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Surgical Neurology 64 (2005) 116–121

SURGICAL NEUROLOGY

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Vascular

Low cerebrovascular reserve capacity in long-term follow-up after subarachnoid hemorrhage

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Received 3 May 2004; accepted 20 December 2004

Abstract

Background: Intradural arteries formerly in vasospasm after subarachnoid hemorrhage (SAH) show structural changes that result in arterial wall thickening and luminal narrowing. To evaluate if these changes lead to maldistribution of cerebral perfusion and reduced cerebrovascular reserve capacity (CVRC) in surviving patients, a long-term follow-up study of 18 adult patients after SAH was performed.

Methods: Eighteen patients were selected for the study, all had shown vasospasm after an early operation on a ruptured aneurysm, were in good neurological condition (GOS [Glasgow Outcome Score] 4 or 5), and had no residual infarcts. A technetium-99m-hexamethyl-propylenamine oxime (HMPAO) single-photon emission computed tomography was performed 15 to 73 months after SAH. To study CVRC, a second investigation after application of acetazolamide was performed 1 week later.

Results: Single-photon emission computed tomography showed areas of focally reduced HMPAO uptake predominantly in the hemisphere ipsilateral to the vessels more affected by posthemorrhagic vasospasm. The thalamus and the basal ganglia, the frontal lobe, and the temporal lobe were the regions most frequently showing reduced uptake. The individual change of HMPAO uptake after acetazolamide application ranged from −7% to 44% (mean, 17% ± 15%).

Conclusions: These results show a remarkable reduction of CVRC compared with findings in healthy individuals. Based on these new findings, further investigations focusing on CVRC in routine SAH follow-up are worth being considered.

Keywords: Subarachnoid hemorrhage; Cerebral vasospasm; Cerebrovascular reserve capacity; HMPAO SPECT; Acetazolamide

1. Introduction

Acute consequential cerebral damage of vasospasm after subarachnoid hemorrhage (SAH) and its clinical appearance have been well studied. Large intradural arteries, formerly in vasospasm after SAH, and small arteries and capillaries in their territory undergo structural changes [5,9]. Immediate changes after spasm encompass myonecrosis of the tunica media, destruction of elastic lamellae, and swelling of the intima. Late changes such as fibrosis and atrophy of the media and fibrosis of the subendothelial intima develop 3 or more weeks later, after vasospasm, and lead to concentric narrowing of the lumen. In small branches and capillaries, immediate stripping of the intima due to subintimal protein and red cells with consecutive late subintimal fibrosis occurs. The final consequence is concentric stenosis and a derangement of the arterial innervation and/or loss of elastic properties of the vessel wall.

The question arises if these documented neuropathological changes are reflected in cerebral function such as maldistribution of the cerebral blood flow (CBF) and

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0090-3019/$ – see front matter © 2005 Elsevier Inc. All rights reserved.
doi:10.1016/j.surneu.2004.12.017

impairment of cerebrovascular reserve capacity (CVRC) in clinical long-term follow-up. To study the regional CBF (rCBF) and the CVRC many years after SAH, a long-term follow-up study of 18 patients using technetium-99m-hexamethyl-propylenamine oxime (Tc-99m-HMPAO) single-photon emission computed tomography (SPECT) was performed. Acetazolamide was used to test CVRC. Intravenous application of acetazolamide used in combination with CBF measurements is a well-established technique to assess cerebral CVRC capacity. Acetazolamide enhances CBF acting as a vasodilatory stimulant. Acidifying of the brain extracellular fluid by a combination of elevation of PCO_2 and H_2CO_3 as a vasodilatory mediator is a probable contributing factor [2].

2. Clinical material and methods

2.1. Patient data

Ten men and 8 women who met the following criteria were included in the study: acute aneurysm surgery after SAH at least 1 year ago followed by cerebral vasospasm, age below 45 years, good neurological outcome (GOS 4 or 5), and follow-up computed tomography (CT) scans without ischemic lesions. Mean age was 36 ± 6 years. Subarachnoid hemorrhage had been diagnosed clinically and by a CT scan. Microsurgical clipping of the ruptured aneurysm was performed within 72 hours after SAH. A preoperative angiogram showed one aneurysm in 15 patients and 2 aneurysms in 3 patients.

