

## Cerebral vasospasm with elevated creatine phosphokinase following surgery of unruptured arteriovenous malformation

Y. Takabatake, J. Yamashita, S. Higashi, T. Yamashima, Y. Yamamoto

Department of Neurosurgery, Kanazawa University, School of Medicine, Kanazawa, Japan

### Summary

Delayed cerebral vasospasm associated with marked elevation of serum creatine phosphokinase (CPK) is reported. A 21-year-old man with unruptured arteriovenous malformation (AVM) in the left temporal lobe developed postoperative symptomatic vasospasm lasting for 2 weeks. A postoperative computerized tomography scan showed intraventricular hematoma without subarachnoid hemorrhage in the basal cistern. On day 5 after surgery, the patient developed motor aphasia due to marked vasospasm around the bifurcation of internal carotid artery. On day 7 and 8, serum CPK was elevated as high as 1175 and 1376 IU/l, respectively. On day 35 when he had completely recovered from cerebral vasospasm both clinically and angiographically, the level of CPK was normalized. The causative factors of symptomatic cerebral vasospasm following surgery of unruptured AVM associated with CPK elevation are discussed.

### Key-Words

Arteriovenous malformation – Cerebral vasospasm – Creatine phosphokinase

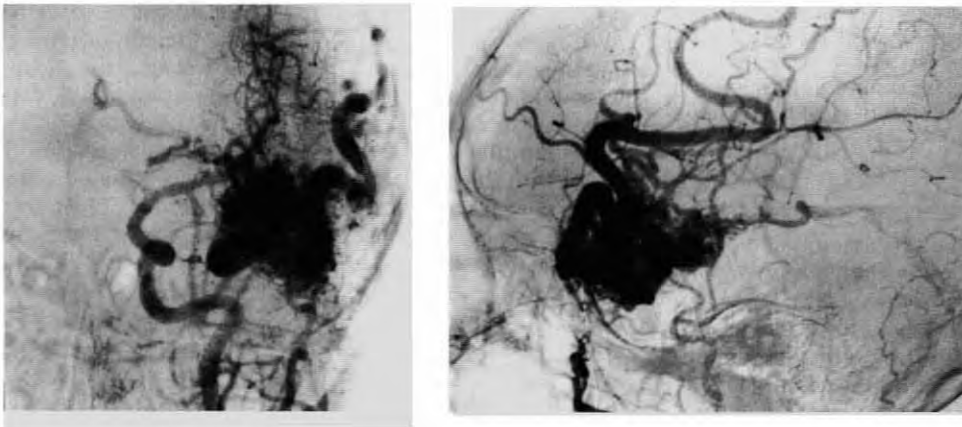
### Zerebraler Vasospasmus bei erhöhter Phosphokinase nach Operation einer intakten arteriovenösen Mißbildung

Die Verfasser berichten über einen verzögerten zerebralen Vasospasmus mit einer ausgeprägten Erhöhung der Serumkreatinphosphokinase. Ein 21-jähriger Mann mit einer intakten arteriovenösen Mißbildung im linken Schläfenlappen entwickelte postoperativ einen 2 Wochen lang anhaltenden symptomatischen Vasospasmus. Postoperative CT zeigte ein intraventrikuläres Hämatom ohne subarachnoidale Blutung in der basalen Zisterne. Am 5. postoperativen Tag entwickelte der Patient eine motorische Aphasie aufgrund eines ausgeprägten Vasospasmus an der Karotisbifurkation. Am 7. und 8. postoperativen Tag war die Serumkreatinphosphokinase auf 1175 bzw. 1376 IE/l erhöht. Am 35. Tag, nach vollständiger klinischer und angiographischer Erholung vom zerebralen Vasospasmus, hatte sich der Serumkreatinphosphokinasespiegel normalisiert. Die ursächlichen Faktoren des symptomatischen zerebralen Vasospasmus nach Operation der intakten arteriovenösen Mißbildung bei gleichzeitig erhöhtem Kreatinphosphokinasespiegel werden erörtert.

