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Delayed ischemic neurological deficit of short duration in patients with subarachnoid hemorrhage

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We retrospectively examined the duration of delayed ischemic neurological deficits (DIND) attributed to vasospasm following subarachnoid hemorrhage (SAH) in order to delineate the nature and involved factors.

Among 605 patients with SAH, 201 developed DIND, and 137 of these had undergone early aneurysmal obliteration. In these 137, duration of DIND was clearly determined in 67 cases. Hypervolemic therapy was instituted only after the onset of DIND.

In the 67 patients, the mean duration of DIND was 5.2 days (ranging from 2 to 13 days); 22 patients had DIND lasting only 2 to 3 days, 26 patients had DIND lasting 4 to 6 days, and in 19, DIND lasted 7 to 13 days. Clinical factors associated with short DIND duration (2 to 3 days) as determined by multivariate analysis included internal carotid artery or middle cerebral artery aneurysm, age under 60, and a good World Federation of Neurological Surgeons grade on admission. No patients developed pulmonary edema from hypervolemic therapy, and the outcomes of all 67 patients were extremely favorable.

In SAH patients developing DIND after early aneurysmal surgery, 16% (22 of 137) had a documented brief duration of DIND. We believe DIND rapidly improved and resolved with hypervolemic therapy because antecedent brain damage from SAH or surgical manipulation had been minimal.

Keywords : Delayed ischemic neurological deficit, Duration, Subarachnoid hemorrhage, Vasospasm

INTRODUCTION

Onset of a delayed ischemic neurological deficit (DIND) due to vasospasm has been well studied, and is usually within the first 2 weeks after subarachnoid hemorrhage (SAH). Duration of DIND, however, has not been studied in detail. The present retrospective study was undertaken to identify factors which might predict the duration of DIND, especially a short duration of 2 to 3 days.

MATERIALS AND METHODS

Patient Population

At Tokai University Hospital, 605 patients with nontraumatic, nonhypertensive SAH were admitted from January 1985 to December 1994. Of these, 33% (201 patients) developed DIND, and of these 137 had undergone early aneurysm surgery within 3 days following SAH. These 137 patients were investigated regarding duration of DIND, falling into four groups: patients with DIND duration of 2 to 3 days, duration of 4 to 6 days, duration exceeding 6 days, and duration unknown.

Diagnostic Tools

Classifications and Scales. The clinical grade of each patient was determined on admission according to the World Federation of Neurological Surgeons (WFNS) [3]. Severity of SAH was graded from the appearance on computerized tomography (CT) according to Fisher *et al.* [4]. Using the Glasgow Outcome Scale [8], the outcome of each patient was classified as either favorable (good recovery or moderate disability) or unfavorable (severe disability,

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vegetative state, or death). Diagnosis of SAH with intracerebral hematoma (ICH) was based on CT evidence of intraparenchymal hemorrhage exceeding 10 ml.

Postoperative Management. In the last 4 years, all SAH patients received continuous intravenous administration of a calcium channel antagonist, either nicardipine or diltiazem, for 7 to 21 days postoperatively. In 43 patients, a single transcisternal injection of urokinase (30000 to 60000 IU) was given 3 to 5 days postoperatively. Cisternal drainage was used for irrigation of the subarachnoid clot.

Diagnosis of DIND. The day after SAH when DIND became manifest was determined by development of a focal neurological abnormality after recovery from the immediate postoperative state, provided that CT showed no evidence of hydrocephalus [9]. In poor-grade SAH patients and patients with ICH, DIND due to vasospasm was often difficult to diagnose by signs of neurological deterioration. In these patients, serial Doppler sonography and angiography were performed to detect DIND. When a patient developed irreversible DIND due to severe vasospasm and resolution of DIND was not apparent, the patient was placed in the unknown duration group.

Management of DIND. Hypervolemic therapy was instituted only after the onset of DIND. Dobutamine [14, 18, 19], with or without dopamine, was administered to all patients who received hypervolemic therapy, which was given according to the previously reported protocol [18, 19]. In the present study, all patients received what we have previously termed "optimum hypervolemic therapy." Immediately after the onset of DIND, the pulmonary wedge pressure and/or central venous pressure was increased by rapid bolus injection of albuminates and glycerol until the neurological deficit was reversed. The hemodynamic profile associated with neurological improvement was determined individually for each patient, and these hemodynamic parameters were maintained at the optimum values until they could be decreased without reappearance of the neurological deficit. If a neurological deficit did not reappear while hemodynamic parameters were decreased from the optimum values, we defined the observation of reversal as the resolution of DIND [18]. In the unknown group, the same management of DIND was carried out when DIND became manifest.

Statistical Analysis

Multiple logistic regression analysis was used to identify independent factors predicting the duration of DIND. Data from patients were compared with respect to duration using the Pearson's chi-square or t-test. All statistical analyses were performed using commercially available software (SPSS, Version 6.1.3; Marija J. Norusis/SPSS, Inc., Chicago, IL).

