

ANGIOPLASTY FOR CEREBRAL VASOSPASM FROM ECLAMPSIA

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Ringer AJ, Qureshi AI, Kim SH, Fessler RD, Guterman LR, Hopkins LN. Angioplasty for cerebral vasospasm from eclampsia. *Surg Neurol* 2001;56:373-9.

BACKGROUND

Neurological deterioration in eclampsia is considered to be secondary to cerebral vasospasm. Magnesium sulfate therapy improves symptoms and controls seizures, possibly related to its vasorelaxive effects in spastic arteries. Some cases, however, are refractory to magnesium therapy. To our knowledge, there is no report of angioplasty for vasospasm from eclampsia in the literature.

METHODS

A 27-year-old woman presented 10 days postpartum with severe mental status changes and left arm and bilateral leg weakness that were refractory to magnesium therapy. Cerebral angiography demonstrated diffuse, severe vasospasm. We treated her with angioplasty of the bilateral middle and posterior cerebral arteries, basilar artery, and bilateral internal carotid arteries.

RESULTS

Angioplasty resulted in excellent angiographic improvement. The patient immediately became responsive and appropriate with improved strength in all extremities. She continued to improve throughout her hospital stay and was discharged 10 days postangioplasty.

CONCLUSIONS

Cerebral angioplasty is an effective treatment for vasospasm from eclampsia refractory to magnesium therapy. Angiography should be considered early in the course of neurological deterioration, but delayed therapy may also be effective. © 2001 by Elsevier Science Inc.

KEY WORDS

Pre-eclampsia, eclampsia, vasospasm, stroke, ischemic, treatment, seizures.

Recent evidence has confirmed the presence of severe cerebral vasospasm in eclampsia [10, 11,21,23]. The presence of elevated transcranial Doppler (TCD) ultrasound velocities in women with

eclampsia but not pre-eclampsia as well as the resolution of these elevated velocities with successful treatment of eclampsia suggest a causative effect [8,18,22,23]. The standard treatment for eclampsia includes control of hypertension and i.v. administration of magnesium sulfate. Magnesium sulfate controls seizures in eclamptic women and improves neurological symptoms. This effect may be related to the ability of magnesium to relax spastic cerebral arteries and improve cerebral blood flow [13,17]. Nonetheless, magnesium therapy is not universally effective, and blindness or other neurological deficits may become permanent in eclamptic women.

Cerebral vasospasm from other causes, such as subarachnoid hemorrhage, has been treated in the past with angioplasty. Angioplasty is effective in improving both angiographic narrowing and cerebral blood flow, with durable results [1,3-6,9]. Patients treated early in the course of neurological deterioration from vasospasm are most likely to improve with treatment [19]. Despite the proven efficacy of angioplasty for vasospasm, we have found no report of angioplasty for vasospasm from eclampsia in the literature. We present our experience with one eclamptic patient who deteriorated neurologically from cerebral vasospasm and responded favorably to angioplasty.

