Possible overlap between reversible cerebral vasoconstriction syndrome and symptomatic vasospasm after aneurysmal subarachnoid hemorrhage

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Abstract A 34-year-old woman with a previous history of severe headache (“thunderclap”) was admitted with a diagnosis of aneurysmal subarachnoid hemorrhage (SAH). The patient developed symptomatic vasospasm on day 5 that resolved rapidly after having increased arterial blood pressure. She experienced also short-lasting excruciating headache. On day 12, while velocities had normalised, as revealed by transcranial Doppler (TCD), for more than 48 h, she developed aphasia and right hemiplegia associated with diffuse segmental vasospasm on the left middle cerebral artery. Intra-arterial infusion of vasodilatory agents was required. Recurrence of symptomatic vasospasm was noted on day 25, with a great number of territories involved as shown in the cerebral angiogram. A second intra-arterial treatment was needed. The patient complained of multiple episodes of extremely severe headache (“thunderclap”), with also transient dysarthria and hemiparesia on day 30. She was discharged on day 38 after full recovery. The clinical and TCD/radiological findings were consistent with a reversible cerebral vasoconstriction syndrome overlapping SAH related symptomatic vasospasm.

Keywords Reversible cerebral vasoconstriction syndrome · Aneurysmal subarachnoid hemorrhage · Vasospasm

Introduction

Reversible cerebral vasoconstriction syndrome (RCVS) is a rare vasculopathy of unknown etiology [1, 2]. It was mainly reported in young women with a history of severe “thunderclap” headache. The clinical picture may mimic subarachnoid hemorrhage (SAH). In addition, unruptured aneurysms have been reported in some patients with RCVS, but not clear causal relationship has been documented [3–5]. We describe a case of aneurysmal SAH for which the differential diagnosis has to be discussed between RCVS and symptomatic vasospasm.

Case report

A 34-year-old woman developed acute-onset occipital headache with loss of consciousness. She had a history of episodic severe headache treated by nonsteroidal anti-inflammatory drugs. There was no clear precipitating factor. The headache was described as generalised and bilateral. The pain was excruciating and lasted usually less than 1 h, being sometimes accompanied by nausea and vomiting.

On arrival, she had a GCS of 15, and also with a mild hypo-esthesia in the left arm. The brain CT confirmed the
diagnosis of SAH (Fisher 3 radiological score), with a focal hematoma in the territory of the left anterior cerebral artery (ACA), blood in the subarachnoid spaces of the left sylvian fissure and into the occipital horn of the left lateral ventricle. The cerebral angiography revealed four distinct aneurysms. The ruptured aneurysm (8 mm × 9 mm) was located on the junction of the A1–A2 segments of the left ACA. The three unruptured aneurysms were on the A1 segment of the left ACA (1.5 mm diameter), on the A2 segment (3 mm × 2 mm) and at the origin of the posterior communicating artery. The clipping of the four aneurysms was performed without peri-operative complications and after extubation the patient presented only neck stiffness and photophobia. She received oral nimodipine and continuous infusion of magnesium sulphate. On day 5 from bleeding, she was found drowsy, with a slurry speech, and a vasospasm on the left middle cerebral artery (MCA) was suspected on transcranial Doppler (TCD). Systolic arterial pressure was increased to 150 mmHg by norepinephrine infusion followed by rapid neurological improvement. She complained on days 9 and 10 of acute-onset but short-lasting excruciating headache. Norepinephrine infusion was tapered down and stopped on day 12. Velocities normalised on TCD performed on days 7 and 10. She was discharged from ICU on day 12 with a normal neurological examination but was readmitted the same night with right hemiparesis. An association between RCVS and SAH-related vasospasm (catecholamines, pheochromocytoma or the use of vasoactive substances like cocaine [1, 2]. In some patients, the presence of an associated intracranial abnormality can be demonstrated, as in our patient who had a ruptured aneurysm leading to SAH.

Obviously, vasospasm, symptomatic or not, is a common complication following aneurysmal SAH. The presence of blood close to the site of the aneurysm locally triggers the vasospasm. The maximal duration of vasospasm, when installed, is usually 4 weeks. However, a delayed recurrence of symptomatic vasospasm is infrequent. Also the clinical symptoms and the TCD and radiological findings were unusual. Recurrent excruciating headache (“thunderclap”) was the main clinical feature. It lasted for approximately one hour and was poorly influenced by major analgesics. It occurred several times during the same journey and seemed to be partly correlated with increased velocities on TCD examination. Cerebral angiography demonstrated migrating segmental vasoconstriction in different cerebral arteries.

We suspected that cerebral vasoconstriction could be triggered by two different mechanisms and postulated that the patient presented an overlap between RCVS and SAH-related vasospasm.