RESULTS

Appearance of DIND

In 131 of 137 patients, it was possible to determine the time of appearance of DIND. The mean days after SAH until DIND became manifest was 7.6; 1 to 7 days in 77 cases (59%), 8 to 14 days in 48 cases (37%), and over 14 days in 6 cases (5%). No significant relationship was evident between the days after SAH until DIND appearance and DIND duration from a t- test (Table 1).

Clinical features and duration of DIND

Among 137 patients with clinical evidence of DIND, the mean duration of DIND was 5.2 days (2 to 3 in 22 patients, 4 to 6 in 26, and 7 to 13 days in [19] in 67 patients and unknown in the other 70 patients because of

Table 1 Onset and duration of DIND

	duration of DIND			
DIND onset	2–3 days	4–6 days	6 days <	unknown
days after SAH	8 ± 4	8 ± 2	7 ± 3	7 ± 3
(range)	(3–20)	(4–15)	(4–18)	(4–17)

Abbreviations; DIND, delayed ischemic neurological deficit; SAH, subarachnoid hemorrhage.
Values are mean ± standard deviation.

severe neurological impairment from the onset or the lack of a clinical improvement during hypervolemic therapy.

Relationship between the clinical features and the duration of DIND is considered in Table 2. In patients with DIND of short duration, past history of hypertension, gender, WFNS grade on admission, Fisher group, intracerebral hemorrhage, and cisternal irrigation with urokinase did not significantly differ between the patient groups according to the Pearson chi-square test ($P>0.05$). An age less than 60 years was frequent among patients with short DIND duration ($P<0.05$). The ruptured aneurysm was not in the anterior cerebral artery (Acom) system in any patient with short DIND duration ($P<0.01$). Incidence of surgical compli-

Table 2 Clinical features and duration of DIND

	duration of DIND			
variable	2–3 days	4–6 days	6 days <	unknown
no. of cases	22	26	19	70
past history of hypertension	8	13	7	32
age < 60 yrs	19*	23	13	42
> 60 yrs	3	3	6	28**
sex (F : M) (NS)	17 : 5	14 : 12	9 : 10	43 : 27
WFNS grade on admission				
1–3	14	20	13	38
4–5	8	6	6	32*
Fisher group				
2	5	8	2	4
3	10	9	10	25
4	7	9	7	41*
ruptured aneurysm				
internal carotid artery	9	6	10	14
anterior cerebral artery	0**	11	6	29
middle cerebral artery	13	9	3	25
posterior circulation	0	0	0	2
intracerebral hemorrhage	4	2	2	17
surgical complication	5*	8	11	40**
cisternal irrigation (urokinase)	6	11	5	21
outcome good recovery	21*	25	12	17**
moderate disability	1	1	5	5
severe disability	0	0	1	9
vegetative state	0	0	0	8
death	0	0	1	31

Abbreviations: WFNS, World Federation of Neurosurgical Surgeons; DIND, delayed ischemic neurological deficit.
Significance was determined according to the chi- square test.
*, $P < 0.05$. **, $P < 0.01$.

cations was significantly less in patients with short DIND duration ($P<0.05$). Favorable outcomes were significantly more frequent in patients with DIND of short duration ($P<0.05$).

On the other hand, patients with DIND of unknown duration frequently were older than 60 years ($P<0.01$), and more often had a WFNS grade on admission of 4 to 5 ($P<0.05$), a Fisher group classification of 4 ($P<0.05$), or a surgical complication ($P<0.01$). Unfavorable outcomes were significantly more frequent in patients with unknown DIND duration.

Systemic Complications Related to Hypervolemic Therapy

Complications of hypervolemic therapy were noteworthy (Table 3). Among 58 patients, a total of 84 complications occurred from hypervolemic therapy. Thirty of these complications were related to pulmonary edema. However, in patients with short DIND duration, no patients developed pulmonary edema from hypervolemic therapy, a significant difference from other duration groups.

Multivariate Analysis and Prediction of Short DIND Duration

The results of multivariate analyses are listed in Table 4. Variables associated with short DIND duration included an aneurysm site in the internal carotid artery (IC) or middle cerebral artery (MCA) system, the absence of surgical complications, age less than 60, and a WFNS grade on admission between I and III.

Table 3 DIND duration and systemic complications during hypervolemic therapy

	duration of DIND			
	2–3 days	4–6 days	6 days <	unknown
number of patients	8	15	9	26
pulmonary edema	0*	7	4	19
sepsis	0	0	0	5
meningitis	7	9	2	11
pneumonitis	1	0	4	8
renal failure	0	0	0	4
hemothorax	0	0	0	1
enterocolitis	0	0	1	1

Abbreviation: DIND, delayed ischemic neurological deficit.
Significance was determined according to the chi-square test.
*, $P < 0.01$.