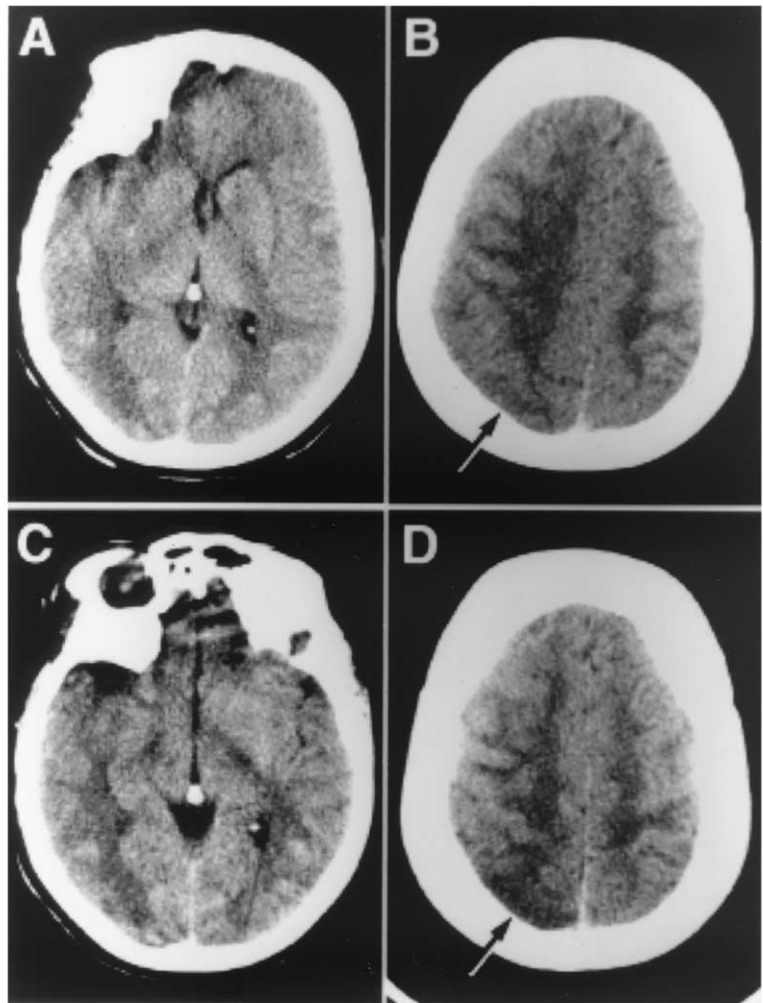
CASE HISTORY

A 27-year-old woman presented to an outside institution with seizures that occurred at home 5 days after a normal spontaneous vaginal delivery of a full-term infant. She had no history of fever, chills, abdominal or leg tenderness, or other signs of infection or deep venous thrombosis. She had complained of episodes of headache and scotoma before presentation. Her medical history was significant for hypertension dur-

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Received January 26, 2001; accepted June 15, 2001.

1 CT performed 3 days (A & B) and 1 day (C & D) before angiography. Sulcal effacement in the occipital and posterior parietal lobes and watershed hypodensity suggest ischemia.



ing the past 2 years. She had been treated with anti-hypertensives but refused to take any medication during her pregnancy for fear of fetal side effects. She was treated for preeclampsia at the time of her delivery and continued to be hypertensive after delivery. When admitted for her postpartum seizures, she was neurologically intact with diffuse hyperreflexia, but no clonus. During her hospital stay, she was treated with magnesium sulfate and antihypertensives and was felt to be medically stable. On the fifth day, just before planned discharge, she became more somnolent and developed left hemiparesis. She was treated with additional infusion of magnesium sulfate, i.v. steroids, and supportive therapy, but her condition gradually deteriorated. On the day that she was transferred to our hospital, she was reportedly unresponsive with a dense left hemiparesis.

Cranial computed tomography (CT) scans obtained 3 days and 1 day before transfer to our institution demonstrated mass effect in the bilateral occipital lobes and watershed hypodensity in the

right posterior temporal lobe (Figure 1). Angiography performed at the referring institution on the day of transfer demonstrated severe, diffuse vasospasm in the entire intracranial posterior circulation, bilateral supraclinoid internal carotid arteries, and bilateral middle and posterior cerebral arteries (Figure 2). Because of her deteriorating clinical condition, she was transferred for consideration of angioplasty.

On arrival at our institution, the patient was awake but did not attempt to speak. She did not track the examiner, answer questions, or follow commands. Her pupils were equal and reactive; her gaze was conjugate; and her face was symmetrical. Other cranial nerves could not be assessed adequately. She demonstrated strong, purposeful movement in her right arm. Her left arm did not move spontaneously but localized briskly to pain. Neither leg moved spontaneously, and she withdrew each leg weakly to painful stimuli. She had significant hypertonicity and hyperreflexia in her legs.



