of epileptic seizures concerning the CT finding [versive seizures ($n = 3$); partial motor seizures ($n = 11$); epilepsia partialis continua ($n = 5$); grand mal ($n = 46$)]. *FRO*, Frontal; *CEN*, central; *PAR*, parietal; *TEM*, temporal; *OCC*, occipital

Table 3. Comparison of patients admitted to hospital after a single seizure, developing epilepsy or not during follow-up of 6 months minimum

		Single seizure	Epilepsy
No. of patients		20	25
Aetiology:	Cardiogenic embolism	15%	16%
	ICA stenosis/occlusion	20%	28%
Seizures:	generalized	75%	76%
	partial	60%	52%
Postictal deterioration		10%	12%
First seizure:	acute state	45%	16%[a]
	chronic state	55%	84%
Anticonvulsant therapy		65%	76%
EEG:	slow focus	80%	80%
	epileptic potentials	35%	40%
Non-lacunar infarct in CT		70%	72%

[a] $P < 0.04$, chi-square test

only 36% of the 40 patients with focal motor seizures and 6 of those 10 with an epilepsia partialis continua actually had an infarction area on CT. Apart from lateralization, the localization of the infarction area in CT gave little information concerning the type of seizure to be expected. The parietal and temporal regions were the main regions of the infarcts, independent of the kind of seizures. Only some of the patients with versive or partial motor seizures had an involvement of the frontal cortex or the central region. Infarcts of patients with epilepsia partialis continua were generally large (Fig. 2).

The Prognosis

Forty-five patients were admitted to hospital after a first seizure, 25 of them suffered from further ones during follow-up. Comparison of the aetiology and localization of the infarcts, kind of seizures, frequency of a slow or epileptic focus in EEG, or therapy of these 25 patients with the group of 20 patients who suffered a single seizure without recurrence revealed no differences. The first seizure of patients without further ones often happened during the acute period after stroke. Patients developing repeated seizures later on predominantly suffered their first seizure in the chronic stage (Table 3).

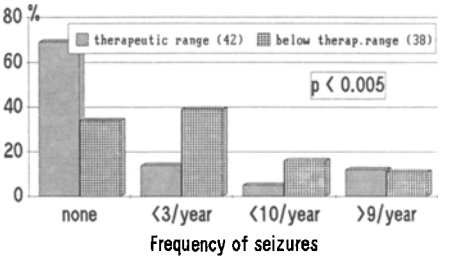

Fig. 3. Frequency of seizures per year depending on anticonvulsant therapy within or without therapeutic serum concentrations

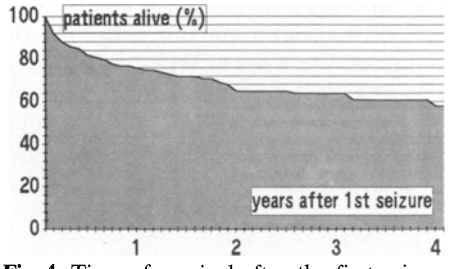

Fig. 4. Time of survival after the first seizure following ischaemic stroke ($n = 100$ patients, mean follow-up 49 months)

Table 4. Comparison of patients with a benign or severe course of poststroke epilepsy [benign course: no further seizures after sufficient (29 patients) or insufficient (13 patients) medical prophylaxis; severe course: frequency of epileptic seizures about 2/year]

		Course of epilepsy	
		Benign	Severe
No. of patients		42	25
Aetiology:	Cardiogenic embolism	10%	16%
	ICA stenosis/occlusion	21%	12%
Seizures:	generalized	74%	68%
	partial	55%	48%
Postictal deterioration		21%	16%
First seizure:	acute state	40%	12%[a]
	chronic state	60%	88%
EEG:	slow focus	83%	60%
	epileptic potentials	29%	56%[b]
Non-lacunar infarct in CT		62%	60%
Mortality		45%	60%

[a] $P < 0.02$, chi-square test; [b] $P < 0.03$

Comparison of the frequency of seizures of 80 patients followed up more than 6 months revealed a significant reduction if antiepileptics were taken in therapeutic dosage. Additionally it becomes evident that most patients have a frequency of seizures below three within 1 year even with subtherapeutic serum levels of antiepileptic medication (Fig. 3).