It is widely accepted that delayed cerebral vasospasm following subarachnoid hemorrhage is usually associated with ruptured aneurysms, but rarely with arteriovenous malformations (AVMs) (2, 3, 4, 6). Furthermore, very few cases of symptomatic vasospasm due to AVMs have been previously reported. This paper is to report a case with symptomatic cerebral vasospasm which was associated with marked elevation of serum creatine phosphokinase (CPK) after surgery of unruptured AVM.

### Case Report

A 21-year-old man was admitted to our hospital on September 30, 1988, because of repeated episodes of dizziness for 7 months. He had a past history of febrile convulsions and head trauma with loss of consciousness for a few days in his childhood. Neurological examination on admission revealed no abnormality except for left external strabismus. A computerized tomography (CT) scan showed a low density area with partial heterogeneous contrast enhancement in the left temporal lobe. A left carotid angiogram showed a large AVM in the left anterior temporal lobe. The nidus measuring 65 × 40 mm in diameter, was fed by the middle cerebral and anterior choroidal arteries, and drained by the veins of Trolard, Rolando, Rosenthal, and Labbé (Fig. 1). According to the Spetzler's grading (5), it was ranked as grade IV. T1 weighted image of magnetic resonance imaging (MRI) showed a hypointensity area with multiple signal void regions in the anterior temporal lobe, and also revealed porencephalic cavity due to old intracerebral bleeding.

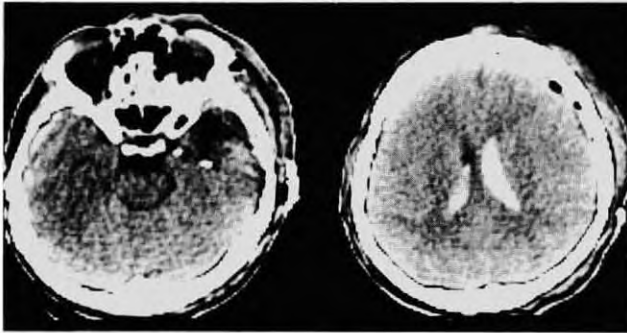


**Fig. 1** Left carotid angiogram showing a large arteriovenous malformation (65 × 40 mm in diameter) in the anterior portion of temporal lobe. Anterior view (left) and lateral view (right).

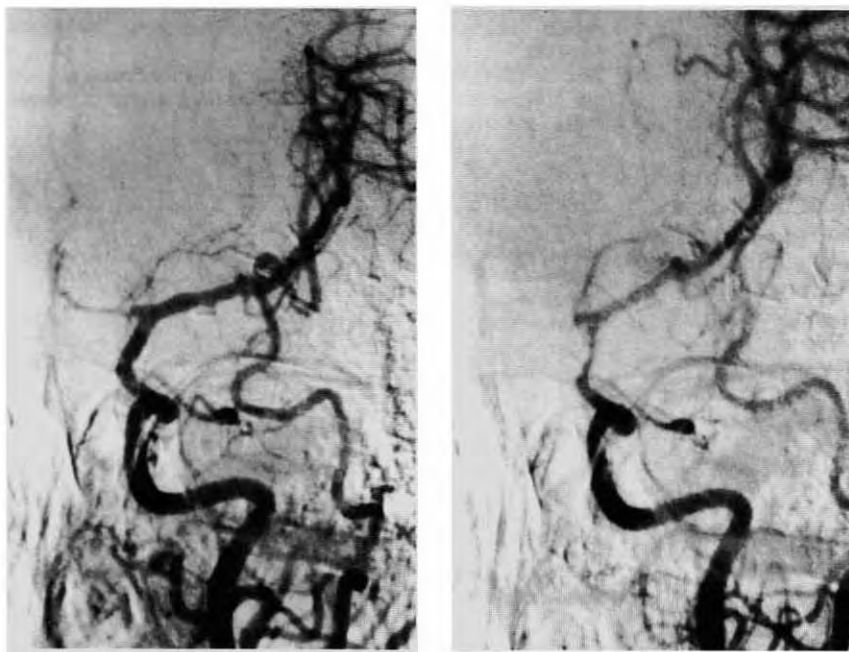
A left fronto-temporal craniotomy was performed for resection of the AVM on October 13. The superficial sylvian veins were reddish, dilated and were drained to the dilated vein of Trolard. Three main feeders from the middle cerebral and anterior choroidal arteries were coagulated and clipped via the transsylvian route. At the rear of the nidus was a large porencephalic cyst. As the