2 Cerebral angiography demonstrating severe vasospasm in the right carotid (A), left carotid (B), and vertebro-basilar (C) distributions.

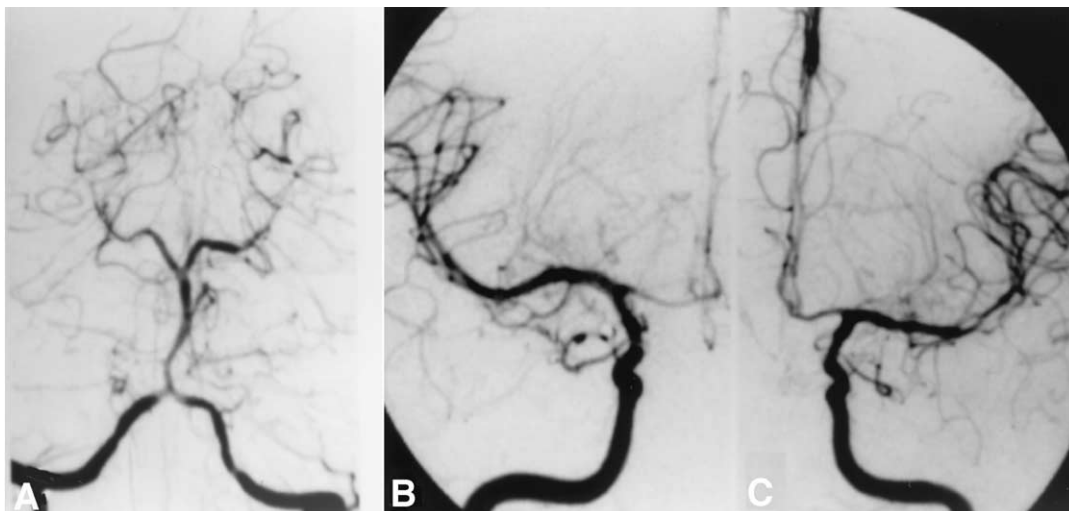
During diagnostic angiography at our institution, the patient's movement could not be adequately controlled and her blood pressure began to fluctuate. We intubated the patient for airway protection and to permit adequate sedation. The remainder of the procedure was performed with continuous fentanyl infusion and a heparin bolus (50 U/kg) to maintain an activated coagulation time within the range of > 250 to 300 seconds. We began endovascular therapy by placing a 6-French guide catheter (Envoy, Cordis Endovascular, Miami, FL) into the distal left vertebral artery (VA). A 2.25 × 10-mm angioplasty balloon (Ninja, Cordis) was advanced over a 0.014-inch guidewire (Transcend, Cordis) into the left posterior cerebral artery. With the guidance of roadmap imaging, we performed multiple manual inflations, withdrawing the balloon after each inflation, to sequentially dilate the P1 segment of the posterior cerebral artery, the basilar artery, and the V4 segment of the left VA. Inflation pressures were not measured, and each inflation was held for approximately 30 seconds. The wire was then advanced into the right posterior cerebral artery, and the P1 segment was treated with the same balloon. After withdrawal into the left VA, the wire was advanced through the vertebrobasilar junction into the contralateral VA; and multiple manual inflations were performed again. Final left vertebral angiography demonstrated excellent restoration of flow in all treated segments with normal distal filling (Figure 3A).

We then entered the right internal carotid artery (ICA) with the guide catheter. The wire and balloon were advanced into the superior division of the right middle cerebral artery (MCA). Using the same angioplasty balloon, we performed multiple manual inflations in the MCA, withdrew the balloon gradually into the supraclinoid segment of the ICA, and

then inflated it manually over the entire distance. Multiple attempts to readvance the balloon into the anterior cerebral artery (ACA) were unsuccessful. Final right ICA angiography demonstrated normal diameters in the ICA and MCA, with moderate residual vasospasm in the right ACA (Figure 3B).