During follow-up 27 of the 100 patients suffered a new stroke and 52 died. The predominant cause of death was cardiac failure, sometimes following myocardial in-

farction (30 patients). Twelve patients died after another stroke and only 4 in relation to an epileptic fit, 1 of these in grand mal status. Twenty-six patients died within the 1st year after manifestation of epilepsy; altogether 40 died within 4 years (Fig. 4).

To obtain information about prognostic factors in poststroke epilepsy, data of 42 patients with a benign course were compared with those of 25 patients with a more severe course. Patients of the first group did not suffer further seizures after medical treatment, which was sufficient regarding serum concentration of the anticonvulsant drug in 29 cases. Patients of the second group suffered from more than two seizures within 1 year. The groups were not different concerning the aetiology or localization of the infarcts, the kind of seizures, the frequency of a slow focus in EEG, a postictal deterioration, or the mortality during follow-up. Patients with a severe course more often had epileptic potentials in EEG, and the first seizure later than 2 weeks after stroke (Table 4).

Discussion

The incidence of epileptic seizures caused by cerebrovascular disorders has been reported to be between 4% and 28% in the literature (Table 5) [3, 5, 6, 8, 10, 14–17, 19–21, 23], depending on the underlying disease. The frequency of seizures for stroke patients in general has ranged between 7.7% and 12.5% [19–21]. It is higher in cases with occlusive disease of the large cerebral arteries [3, 5, 6, 14, 23]. Contrary to the assumption of some authors [2, 10], patients with cerebrovascular disorders are not threatened by epilepsy less than those with cerebral trauma. In a recent study the risk of post-traumatic seizures was 11.5% within 5 years [1]. Older studies reporting a higher incidence of post-traumatic epilepsy mostly analysed patients with war injuries. These are only roughly comparable with stroke patients because of a high proportion of penetrating brain trauma [13].

Table 5. Frequency of epileptic seizures in ischaemic cerebrovascular disease

Author	Diagnosis	Patients	Incidence
Kehrer and Aretz [15]	Cerebral arteriosclerosis	1660	4.6%
Fischer [10]	Cerebral arteriosclerosis	1225	4.0%
Louis and McDowell [19]	Nonembolic infarction	1000	7.7%
Moskowitz et al. [20]	Stroke	518	9.5%
Knüpling and Schliack [16]	ICA/MCA circulation disorders	277	13.7%
Barolin et al. [3]	Occlusive cerebrovascular disease	229	11.7%
Cocito et al. [5]	ICA/MCA occlusion/stenosis	141	15.6%
De Carolis et al. [6]	ICA/MCA occlusion	124	14.5%
Johnson and Walker [14]	ICA occlusion/stenosis	107	20.0%
Richardson and Dodge [21]	Cerebral infarcts + haemorrhage	104	12.5%
Krayenbühl and Yasargil [17]	Cerebral embolism	100	8.0%
Silverstein [23]	ICA occlusion/stenosis	50	28.0%

It is generally accepted that a single epileptic seizure does not warrant the diagnosis of epilepsy. Nevertheless, patients with only one fit were included in this study as they were previously in a study of post-traumatic epilepsy [1] because of an increased use of anticonvulsant medication for single seizures.

Some pathogenetic theories of vascular epilepsy may be discussed. An important factor for the occurrence of an epileptic fit might be a localized hypoxaemia surrounding the infarction area [7]. Hyperexcitability of neurons during ischaemia has been demonstrated in animal experiments [12]. The vulnerability of the tissue around the infarction area is evident from the high percentage of a postictal worsening of the neurological deficit in this series, a phenomenon known for many years [9]. Patients with occlusive disease of the large cerebral arteries were threatened particularly by a postictal deterioration, which, however, was reversible completely in all cases. The reversibility in every case in our series would not support the hypothesis that minor embolization from arteriosclerotic plaques may account for epileptic seizures, which has been considered as a reason for vascular epilepsy in carotid occlusive disease [5]. Denervation hypersensitivity developing in the brain after tissue injury has also been assumed to be a cause of poststroke epilepsy for many years [19]. More recently, the causative role of blood components in the development of a chronic epileptic focus has been emphasized [6]. Epileptic foci in the EEG have been found in animals after ferric chloride injection into the cortex [24]. However, these findings could not be confirmed from a study of conducting single neuron patterns [18]. Accordingly, epileptic seizures seem to be even less frequently associated with intracerebral haematoma than with infarction [21]. In our series there was no evidence of haemorrhagic infarction in most patients.

