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Incidence of Late Seizure after Coil Embolization of Ruptured Cerebral Aneurysms

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= 국문초록 =

파열된 뇌동맥류에 대한 코일색전술후 발생한 지연 발작의 빈도

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목 적 : 이 연구는 동맥류 파열로 인한 지주막하출혈 후 시행되는 결찰술과 코일색전술후 발생하는 지연 발작의 발생빈도를 비교하여 향 후 선택된 환자에게 적용할 수 있는 치료 방침을 얻고자 한다.

방 법 : 2004년 8월부터 2007년 12월 사이에 동맥류 파열로 인한 지주막하출혈로 내원한 61명의 환자를 상대로 후향적으로 분석하였다. 지연 발작의 정의는 수술 후 2주 후 발생하는 발작을 의미한다. 환자의 추적관찰 기간은 평균 23.5개월(범위 6~48개월)로 최대 4년까지 추적 관찰 하였다. 발작의 빈도는 기존의 논문과 비교분석할 것이고, 이와 관련된 임상적인 관계도 분석할 것이다.

결 과 : 추적관찰 기간 동안에 61명의 환자 중에 3명(5%)의 환자가 발작을 경험하였다. 이 중 2명은 30일이내 발생하였고, 나머지 1명은 2년이 지난 후에 발생하였다.

결 론 : 본원에서 분석한 동맥류 파열로 인한 지주막하출혈 후 시행되는 코일색전술후 발생하는 발작의 낮은 빈도가 수술 후 사용되는 예방적 항간질제의 사용을 정당화하지는 않는다고 생각된다. 향후 보다 많은 환자수와 전향적인 연구가 본 연구결과를 증명하는데 필수적이라 판단된다.

중심 단어 : 동맥류 · 지주막하출혈 · 코일색전술 · 발작.

Introduction

Aneurysmal subarachnoid hemorrhage may result in significant morbidity and mortality, as well as, complications that including late seizures. The reported overall incidence of late seizure after aneurysmal subarachnoid hemorrhage (SAH) treated with craniotomy varies between 4 and 27.5% in different series[1)3)8)9)12)15)20)23)27)28)]. Seizure in patients who underwent surgery for aneurysmal subarachnoid hemorrhage may have delayed features although most seizure occur within 2 years. Furthermore, one study has demonstrated that incidence of seizure falls to very low levels after 12 months[4)]. Endovascular treatment with coil embolization of ruptured aneurysms could avoid craniotomy, ressulting in reduceed risk of potential postoperative seizures owing to less

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cortical damage[7)10)29)]. To date, a few data has been reported the incidence of late seizure after aneurysmal subarachnoid hemorrhage treated with endovascular treatment[6)].

The present study gains its importance because it critically assess the incidence of seizures in patents undergoing endovascular therapy for ruptured intracranial aneurysms. As endovascular approaches to treat aneurysmal subarachnoid hemorrhage is becoming more common, studies related to treatment out will be more important in determining appropriate management strategies. This will also help to guide neurosurgeons as to which approach to choose, and could show important benefits of treating this disease entity with an endovascular approach rather than invasive craniotomy.

Patients and Methods

A total of 91 patients, who underwent coil embolization with aneurysmal subarachnoid hemorrhage admitted the our hospital. Among them, 30 patients were excluded by exclusion criteria ; initial negative angiogram from SAH in 6 patients, presenting Hunt Hess grade 5 in 3 patients, not at least flex to pain after resuscitation in 2 patients, non-aneurysmal SAH in 11 patients, rebleeding before embolization in 3 patients, embolization performing after 21 days in 2 patients, die after coil embolzation during hospital stay in 3 patients.

Sixty-one patients who underwent coil embolization for ruptured intracranial aneurysms by exclusion criteria were identified between August 2004 and December 2007 in our hospital. Intracranial aneurysms were confirmed by computed tomography and cerebral angiography in all patients. Inclusion criteria for the study population is that the patient who had underwent a coil embolzation to secure a ruptured intracranial aneurysm and also survived to be discharged from acute neurosurgical care.

Anticonvulsant Treatment Policy

Prophylactic anticonvulsant drug were prescribed from event of aneurysmal subarachnoid hemorrhage until second week from the event. With the early seizure (within two weeks of hemorrhage), anticonvulsant therapy was continued up to 24 months. When the late seizure occurred after 24 months, anticonvulsant therapy was continued there after.

Results

1. Patient demographics

Sex ratio was 1 : 1.65 (men 23 patients, women 38 patients). Twenty eight patients (45.9 %) were between age of 40 and 59 years, 29 patients (47.5%) were older than 59 years, with the remaining 4 patients (6.5%) were younger than 40 years. No patients had preexisting seizure. Mean follow-up periods was 23.5 months (range 6−48 months).

2. Incidence of early vs late-seizure

Of the total 61 patients of study population, 6 patients experienced early seizure after immediate postoperative periods, which means that AED concentrations had not got the level of therapeutic range and, only 3 patients had late seizure during follow-up periods (0.05%). Two of them had seizure onset within 30 days of the event and the other patient had seizure onset more than 2 years after (Table 1).

Discussions

Late seizure has long been recognized as a sequela of head trauma and major brain surgery, its severity depending on localization, extent of underlying lesion and the nature of the operation. The reported incidence of post-surgical late seizure in patients with ruptured intracranial aneuryms has varied between 4.5 and 22%[1)3)8)9)12)15)20)23)27)28)].

The results of our study (0.05%) shows a much lower incidence of late epilepsy compared with other previous published series.