After selectively catheterizing the left ICA, we attempted to advance the same angioplasty balloon into the spastic segment of the supraclinoid ICA. We were unable to negotiate the cavernous segment, despite exchanging the soft Transcend guidewire for a 0.014-inch wire with greater proximal support (Balance lightweight, Guidant, Menlo Park, CA). After exchanging the angioplasty balloon over the Balance guidewire for another of the same type and dimensions, we were able to advance the balloon into the M1 segment of the MCA and perform angioplasty. Once again, we continued to perform manual inflations while withdrawing the balloon into the supraclinoid ICA. Additional attempts to enter the ACA were unsuccessful. Final left ICA angiography showed dramatic improvement in vessel diameter and distal filling (Figure 3C).

Following treatment, the patient was more alert, actively tracking the examiner, and followed commands with her right hand. She remained densely paretic on the left side. She was admitted to our neurological intensive care unit, where we continued treatment with magnesium sulfate and blood pressure control. We permitted hypertension at a moderate level by withholding antihypertensive medications and maintained mild hypervolemia, which was monitored by a central venous catheter. She was successfully extubated 1 day after the intervention, and magnesium therapy was discontinued the next day. Over the next several days, her strength improved in the left arm and she began to speak, answering questions appropriately. At the



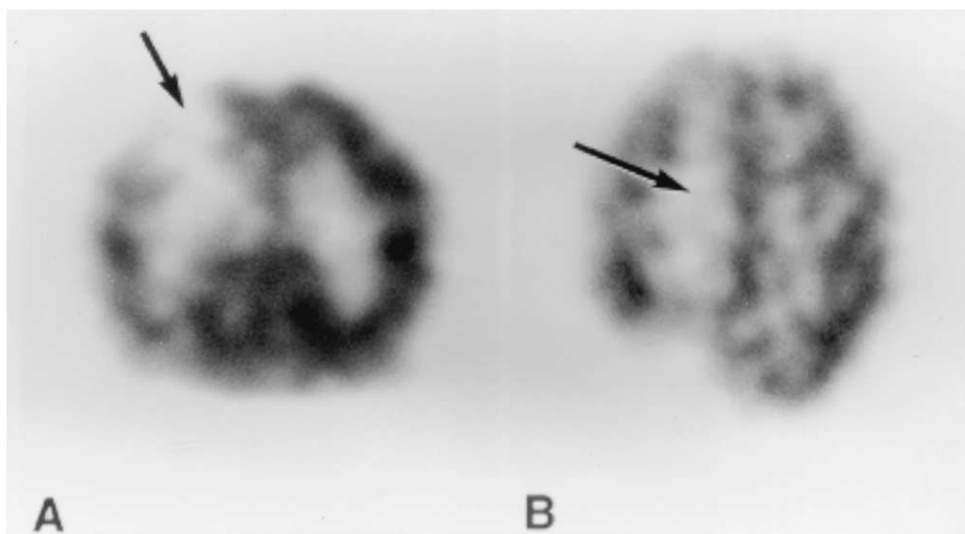
3 (A) Left vertebral angiography after balloon angioplasty performed in both posterior cerebral arteries, the basilar arteries, and the intracranial portions of both VAs. (B) Right internal carotid angiography performed after angioplasty in the MCA and the supraclinoid portion of the ICA. The treated arterial segments are significantly dilated compared to the pretreatment angiogram. (C) Left internal carotid angiography performed after angioplasty in the MCA and the supraclinoid portion of the ICA. The treated arterial segments are significantly dilated compared to the pretreatment angiogram. Residual vasospasm can be seen in both ACAs (B & C).

time of discharge 10 days after angioplasty, she had normal strength in the right leg, antigravity strength in the left arm, and could move her toes and rotate her hip on the left side. We started warfarin therapy for a deep venous thrombosis at the central venous catheter site.