Forty-six percent of our patients had grand mal only, 24% partial seizures and the remaining 30% both. A predominance of generalized seizures in vascular epilepsy has been reported by several authors [3, 6, 10, 15], but in some series a larger number of partial fits has been found [5, 16, 19]. The focal character of poststroke epilepsy becomes evident from the findings in the interval EEG. If epileptic potentials occurred, they were nearly always locally restricted with an affinity to an eventual slow focus caused by the infarct.

Beside demonstration of an infarct, CT contributes little information in poststroke epilepsy. As should be expected from the literature [2, 21], cortical infarcts could not always be demonstrated. A few patients even had lacunar infarcts only. Furthermore, CT sometimes failed to demonstrate any infarction area despite a persisting neurological deficit and a slow focus in the EEG indicating partial neuronal necrosis. It was not uncommon for the infarcts of patients with certain partial fits to spare the anatomical region to be expected from the type of seizure. It could be assumed from this observation that sometimes the cerebrovascular disease itself causing

focal hypoxaemia is the cause of epileptic activity and not the lesion caused by an infarct.

The prognosis concerning the frequency of seizures of poststroke epilepsy was favourable in this series, in accordance with earlier experience [21]. Vascular epilepsy can be controlled well by therapy [6, 9, 11]. Most of our patients experienced a significant reduction of seizure frequency by single anticonvulsant drug medication. Nevertheless, a small number of patients suffered from generalized seizures occurring in series or even status. No criteria were evident to recognize these patients with an increased risk.

The long-term prognosis of patients with epilepsy following cerebral infarction was characterized by recurrent stroke in about a quarter of the patients during a 4-year follow-up on average and a mortality of 40% during this time. In accordance with experience in cerebrovascular disease in general, most patients died in consequence of cardiac failure, and actually only a few in relation to an epileptic fit.

Little is known about prognostic factors in poststroke epilepsy. Analysis of different clinical, CT and EEG parameters in this series revealed the occurrence of epileptic potentials in EEG and the interval from stroke to the first fit as the only reliable predictors for the severity of epilepsy. Epileptic potentials in EEG were combined with a higher frequency of seizures. Furthermore, the beginning of epilepsy in the chronic state after the stroke was more frequent in patients with a severe course. Accordingly, the risk of further fits was significantly lower if the first seizure occurred within the first 2 weeks after stroke [22]. This pattern in the development of seizures is similar to that seen with post-traumatic epilepsy, where early seizures are frequently not repeated, while seizures occurring after the first 2 weeks usually presage chronic epilepsy [13, 19]. Different mechanisms causing epileptic fits are assumed for the acute and the chronic state after stroke [5, 6]. Nevertheless, in this series patients with a first seizure within the first 2 weeks after the infarct did not differ from those with a first fit later on concerning aetiology of stroke, kind of seizures, demonstration and localization of the infarct in CT and the occurrence of a slow or epileptic focus in EEG.

An important question is whether or not to give anticonvulsants after a first seizure following stroke. In this series the risk of further fits was independent of the aetiology of the infarct, the kind of seizure, the CT and EEG findings. As only 14% of the patients with a first seizure within 2 weeks after stroke experience further ones, prophylactic medication after the first fit is not imperative. At least leaving out medication after 6 months without a seizure seems justified. On the other hand, a risk of about 50% for further seizures after a first fit in the chronic state after stroke makes long-term medical prophylaxis indispensable in such cases.