inferior horn of the left lateral ventricle was opened during surgery, a moderate amount of blood flowed into the lateral ventricle.

His postoperative recovery was good. A postoperative CT scan taken on day 2 showed intraventricular hematoma due to surgery, but no hemorrhage in the subarachnoid space (Fig. 2). Cerebral blood flow (CBF) study on day 4 showed a diffuse decrease of CBF in both frontal and temporal lobes on the left side. On day 5 the patient had a transient episode of motor aphasia lasting for 5 minutes. Serum CPK on that day was 75 IU/l (normal range: 0–93 IU/l). The value of CPK was elevated as high as 1155 IU/l on day 7 and up to 1376 IU/l on day 8. At the same time, his motor aphasia became persistent and more severe. Phenobarbital was given intramuscularly for the purpose of sedation in dose of 100 mg three times a day from day 5 to day 7. Intracranial pressure measured by lumbar puncture on day 9 was 280 mmH<sub>2</sub>O. Cerebrospinal fluid (CSF) was xanthochromic, containing 47 mg/dl of protein, 51 mg/dl of sugar and 25 leucocytes/mm<sup>3</sup>. On day 10, his neurological conditions further deteriorated with total aphasia, perseveration and literal paraphasia. Surprisingly a left carotid angiogram on day 12 showed severe cerebral vasospasm around the bifurcation of internal carotid artery (Fig. 3 left). Then CPK isozyme patterns were analyzed twice. There was no CPK-BB at all and CPK-MB was no more than 2% (see below). There were no



**Fig. 2** Computerized tomography scan 2 days after operation showing intraventricular hemorrhage (right), but no hemorrhage in the basal cistern (left).



**Fig. 3** Left carotid angiograms showing severe cerebral vasospasm around the bifurcation of internal carotid artery on day 12 (left), which had subsided on day 35.

electrocardiographic changes. CBF study on day 14 showed diffuse decrease in both hemispheres. However, all of his neurological symptoms gradually disappeared. On day 35, a left carotid angiogram showed complete recovery from the vasospasm (Fig. 3 right), and both CBF and CPK were also normalized. He was discharged on day 46 without neurological deficits.

### Comments

It is well known that the amount of blood in the basal cistern is closely related to the development of cerebral vasospasm in ruptured aneurysms (7). In case of AVMs, less amount of blood extends to the basal cistern because of their distant location (3). Accordingly, symptomatic cerebral vasospasm occurs far less frequently following rupture of AVMs. The incidence of angiographic cerebral vasospasm in ruptured AVMs was variously reported as 8–31% (2, 3, 4, 6). However, the majority of previously reported cases were clinically asymptomatic. Although the CT scan on day 2 disclosed no hemorrhage in the basal cistern, the present case developed symptomatic cerebral vasospasm lasting for 2 weeks. Two possible factors may emerge as a cause of the vasospasm.

Firstly, as the temporal horn was incidentally opened during surgery through a preexisting porencephalic cavity in the temporal lobe, a moderate amount of blood directly flowed into the temporal horn. Consequently chemical mediators such as serotonin, oxyhemoglobin, prostaglandins, etc. might have dissolved from the clots in the lateral ventricle and entered into the basal cistern.

Secondly, the AVM was located only a few centimeters distal to the bifurcation of the middle cerebral artery, surgical procedures might have damaged perforating arteries to the hypothalamus. The resultant hypothalamic disturbance might have induced the liberation of various vasoactive agents into the basal cistern, or stimulated widespread sympathetic discharge with increased level of circulating catecholamines (11).