Postoperative imaging included a cranial CT scan and a single-photon emission CT (SPECT) scan to evaluate cerebral perfusion. The CT scan showed

some improvement in the watershed hypodensity with no progression to infarction. The SPECT scan demonstrated mild hypoperfusion in both frontal lobes with essentially normal perfusion in the posterior circulation and both MCA territories (Figure 6).

One month after angioplasty, the patient was improving while an inpatient at a rehabilitation center. She was walking with a cane and performing all



4 SPECT scan performed 1 day after angioplasty for diffuse, severe vasospasm. Axial (A) and coronal (B) images show fixed hypoperfusion in the right ACA-MCA watershed area (arrows) that match CT changes. Perfusion in the remainder of the brain is normal.

activities of daily living independently. Higher cognitive functions have nearly returned to her baseline. Neuropsychological testing has detected a subtle spatial memory deficit but is otherwise normal.

DISCUSSION

Progression from preeclampsia to eclampsia is marked by the development of seizures or other neurological symptoms, including mental status changes and focal deficits. Recent studies suggest that the development of eclampsia is associated with cerebral vasospasm. Trommer et al first reported angiographic evidence of vasospasm in an eclamptic patient [21]. Williams and McLean subsequently described TCD evidence of vasospasm with elevated mean flow velocities [23]. Qureshi et al demonstrated that TCD velocities are significantly higher in eclamptic women with neurological symptoms than in normotensive pregnant women [18]. Pre-eclamptic women, however, have TCD velocities similar to normotensive pregnant women [18].

The etiology of vasospasm in eclampsia is unclear. Circulating vasoactive factors, such as angiotensin-II and endothelin-1, have been reported to produce arterial narrowing and seizures similar to eclampsia and have been suggested as possible causes [7,13]. In addition, endothelial cell dysfunction leads to decreased production of vasorelaxing factors prostaglandin I₂ and prostaglandin E₂ in preeclampsia [24, 25]. Other theories include hypercalcemia [12] and autoregulatory vasoconstriction in response to hypertension as seen in animals and humans [2,15]. Despite an apparently different pathophysiology than for vasospasm after subarachnoid hemorrhage, the end result is similar: a spastic, narrowed artery with restriction of blood flow resulting in regional cerebral ischemia. Accordingly, the results after angioplasty for the two entities may be similar.

The diagnosis of cerebral vasospasm in eclampsia can be made with a variety of imaging techniques. As mentioned previously, angiography and TCD may provide evidence of vasospasm during the course of eclampsia. In addition, magnetic resonance angiography may demonstrate both arterial narrowing consistent with vasospasm and resolution of vasospasm [10,11]. Qualitative blood flow measurement, such as is provided by SPECT, may provide evidence of hypoperfusion from vasospasm. In the largest series to date documenting evidence of vasospasm in eclampsia, Naidu et al prospectively evaluated 65 eclamptic women with

CT, TCD, and/or SPECT [16]. They found CT abnormalities in 58.5% of eclamptic women studied, 97.4% of these involving the parietooccipital regions known to be most sensitive to changes with eclampsia. Among those patients evaluated with TCD, elevated velocities were documented in 85.7%, whereas SPECT abnormalities were found in the watershed zones of all eclamptic women, involving the parietooccipital regions in 75%. Although each modality provided unique information, SPECT was felt to be the most sensitive diagnostic tool for obtaining evidence of symptomatic vasospasm in eclampsia.

The cornerstone of treatment for eclampsia has been magnesium sulfate therapy. In a prospective, randomized trial, magnesium sulfate therapy was superior to phenytoin for the treatment of eclamptic seizures [14]. Further evidence suggests that the mechanism for this action is through improvement in cerebral perfusion after administration of a loading dose of magnesium sulfate, a phenomenon not demonstrated after a loading dose of phenytoin in another prospective trial [17]. Magnesium sulfate may improve cerebral perfusion by opposing calcium-dependent arterial constriction, thereby relieving vasospasm [20]. Still, some cases of eclampsia are refractory to treatment with magnesium, as in the case we present. In these cases, additional treatment options must be considered.