References

1. Annegers JF, Grabow JD, Groover RV, Laws ER, Elveback LR, Kurland T (1980) Seizures after head trauma: a population study. Neurology 30:683–689
2. Barolin GS, Reinisch H (1972) Autoptische Befunde bei vaskulären Epilepsien. Wien Z Nervenheilkd 30:8–24
3. Barolin GS, Scherzer E, Schnaberth G (1975) Die zerebrovaskulär bedingten Anfälle. In: Kielholz P, Kaeser H, Klingler M (eds) Aktuelle Probleme in der Psychiatrie, Neurologie, Neurochirurgie, vol 12. Huber, Bern
4. Cerebral Embolism Task Force (1986) Cardiogenic brain embolism. Arch Neurol 43:71–84
5. Cocito L, Favale E, Reni L (1982) Epileptic seizures in cerebral arterial occlusive disease. Stroke 13:189–195
6. DeCarolis P, Alessandro RD, Ferrara R, Andreoli A, Sacquegna T, Lugaresi E (1984) Late seizures in patients with internal carotid and middle cerebral artery occlusive disease following ischaemic events. J Neurol Neurosurg Psychiatry 47: 1345–1347
7. DeReuck J, Krahel N, Sieben G, Orban L, DeCoster W, Vander Eecken H (1980) Epilepsy in patients with cerebral infarcts. J Neurol 224:101–109
8. Dodge PR, Richardson EP, Victor M (1954) Recurrent convulsive seizures as a sequel to cerebral infarction: a clinical and pathological study. Brain 77:610–638
9. Fine W (1967) Post-hemiplegic epilepsy in the elderly. Br Med J 10:199–201
10. Fischer H (1959) Symptomatische Epilepsie bei zerebralen Gefäßprozessen. Arch Psychiatr Nervenkr 199:296–310
11. Gupta SR, Naheedy MH, Elias D, Rubino FA (1988) Postinfarction seizures – a clinical study. Stroke 19:1477–1481
12. Heiss WD, Hayakawa T, Waltz AG (1976) Cortical neuronal function during ischemia – effects of occlusion of one middle cerebral artery on single unit activity in cats. Arch Neurol 33: 813–820
13. Jennet B (1979) Posttraumatic epilepsy. Adv Neurol 22:137–147
14. Johnson HC, Walker AE (1951) The angiographic diagnosis of spontaneous thrombosis of the internal and common carotid arteries. J Neurosurg 8:631–643
15. Kehrer HE, Aretz U (1963) Epileptische Anfälle bei zerebraler Gefäßsklerose – ein Beitrag zur Pathogenese der „Spätepilepsie". Psychiatr Neurol 146:265–272
16. Knuepling R, Schliack H (1972) Epileptische Anfälle bei cerebralen Durchblutungsstörungen. Z Neurol 201:196–200
17. Krayenbühl H, Yasargil MG (1964) Verschluß der Arteria cerebralis media – Ergebnisse der klinischen und katamnestischen Untersuchungen. Schweiz Arch Neurol Neurochir Psychiatr 94:287–296
18. Lange SC, Neafsex ES, Wiler AR (1980) Neuronal activity in chronic ferric chloride epileptic foci. Epilepsia 21:251–254
19. Louis S, McDowell F (1967) Epileptic seizures in nonembolic cerebral infarction. Arch Neurol 17:414–418
20. Moskowitz E, Lightbody FEH, Freitag NS (1972) Long-term follow-up of the poststroke patient. Arch Phys Med Rehabil 53:167–172
21. Richardson EP, Dodge PR (1954) Epilepsy in cerebrovascular disease – a study of the incidence and nature of seizures in 104 autopsy-proven cases of cerebral infarction and hemmorhage. Epilepsia 3:49–65
22. Shinton RA, Gill JS, Melnick SC, Gupta AK, Beevers DG (1988) The frequency, characteristics and prognosis of epileptic seizures at the onset of stroke. J Neurol Neurosurg Psychiatry 51:273–276
23. Silverstein A (1959) Occlusive disease of the carotid arteries. Circulation 20:4–12
24. Willmore LJ, Sypert GW, Munson SB (1978) Recurrent seizures induced by cortical injection: a model of post traumatic epilepsy. Ann Neurol 4:329–336