Demographic and clinical data such as neurological condition on admission (Hunt-Hess score), amount of blood on initial CT scan (Fisher scale), aneurysm site, and grade of vasospasm of all study patients were collected retrospectively from the patients' charts and are shown in Table 1. Patients' histories were free of cerebrovascular risk factors and medical examination revealed no obvious vascular disease. No vasospasm was seen in the preoperative angiograms. Postoperatively, all patients had well-documented daily transcranial Doppler (TCD) recordings. Mean blood flow velocity (BFV) of more than 50% of the initial level and above 120 cm/s as indicative for vasospasm was seen in all patients. Vasospasm was graded as follows: mean BFV between 120 and 160 cm/s as grade 1, between 160 and 200 cm/s as grade 2, and mean BFV higher than 200 cm/s as grade 3. Seven patients developed a transient neurological deficit due to vasospasm. All were treated with 1 to 2 mg/h of nimodipine intravenously and with induced hypertension and hypervolemia when indicated.

The follow-up investigation included a clinical investigation, a CT scan, and a Tc-99m-HMPAO SPECT study, including one after acetazolamide application.

2.2. Single-photon emission computed tomography

Using a dual-head gamma camera (Siemens Dual Rota ZLC 37, Siemens, Germany), a baseline HMPAO SPECT study was performed on each patient. To test CVRC in answer to acetazolamide, a second study was done 1 week later.

Table 1
Demographic and clinical data of 18 patients after SAH caused by aneurysm rupture

Patient	Sex	Age (y)	Hunt-Hess score	Fisher scale	Aneurysm site	Vasospasm grade
1	F	39	II	1	ACoA	1
2	M	40	I	1	ACoA	1
3	M	31	III	3	ACA r	2
4	F	45	III	3	ICA r (+l)	1
5	F	42	I	1	MCA l (+r)	2
6	M	42	II	1	ACoA	1
7	M	34	I	1	ACoA	1
8	M	38	I	1	ACoA	1
9	M	39	I	1	ACoA	1
10	M	39	III	3	MCA r	1
11	M	27	I	1	ACoA	1
12	F	38	I	1	Apc r	2
13	M	38	II	3	ACoA	1
14	F	29	I	1	ICA r	1
15	F	28	I	1	MCA l	1
16	F	23	I	3	ICA r	3
17	M	34	I	1	ACoA + (ICA r)	1
18	F	35	IV	4	ICA r	3

F indicates female; M, male; ACA, anterior cerebral artery; r, right; l, left; Apc = pericallosal artery.

Rotation started 15 minutes after intravenous injection of 1 g of acetazolamide over a period of 30 minutes. We quantified the individual global HMPAO uptakes in both hemispheres. For this purpose, the camera system was calibrated using a Lucite phantom 20 cm in diameter filled with a Tc-99m solution (2.8 MBq Tc-99m/100 mL water). Thus, it was possible to convert counts per voxel obtained in patient SPECT studies into megabecquerel per voxel and to express the HMPAO brain uptake in percentage (%) of the known injected tracer amount per 100 g brain tissue. The injected tracer dose was estimated correctly by subtracting the decay-corrected tracer amount remaining in the syringe and needle from the initial syringe content.

The intraindividual increase of global HMPAO uptake after injection of acetazolamide was calculated in percentage (%) of the HMPAO uptake at rest to indicate the individual CVRC. The test-retest range of 2 baseline studies within 1 week is 13% (=double SD) [15]. Thus, an increase below 13% after injection of acetazolamide was considered as not significant and as indicative for low CVRC. Areas of regionally reduced uptake were evaluated by visual judgement by an independent, experienced investigator (IP).

3. Results

The follow-up investigations were performed 15 to 73 months after SAH (mean, 39.8 ± 19.5 months). All patients were able to live independently and work in their former profession. Three patients showed mild cognitive impairment with lack of concentration and, in addition, with