Wilkins reported that increased catecholamines might provoke autonomic dysfunction, myocardial necrosis (8, 9), and elevated CPK. CPK is a dimer consisting of 2 subunits, M (muscle) and B (brain), while isozymes of CPK are MM, BB, and MB. CPK-MM is mainly involved in the skeletal muscles, CPK-BB in the brain, and CPK-MB in the myocardium. *Yuu* noted marked elevation of CPK as high as 2.1–12.9 fold of normal value, after intramuscular injection of 100mg of phenobarbital (12). However, we have observed only mild elevation of CPK after intramuscular injection of phenobarbital in our several patients. *Greenblatt* reported that cerebral vasospasm does not cause an elevation of CPK in the CSF unless it induces cerebral infarction. Elevat-

ed CPK levels in the CSF was previously assumed to be indicative of parenchymal damage (1). Although intramuscular injections of phenobarbital might be one of the causative factors, it is unlikely that marked elevation of CPK was solely due to that. It alone cannot explain dynamic CPK changes in this case. Dynamic CPK changes were closely related with the time course of cerebral vasospasm in this case. The exact mechanism of elevated serum CPK in this case still remains obscure. In summary, we would like to draw attention to possible relationship between CPK and cerebral vasospasm.

### References

- Greenblatt, S. H.*: Cerebrospinal fluid creatine phosphokinase in acute subarachnoid hemorrhage. *J. Neurosurg.* 44 (1976) 50–54
- Matsumori, K., S. Asahi, K. Nakayama, Y. Miyasaka, T. Beppu.*: Cerebral vasospasm after subarachnoid hemorrhage from arteriovenous malformation. *No Shinkei Geka* 11 (1983) 829–834
- Nishimura, K., T. D. Hawkins.*: Cerebral vasospasm with subarachnoid hemorrhage from arteriovenous malformations of the brain. *Neuroradiology* 8 (1975) 201–207
- Sasaki, T., Y. Mayanagi, H. Yano, S. Kim.*: Cerebral vasospasm with subarachnoid hemorrhage from cerebral arteriovenous malformations. *Surg. Neurol.* 16 (1981) 183–187
- Spetzler, R. F., N. A. Martin.*: A proposed grading system for arteriovenous malformations. *J. Neurosurg.* 65 (1986) 476–483
- Stornelli, S. A., J. D. French.*: Subarachnoid hemorrhage-factors in prognosis and management. *J. Neurosurg.* 21 (1964) 769–780
- Symon, L., B. A. Bell, B. Kendall.*: Relationship between effused blood and clinical course and prognosis in aneurysmal subarachnoid hemorrhage: A preliminary computerized tomography scan study. In: *Wilkins, R. H. (ed.) Cerebral Arterial Spasm.* Williams & Wilkins, Baltimore (1980) 409–411
- Wilkins, R. H.*: Hypothalamic dysfunction and intracranial arterial spasm. *Surg. Neurol.* 4 (1975) 472–480
- Wilkins, R. H.*: The possible role of the hypothalamus in the development of intracranial arterial spasm. In: *Wilkins, R. H. (ed.) Cerebral Arterial Spasm.* Williams & Wilkins, Baltimore (1980) 266–269
- Wilson, J. L., J. R. Feild.*: The production of intracranial vascular spasm by hypothalamic extract. *J. Neurosurg.* 40 (1974) 473–479
- Yamashima, T., S. Yamamoto.*: Cerebral arterial pathology in experimental subarachnoid hemorrhage. *J. Neurosurg.* 58 (1983) 843–850
- Yuu, H.*: Diagnostic significance of serum creatine kinase isoenzyme, MB fraction (CK-MB) in acute myocardial infarction. *Nippon Naika Gakkai Zasshi* 67 (1978) 10–16

*Tetsumori Yamashima, M.D.*

Department of Neurosurgery  
Kanazawa University  
School of Medicine  
Takaramachi 13-1  
Kanazawa city, 920  
Japan