Table 4 Stepwise logistic regression analysis of clinical factors associated with short duration (2 to 3 days) of delayed ischemic neurological deficit

variable	Odds Ratio	95% CI	p Value
site of aneurysm			
(IC or MCA system)	1.766	1.503–2.075	0.001
absence of surgical complication	1.617	1.201–2.177	0.007
age (< 60 yrs)	1.414	1.133–1.766	0.015
WFNS grade I to III	1.209	1.020–1.432	0.034

Abbreviations: CI, confidence interval; WFNS, World Federation of Neurosurgical Surgeons; IC, internal carotid artery; MCA, middle cerebral artery

On the other hand, in patients with DIND of unknown duration, no significant variables were identified by multivariate analysis.

DISCUSSION

Diagnosis of onset and resolution of DIND

DIND arising from vasospasm usually become apparent clinically and radiologically within 2 weeks of SAH. A few reports have detailed the angiographical duration of delayed vasospasm [23]. Drake and Allcock concluded that angiographical vasospasm resolved in 7 to 10 days [2]. However, we could not find a specific study of the clinical duration of DIND from vasospasm in previous literature. Many neurosurgeons use a prophylactic hypervolemic protocol, creating difficulty in identifying the onset and resolution of DIND [16, 17, 21]. Duration of DIND is difficult to assess from angiographical narrowing because such vasospasm may be asymptomatic.

Our protocol for hypervolemic therapy, on the other hand, facilitated determination of the onset and resolution of DIND. In the present study, 131 of 137 patients (96%) had a well-defined onset of DIND, and 67 of 137 patients (49%) had a clearly defined resolution of DIND. However, clinical diagnosis of the onset and resolution of vasospasmic DIND is difficult in poor-grade patients. Diagnostic procedures cannot fully resolve this problem. Angiographic narrowing reportedly does not correlate with DIND except when diffuse vasospasm is present [7, 24]. Additionally, an angiogram cannot reveal small-vessel spasm [11]. Similarly, Doppler sonographic findings do not correlate well with decreased cerebral blood flow or presence of DIND due to vasospasm [1, 13, 22]. Therefore, we lack a dependably accurate diagnostic method for DIND due to vasospasm, especially in patients with severe preexisting neurological deficits [18].

Clinical features of short duration DIND

In the present study, clinical factors associated with short DIND duration were an aneurysmal rupture site in an IC or MCA distribution, the lack of surgical complications, age under 60, and a WFNS grade of I to III on admission. In general, patients with a ruptured Acom system aneurysm are susceptible to diffuse SAH, and in these patients aneurysm surgery is more difficult than in patients with ruptured IC or MCA aneurysms. Therefore, brain injury due to retraction or intraoperative aneurysmal rupture is more likely for Acom aneurysms [5, 15]. Accordingly, patients with a ruptured Acom aneurysm tend to have more frequent surgical complications, such as brain edema. We could not directly link diffuse SAH to duration of DIND, as duration of DIND and extent of subarachnoid clot by CT (Fisher group) did not show a significant correlation.

On the other hand, surgical complications and clinical grade on admission correlate with the degree of brain damage present before DIND due to vasospasm. We have reported that the prognosis of DIND is determined by the degree of antecedent brain damage, including such poor-grade SAH, intracerebral hematoma, surgical complications, and DIND following rerupture [20]. We believe that a rapid resolution of DIND requires minimal antecedent brain damage.

In older patients with DIND, it is difficult to increase cardiac output by hypervolemic, hyperdynamic therapy using dobutamine. In addition, older patients have more systemic complications from hypervolemic therapy such as pulmonary edema. Ischemia from vasospasm also may develop more easily into irreversible DIND due to infarction in older patients, because reserve capability to withstand cerebral ischemia decreases in old age [12].

Duration of DIND and outcome

Outcome was highly favorable, not only in patients with brief DIND, but also in all patients with a known duration of DIND. Because DIND resolution is diagnosed after establishment of optimal hemodynamic parameters, and the parameters based on neurological improvement with hemodynamic hypervolemic therapy, patients with a well-defined DIND resolution do not include those without a clear response to hypervolemic therapy. Patients not responding, with resulting unknown duration of DIND, most likely had unfavorable outcomes. We believe that immediate improvement with hypervolemic therapy is an important prognostic factor in DIND. In patients not responsive to hypervolemic therapy, transluminal angioplasty or intra-arterial papaver-

ine infusion may improve the outcome [6, 10].

We suggest that an additional reason for favorable outcome in patients with short duration DIND is a shorter period of therapy with less opportunity for systemic complications such as pulmonary edema.

CONCLUSION

We found that DIND had a short duration in 15 % of cases. IC or MCA system aneurysm, the lack of surgical complications, age under 60, and low WFNS grade on admission were associated with short DIND duration. We believe that antecedent brain damage has a major influence on both the duration and outcome of DIND.

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