Subarachnoid hemorrhage–associated cerebral vasospasm (CVS) is a devastating condition. Unfortunately, 66% of patients with aneurysmal subarachnoid hemorrhage (SAH) develop moderate to severe angiographic vasospasm.1 In the management of CVS, the combination of induced hypertension, hypervolemia, and hemodilution (triple-H therapy) is often used to treat cerebral vasospasm. However, hypertensive treatment may carry significant medical morbidity, including cardiopulmonary, renal, and intracranial complications. Posterior reversible encephalopathy syndrome (PRES) is a reversible intracranial complication that has rarely been reported in the setting of induced hypertension.

Methods—We present an illustrative case of PRES in a patient with induced hypertension for SAH-related cerebral vasospasm and performed a systematic review. Furthermore, the electronic database MEDLINE was searched for additional data in published studies of PRES after induced hypertension.

Results—Overall, 7 case reports presenting 10 patients who developed PRES secondary to induced hypertension were found. Eighty-two percent of the patients were women. In all cases, the clinical symptoms were attributed to cerebral vasospasm before the diagnosis of PRES. The time from onset of induced hypertension to the development of PRES was 7.8±3.8 days. After the diagnosis of PRES and careful taper down of the blood pressure, the neurological symptoms resolved almost completely within a few days in all patients.

Conclusions—PRES in the setting of SAH is an overlooked complication of hypertensive therapy for the treatment of vasospasm. However, the diagnosis of this phenomenon is crucial given the necessity to reverse hypertensive therapy, which is contrary to the usual management of patients with vasospasm. (Stroke. 2016;47:519-522. DOI: 10.1161/STROKEAHA.115.011697.)

Key Words: intracranial aneurysm ■ posterior reversible encephalopathy syndrome ■ subarachnoid hemorrhage ■ vasospasm, intracranial

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of PRES are similar to the symptoms of CVS and can, therefore, mimic delayed ischemic neurological deficit or the clinical symptoms of CVS.

Materials and Methods

We present an illustrative case of PRES secondary to induced hypertension after SAH and performed a literature review.

Literature Search

Two reviewers (S.M. and E.G.) performed an independent MEDLINE search of published studies written in English and German till December 2014. The following key words were used in relevant combinations: PRES, posterior reversible encephalopathy, SAH, subarachnoid hemorrhage, vasospasm, and induced hypertension. We found 58 articles in total. The search was restricted to human studies and case reports on PRES after SAH and induced hypertension. Full-text versions of published reports were obtained for all studies considered to be potentially relevant by both reviewers. The references of all relevant studies were manually searched for additional studies until no further publications were found.

Results

Case and Treatment Protocol

A 67-year-old woman presented to the neurosurgical department after development of sudden headache and nausea. On admission, her blood pressure was 160/90 mm Hg with a history of arterial hypertension. A cranial computed tomographic (CT) scan revealed SAH with no signs of hydrocephalus (Hunt and Hess grade III, Fisher III). The digital subtraction angiography revealed a posterior communicating artery aneurysm (6×3 mm), which was successfully treated by coiling on the day of admission.

On day 1 after coiling, the patient was alert, without further motor deficit. Her mean arterial blood pressure (MAP) was between 80 and 90 mm Hg (Figure 1). On day 4, the patient developed a hemiparesis on the left side. A CT scan showed no rebleeding or hydrocephalus. The CT angiography showed slight multifocal CVS. Considering vasospasm-associated neurological decline, the MAP was maintained ≈110 mm Hg. The patient recovered slowly from her hemiparesis during the next 6 days of induced hypertension. On day 10, the patient again started deteriorating neurologically. She was confused, and after focal seizure, she was intubated. CT perfusion and CT angiography scans did not show any significant perfusion deficits but slight residual CVS. At this time, our patient was spontaneously hypertensive. Because of the suspected residual CVS, we did not actively treat her hypertension. A follow-up

Figure 1. Mean arterial blood pressure averaged for 24 hours from admission to day 20. Data from every second day is presented; neurological symptoms and diagnostic and therapeutic procedures are indicated in boxes. MRI indicates magnetic resonance imaging; PRES, posterior reversible encephalopathy syndrome; and SAH, subarachnoid hemorrhage.

Figure 2. Magnetic resonance imaging (MRI) scan showing posterior reversible encephalopathy syndrome (PRES) secondary to induced hypertension. The first MRI (A and B) confirmed extensive hyperintense lesions in T12 sequence (vasogenic edema) with involvement of the frontal, temporal, and parietal lobes. Control MRI (C and D) proofs the diagnosis of PRES as it shows that the lesions are widely reversible, as reversibility is 1 hallmark of PRES.
CT scan showed bilateral posterior subcortical edema in the watershed zone and additional frontal and parietal edema leading to the suspicion of underlying PRES. A cranial magnetic resonance imaging scan confirmed the bihemispheric supratentorial vasogenic edema typical for PRES and further showed brain stem and cerebellar edema, which is less common in PRES (Figure 2). CVS could be ruled out by magnetic resonance angiography and perfusion weighted imaging and because of the lack of cytotoxic edema in diffusion-weighted imaging. A slow taper down of the MAP to \(\approx 80\) mm Hg resolved the hemiparesis on day 21. A follow-up magnetic resonance imaging scan on day 24 showed that the vasogenic edema was widely reversed with remaining minimal residual changes. With proof of reversibility, the diagnosis of PRES finally could be confirmed. The patient was transferred to the normal ward with a modified Rankin score of 3 on day 28.