It has been suggested that some factors known to be involved in SAH-related vasospasm (catecholamines, endothelin-1, serotonin, nitric oxide, and prostaglandins) could play a similar role in the pathophysiology of vasoconstriction in RCVS [1, 2].

SAH without intracranial aneurysm is not infrequently encountered in RCVS, perhaps in up to one in four cases, and typically overlies the lateral-superior cortical surface [3–6]. In RCVS, SAH is usually minimal or moderate in amount and should not be considered the cause of the segmental vasoconstriction, which affects artery remote to the site of bleeding. An association between RCVS and unruptured intracranial aneurysm has also been reported [5].

By definition, RCVS usually shows diffuse areas of multiple stenosis and dilatation involving intracranial
Table 1  Clinical course, TCD and radiological findings, and therapy

| Day from bleeding | TCD Mean velocity (cm/s) (left MCA/right MCA) | Symptoms | Brain CT or MR angiography Vasospasm | Treatment |
|-------------------|-----------------------------------------------|----------|-------------------------------------|-----------|
| D1                | Headache, loss of consciousness               |          |                                     | Nimodipine |
| D2                | (Clipping)                                     |          |                                     | Nimodipine, MgSO₄ |
| D3                |                                               |          |                                     | Nimodipine, MgSO₄ |
| D4                | 130/111                                       | Headache |                                     | Nimodipine, MgSO₄ |
| D5                | 154/123                                       | Headache | Left MCA(P)                          | Nimodipine, MgSO₄, THT |
| D6                | 160/135                                       |          |                                     | Nimodipine, MgSO₄, THT |
| D7                | 105/88                                        |          |                                     | Nimodipine, MgSO₄, THT |
| D8                |                                               |          |                                     | Nimodipine, MgSO₄, THT |
| D9                |                                               |          |                                     | Nimodipine, MgSO₄, THT |
| D10               | 95/88                                         |          |                                     | Nimodipine, MgSO₄, THT |
| D11               |                                               |          |                                     | Nimodipine, MgSO₄ |
| D12               |                                               |          |                                     | Nimodipine, MgSO₄ |
| D13               | 174/109                                       | Aphasia, right hemiplegia | Left ACA(C), diffuse D on left M1 and right M1–M2 | Nimodipine, MgSO₄, THT-IA nimodipine, IV milrinone |
| D14               | 99/62                                         | Right leg plegia |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D15               | 92/63                                         | Motor recovery |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D16               |                                               |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D17               | 105/60                                        |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D18               | 140/60                                        | Headache |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D19               | 145/88                                        | Headache |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D20               | 121/80                                        |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D21               | 122/62                                        |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D22               |                                               |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D23               |                                               |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D24               | 89/71                                         |          |                                     | Nimodipine, MgSO₄, THT |
| D25               | 150/220                                       | Confusion, agitation, headache +++ | See Fig. 1 | Nimodipine, MgSO₄, THT-IA + IV milrinone |
| D26               | 109/165                                       | Headache |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D27               | 96/100                                        | Headache |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D28               | 78/130                                        | Headache |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D29               |                                               |          |                                     | Nimodipine, MgSO₄, THT, milrinone |
| D30               |                                               | Transient dysarthria and right hemiparesia | RP1, focal BT, segmental left M1, right M1 | Nimodipine, MgSO₄, THT |
| D31               | 96/166                                        |          |                                     | Nimodipine, MgSO₄, THT |
| D32               | 83/152                                        |          |                                     | Nimodipine, MgSO₄, THT |
| D33               |                                               |          |                                     | Nimodipine |
| D34               | 94/171                                        |          |                                     | Nimodipine |
| D35               |                                               |          |                                     | Nimodipine |
| D36               |                                               |          |                                     | Nimodipine |
| D37               |                                               |          |                                     | Nimodipine |
| D38               | 87/145                                        | Full recovery |                                     | Nimodipine |

*TCD* transcranial Doppler, *left ACA* left anterior cerebral artery, *left MCA* left middle cerebral artery, *right MCA* right middle cerebral artery, *LM1* segment M1 of left MCA, *RM1–2* segments 1–2 of right MCA, *RP1* segment P1 of the right posterior cerebral artery, *BT* basilar trunk, *P* proximal, *C* complete, *D* distal, *THT* triple-H therapy, *IA* intra-arterial (in loco), *IV* intravenous
arteries [1, 2, 6]. These abnormalities are reversible within days to weeks. In SAH, vasospasm typically is not multifocal, affects one or two medium arteries, and peaks between days 4 and 11.

The pharmacological treatment of SAH-related vasospasm relies on the so-called “triple-H therapy” (hypertension, hypervolemia, hemodilution), where hypertension induced by norepinephrine may play a major role. It can not be excluded that vasoactive substances like norepinephrine may aggravate RCVS [6]. The place of “rescue” therapy with intra-arterial vasodilatory agents is not yet defined [7].

Conflict of interest None.

References

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