Angioplasty has been proposed as the treatment of choice for symptomatic vasospasm secondary to subarachnoid hemorrhage refractory to hyperdynamic therapy [5]. Cerebral blood flow improves after angioplasty for vasospasm with durable results [4]. To our knowledge, no report of angioplasty for vasospasm in eclampsia has been reported. Given the clinical similarities between symptomatic vasospasm from subarachnoid hemorrhage and eclampsia, one might expect a similar benefit from angioplasty in the two conditions. In our case, the patient improved rapidly and dramatically. Furthermore, given the finding that magnesium sulfate improves intracerebral flow dynamics, as measured by TCD, after the initial loading dose [17], failure to improve after magnesium loading may be sufficient indication to pursue cerebral angiography with consideration of angioplasty. This is consistent with the finding that angioplasty for vasospasm secondary to subarachnoid hemorrhage is most effective if performed within 3 hours of symptom onset [18]. Delayed angioplasty should not be ruled out, however, as our patient was treated several days after deteriorating with favorable results.

We conclude that intracranial angioplasty is an effective method of treatment for severe eclampsia

refractory to magnesium therapy. Pregnant and postpartum women with severe hypertension and neurological deterioration should be rapidly given an initial loading dose of magnesium sulfate. Baseline evaluation with TCD or magnetic resonance angiography should be considered to monitor therapy. Failure to respond clinically to magnesium therapy is an indication to consider angiography and angioplasty. Angioplasty should be considered early, possibly after administering a loading dose of magnesium sulfate if no improvement is noted, but delayed therapy may also be effective.

The authors thank Paul H. Dressel for preparation of the illustrations. This department receives research support from Cordis Endovascular and Guidant Corporation.