**Literature Review**

The MEDLINE search yielded 7 articles reporting on 10 patients with PRES after hypertensive therapy of CVS.6–11 Patient characteristics are detailed in Table.

Including our case, 9 of 11 patients (82%) were women. Four of 7 patients (57%) were admitted to the hospital with Hunt and Hess grades I or II. In seven of 10 (70%) of the cases, the aneurysm was located at the anterior or posterior communicating artery. Six of 10 (60%) of the patients were treated by clipping. The time to development of PRES after starting hypertensive treatment was 7.8±3.8 days (range, 1–13 days). Clinical symptoms of PRES were lethargy, confusion, aphasia, focal neurological deficit, and seizure. Radiological signs of PRES were distributed in the parietooccipital region and, in 3 cases, additionally in the cerebellum. In all patients, the clinical symptoms reversed within few days after normalization of the blood pressure.

**Clinical Outcome**

Seven of 11 patients (64%) left the hospital without significant disability (modified Rankin scale score, 1), 1 patient died because of rebleeding of the aneurysm, and 3 patients had moderate to severe disability at hospital discharge.

**Discussion**

Sixty-six percent of patients develop angiographic vasospasm after SAH,6 which is the main cause of secondary neurological decline.7 The main goal of therapy during vasospasm is to sustain cerebral perfusion through narrowed arterioles by induced hypertension, keeping the MAP >110 mm Hg. Unfortunately, there is no ceiling MAP established to be safe during induced hypertensive therapy of vasospasm. Complex situations, where despite increased MAP, the symptoms of the patient do not resolve, may lead to aggressive hypertensive treatment with consequent autoregulatory failure and development of complications, for example, PRES.

PRES in the setting of induced hypertension caused by CVS is an overlooked condition, described in 10 cases in the world literature, except the present case, to date.6–11 Literature review revealed that 80% of the patients with PRES after induced hypertension were women. However, this might be because of a higher incidence of SAH in women, amplified by the fact that PRES is generally more frequent in women. Previous history of hypertension may play a role in the development of PRES, as only 4 of the 11 patients had no previous history of hypertension. Hypertension can lead to endothelial damage and breakdown of blood–brain barrier that can ultimately lead to formation of vasogenic edema. Impaired

### Table. Summary of Patient Characteristics in Patients With SAH and PRES

<table>
<thead>
<tr>
<th>Study</th>
<th>Sex</th>
<th>Age</th>
<th>Aneurysm Location</th>
<th>Treatment</th>
<th>Target BP (mm Hg)</th>
<th>PRES (Days After SAH)</th>
<th>PRES (Days After HT)</th>
<th>History of Hypertension</th>
<th>Clinical Outcome (mRS)</th>
<th>Symptoms During PRES/CVS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amin-Hanjani et al5</td>
<td>F</td>
<td>52</td>
<td>MCA (l)</td>
<td>Clipping</td>
<td>SBP, =200</td>
<td>13</td>
<td>7</td>
<td>No</td>
<td>1</td>
<td>Lethargy</td>
</tr>
<tr>
<td>M</td>
<td>66</td>
<td>No</td>
<td>No</td>
<td>SBP, =200</td>
<td>12</td>
<td>10</td>
<td>Yes</td>
<td>6</td>
<td>Lethargy, aphasia, seizure, HP</td>
<td></td>
</tr>
<tr>
<td>Sanelli et al8</td>
<td>F</td>
<td>49</td>
<td>Acom</td>
<td>Clipping</td>
<td>SBP, 140–200</td>
<td>17</td>
<td>13</td>
<td>NA</td>
<td>1</td>
<td>Lethargy</td>
</tr>
<tr>
<td>Wartenberg et al11</td>
<td>F</td>
<td>73</td>
<td>ICA (l)</td>
<td>Clipping</td>
<td>SBP, 140–200</td>
<td>10</td>
<td>7</td>
<td>Yes</td>
<td>4</td>
<td>Coma with decorticating posture</td>
</tr>
<tr>
<td>Jang et al8</td>
<td>F</td>
<td>65</td>
<td>Pcom</td>
<td>Clipping</td>
<td>SBP, =165</td>
<td>7</td>
<td>1</td>
<td>No</td>
<td>1</td>
<td>Confusion, headache, and loss of vision</td>
</tr>
<tr>
<td>Girald et al7</td>
<td>F</td>
<td>62</td>
<td>Acom</td>
<td>Clipping</td>
<td>MAP, =115</td>
<td>12</td>
<td>6</td>
<td>No</td>
<td>1</td>
<td>Lethargy, headache, and retroorbital pain</td>
</tr>
<tr>
<td>F</td>
<td>70</td>
<td>Acom</td>
<td>Clipping</td>
<td>MAP, =120</td>
<td>12</td>
<td>11</td>
<td>Yes</td>
<td>1</td>
<td>Lethargy and seizure</td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>62</td>
<td>Acom</td>
<td>Clipping</td>
<td>SBP, =180</td>
<td>14</td>
<td>13</td>
<td>Yes</td>
<td>4</td>
<td>Lethargy</td>
<td></td>
</tr>
<tr>
<td>Dhar et al6</td>
<td>F</td>
<td>47</td>
<td>Pcom (r)</td>
<td>Clipping</td>
<td>MAP, =120</td>
<td>13</td>
<td>7</td>
<td>No</td>
<td>1</td>
<td>Lethargy, confusion, left facial droop, aphasia, and HP</td>
</tr>
<tr>
<td>Voetsch et al13</td>
<td>F</td>
<td>35</td>
<td>MCA (r)</td>
<td>Clipping</td>
<td>MAP, 120–130</td>
<td>7</td>
<td>4</td>
<td>NA</td>
<td>3</td>
<td>Headache, seizure, and declined arousal</td>
</tr>
<tr>
<td>Current report</td>
<td>F</td>
<td>67</td>
<td>Pcom (r)</td>
<td>Clipping</td>
<td>MAP, =110</td>
<td>11</td>
<td>7</td>
<td>Yes</td>
<td>3</td>
<td>Lethargy, seizure, and HP</td>
</tr>
</tbody>
</table>