It is generally accepted that there is increased risk of seizure and subsequent tendency for the epilepsy after supratentorial craniotomy and that this risk is particularly high after aneurysm clipping. The risk of seizure may arise from subarachnoid hemorrhage itself and the craniotomy and microsurgery, or both. The evolution of

Table 1. Incidence of late seizure related to Hunt and Hess grade, Glasgow outcome score, and site of aneurysm(n=61)

Variable		Incidence of epilepsy(%)	n
Hunt & Hess grade	1		1
	2		36
	3	1(0.05)	19
	4	2(0.2)	5
GOS at 6 months	5	1(0.02)	42
	4		10
	3		6
	2	2(0.25)	3
Site of aneurysm	ACAA	1(0.07)	13
	MCAA	2(0.14)	14
	PCAA		17
	Ant Choroid AA		2
	ICAA		3
	Pericall AA		4
	BAA		3
	SCAA		2
	VAA		3

GOS : Glasgow outcome score, ACAA : anterior communicating artery aneurysm, ICAA : internal carotid artery aneurysm, MCAA : middle cerebral artery aneurysm, Ant Choroid AA : anterior choroidal artery aneurysm, PCAA : posterior communicating artery aneurysm, Pericall AA : pericallosal artery aneurysm, BAA : basilar artery aneurysm, SCAA : superior cerebellar artery aneurysm, VAA : vertebral artery aneurysm

management paradigms and microsurgical techniques over the last 30 years may be associated with reduced morbidity and mortality rates including occurrence of late seizure [9)13)].

Several pathophysiological mechanisms although requiring further elucidation, are implicated in the occurrence of seizures after aneurysmal subarachnoid hemorrhage including first, large amounts of subarachnoid blood and damage to the motor cortex or the insula, a combination of the sudden development of a space occupying lesion with mass effect, focal ischemia, and blood products may be involved in the onset of late seizures[14)16)17)19)22)], second, a variety of surgical techniques or neurological complications such as rebleeding, hyponatremia, delayed ischemic deficit, or hydrocephalus may be present individually or together that provoke late seizures[11)18)21)], third, late seizures may be due to gliosis and the development of a meningocerebral cicatrix created by craniotomy and microsurgery[2)].

Butzkueven et al. found a large amount of subarachnoid cisternal blood seemed to be significantly more common in patients with subarachnoid hemorrhage who suffered late seizures. The mechanical effect of the blood near motor cortex or insula, the release of large amounts of glutamate and the generation of lipid peroxidase from oxygen-free radical reactions catalyzed by iron and by hemoglobin degradation products, as well as by oxidative catabolism of arachidonic acid, may account for the occurrence of seizures of post subarachnoid hemorrhage. The exact mechanism, however, await further elucidation[5)].

The presence of an late seizure is nonetheless very strongly associated with poor functional recovery. It is likely, therefore, that the seizure is a surrogate marker for the severity of cerebral insult. Late seizure is unlikely to be a surrogate marker for the initial amount of intracranial blood. The other major insult to the brain is acute subarachnoid hemorrhage induced ischemia. There was no association between onset of seizure and delayed symptomatic vasospasm. However, it is still plausible that onset of seizure are indicators of the severity of very early brain ischemia. A recent study demonstrated 'ultra-early arterial spasm' was associated with poor outcome at 3 months[22)]. Future studies may clarify the possible relationship between angiographic ultra-early vasospasm and onset of seizure. Several studies have also demonstrated increased neurological mortality and morbidity among patients with aneurysmal subarachnoid hemorrhage. Several mechanisms are implicated in poor outcome. First, the possibility of seizures precipitating rebleeding of the aneurysm secondary to increased blood pressure and second, seizure could cause excessive cerebral metabolic demand and increase intracranial pressures. The possible benefit of antiepileptic drug is reduction of functional morbidity after seizure following aneurysmal subarachnoid hemorrhage[24)25)].

Recanalization and rebleeding from coiled aneurysms is another important factor that needs to be considered in a person with an apparently well protected aneurysm. Because rebleeding in coiled aneurysm is highly related with development of late seizure. However, the implications of the possibility of rebleeding of treated aneurysms require analysis. The experience of past decade has shown

that the vast majority of the patients are protected against rebleeding by coil embolization, despite an appreciable angiographic failure rate.

Several limitations of our study deserve to mention. The major weakness is that our study is retrospective, not prospective organized study. Another major limitation is that the diagnosis of late seizure had to be made by patient report and without an in-depth neurological examination and EEG study. And, most patients with coil embolization in this study were treated with anticonvulsant medication for 2 weeks after their acute symptomatic aneurysmal subarachnoid hemorrhage. So, the effect of high predictive factor such as, poor preoperative neurological state, blood in cisternal space, middle cerebral artery aneurysm, ischemia and postoperative vasospasm, rebleeding, and, intraventricular hemorrhage is unclear. However, our finding in this study that may have implications for clinical management and future prognosis.

Conclusion

This data are suggestive that overall incidence of late seizures may be less common after endovascular therapy as compared with craniotomy and microsurgery.

However, direct comparison of characterization of late seizure after aneurysmal subarachnoid hemorrhage between clipping and coil embolization is inadequate. The indications, efficacy, regimens, and length of anticonvulsant therapy as well as treatment modality should be re-evaluated and further study is warranted to clarify these issues. And, the low incidence of late seizure does not justify the use of prophylatic antiepileptic drug after aneurysmal subarachnoid hemorrhage in patients treated only with coil embolization. These warrant further investigation in larger prospective studies to determine whether there is a role for anticonvulsant drugs in this population.

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