REFERENCES

- Bracard S, Picard L, Marchal JC, Ducrocq X, Per A, Czorny A, Islak C, Roy D, Roland J, Lepoivre J. Role of angioplasty in the treatment of symptomatic vascular spasm occurring in the post-operative course of intracranial ruptured aneurysms. *J Neuroradiol* 1990; 17:6-19.
- Byrom F. The calibre of the cerebral arteries in experimental hypertension. *Proc R Soc Med* 1968;61: 605-6.
- Coyne TJ, Montanera WJ, Macdonald RL, Wallace MC. Percutaneous transluminal angioplasty for cerebral vasospasm after subarachnoid hemorrhage. *Can J Surg* 1994;37:391-6.
- Elliott JP, Newell DW, Lam DJ, Eskridge JM, Douville CM, Le Roux PD, Lewis DH, Mayberg MR, Grady MS, Winn HR. Comparison of balloon angioplasty and papaverine infusion for the treatment of vasospasm following aneurysmal subarachnoid hemorrhage. *J Neurosurg* 1998;88:277-84.
- Eskridge JM, McAuliffe W, Song JK, Deliganis AV, Newell DW, Lewis DH, Mayberg MR, Winn HR. Balloon angioplasty for the treatment of vasospasm: results of first 50 cases. *Neurosurgery* 1998;42:510-6.
- Firlik AD, Kaufmann AM, Jungreis CA, Yonas H. Effect of transluminal angioplasty on cerebral blood flow in the management of symptomatic vasospasm following aneurysmal subarachnoid hemorrhage. *J Neurosurg* 1997;86:830-9.
- Halim A, Kanayama N, el Maradny E, Maehara K, Shimoyama I, Sumimoto K, Terao T. Eclampsia-like seizures and electroencephalographic changes in pregnant rabbits with endothelin-1 injections. *Gynecol Obstet Invest* 1995;39:1-7.
- Hansen WF, Burnham SJ, Svendsen TO, Katz VL, Thorp JM Jr, Hansen AR. Transcranial Doppler findings of cerebral vasospasm in preeclampsia. *J Matern Fetal Med* 1996;5:194-200.
- Higashida RT, Halbach VV, Cahan LD, Brant-Zawadzki M, Barnwell S, Dowd C, Hieshima GB. Transluminal angioplasty for treatment of intracranial arterial vasospasm. *J Neurosurg* 1989;71:648-53.
- Ito T, Sakai T, Inagawa S, Utsu M, Bun T. MR angiography of cerebral vasospasm in preeclampsia. *AJNR Am J Neuroradiol* 1995;16:1344-6.
- Kanayama N, Nakajima A, Maehara K, Halim A, Kajiwara Y, Isoda H, Masui T, Terao T. Magnetic resonance imaging angiography in a case of eclampsia. *Gynecol Obstet Invest* 1993;36:56-8.
- Kaplan PW. Reversible hypercalcemic cerebral vasoconstriction with seizures and blindness: a paradigm for eclampsia? *Clin Electroencephalogr* 1998;29: 120-3.
- Kemp PA, Gardiner SM, Bennett T, Rubin PC. Magnesium sulphate reverses the carotid vasoconstriction caused by endothelin-1, angiotensin II and neuropeptide-Y, but not that caused by NG-nitro-L-arginine methyl ester, in conscious rats. *Clin Sci (Colch)* 1993;85:175-81.
- Lucas MJ, Leveno KJ, Cunningham FG. A comparison of magnesium sulphate with phenytoin for the prevention of eclampsia. *N Engl J Med* 1995;333:201-5.
- MacKenzie ET, Strandgaard S, Graham DI, Jones JV, Harper AM, Farrar JK. Effects of acutely induced hypertension in cats on pial arteriolar caliber, local cerebral blood flow, and the blood-brain barrier. *Circ Res* 1976;39:33-41.
- Naidu K, Moodley J, Corr P, Hoffmann M. Single photon emission and cerebral computerised tomographic scan and transcranial Doppler sonographic findings in eclampsia. *Br J Obstet Gynaecol* 1997;104: 1165-72.
- Naidu S, Payne AJ, Moodley J, Hoffmann M, Gouws E. Randomised study assessing the effect of phenytoin and magnesium sulphate on maternal cerebral circulation in eclampsia using transcranial Doppler ultrasound. *Brit J Obstet Gynaecol* 1996;103:111-6.
- Qureshi AI, Frankel MR, Ottenlips JR, Stern BJ. Cerebral hemodynamics in preeclampsia and eclampsia. *Arch Neurol* 1996;53:1226-31.
- Rosenwasser RH, Armonda RA, Thomas JE, Benitez RP, Gannon PM, Harrop J. Therapeutic modalities for the management of cerebral vasospasm: timing of endovascular options. *Neurosurgery* 1999;44:975-9.
- Sadeh M. Action of magnesium sulfate in the treatment of preeclampsia-eclampsia. *Stroke* 1989;20: 1273-5.
- Trommer BL, Homer D, Mikhael MA. Cerebral vasospasm and eclampsia. *Stroke* 1988;19:326-9.
- Vliegen JH, Muskens E, Keunen RW, Smith SJ, Godfried WH, Gerretsen G. Abnormal cerebral hemodynamics in pregnancy-related hypertensive encephalopathy. *Eur J Obstet Gynecol Reprod Biol* 1993;49: 198-200.
- Williams K, McLean C. Maternal cerebral vasospasm in eclampsia assessed by transcranial Doppler. *Am J Perinatol* 1993;10:243-4.
- Zahradnik H, Schafer W, Wetzka B, Beckwoldt M. Hypertensive disorders in pregnancy: the role of eicosanoids. *Eicosanoids* 1991;4:123-36.
- Zammit VC, Whitworth JA, Brown MA. Endothelium-derived prostacyclin: effect of serum from women with normal and hypertensive pregnancy. *Clin Sci (Colch)* 1992;82:383-8.

COMMENTARY

This is an extremely important case report of severe symptomatic vasospasm associated with