Acom indicates anterior communicating artery; CVS, cerebral vasospasm; F, female; HP, hemiparesis; HT, hypertension, ICA, internal carotid artery; l, left; M, male; MAP, mean arterial blood pressure; MCA, middle cerebral artery; mRS, modified ranking scale; Pcom, posterior communicating artery; PRES, posterior reversible encephalopathy syndrome; r, right; SBP, systolic blood pressure; and SAH, subarachnoid hemorrhage.
autoregulation of blood pressure in patients with SAH may further increase the susceptibility to develop vasogenic edema and PRES. Induced hypertension can increase the perfusion in the territory of CVS, but at the same time, it may lead to high pressure in vessels not involved in CVS and therefore may increase the vulnerability to develop PRES. CT perfusion findings demonstrated that there is an increased cerebral blood flow and cerebral blood volume and decreased mean transient time compatible with hyperemia in the PRES-related areas.

According to the review of literature, anterior circulation aneurysms may be more susceptible to develop PRES during the treatment of CVS. However, PRES may be overlooked in posterior circulation aneurysms because of the lack of typical clinical symptoms, such as hemiparesis. Furthermore, the prevalence of posterior circulation aneurysms is lower compared with anterior circulation aneurysms, and the frequency of CVS is significantly lower after rupture of posterior circulation aneurysms when compared with anterior circulation aneurysms that may shift the incidence of PRES during treatment of CVS toward anterior circulation aneurysms.

The present case has many similarities to the cases reported in the literature. The patient was of female sex with a previous history of hypertension, harboring a posterior communicating artery aneurysm.

The diagnosis of PRES led to a change in the therapy regime with clinical and radiological improvement. In the present case, the patient developed PRES after 7 days of hypertensive treatment, which is in line with the data of the literature.

The mechanisms of induced hypertension–related PRES are not well understood and have been controversially discussed in the literature. It is suggested that PRES develops secondary to induced hypertension, probably exceeding the autoregulatory limits. However, immunosuppressive drugs, for example, tacrolimus, catecholamines, and ciclosporin, can also cause PRES that is associated with altered cerebral blood flow and endothelial dysfunction. Moreover, PRES can also develop after SAH without induction of hypertension. The patient presented had a history of hypertension for many years and was hospitalized in the past because of hypertensive crises. She may have already endothelial dysfunction caused by longstanding hypertension and might be more prone to develop blood–brain barrier disruption after induced hypertension.

In this systematic review with illustrative case, induced hypertension did not resolve the secondary neurological decline in patients with SAH-related CVS. Moreover, induced hypertension rather worsened the clinical symptoms by the induction of PRES. Therefore, the possibility of complications of induced hypertension (eg, PRES) should be kept in mind, whenever clinical symptoms rather worsen after the augmentation of blood pressure.

Conclusions

PRES in the setting of SAH is an overlooked complication of hypertensive therapy for the treatment of vasospasm. However, the diagnosis of this phenomenon is crucial given the necessity to reverse hypertensive therapy or actively treat spontaneously hypertensive patients, which is contrary to the usual management of patients with vasospasm.

Disclosures

None.

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Posterior Reversible Encephalopathy Syndrome as an Overlooked Complication of Induced Hypertension for Cerebral Vasospasm: Systematic Review and Illustrative Case
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