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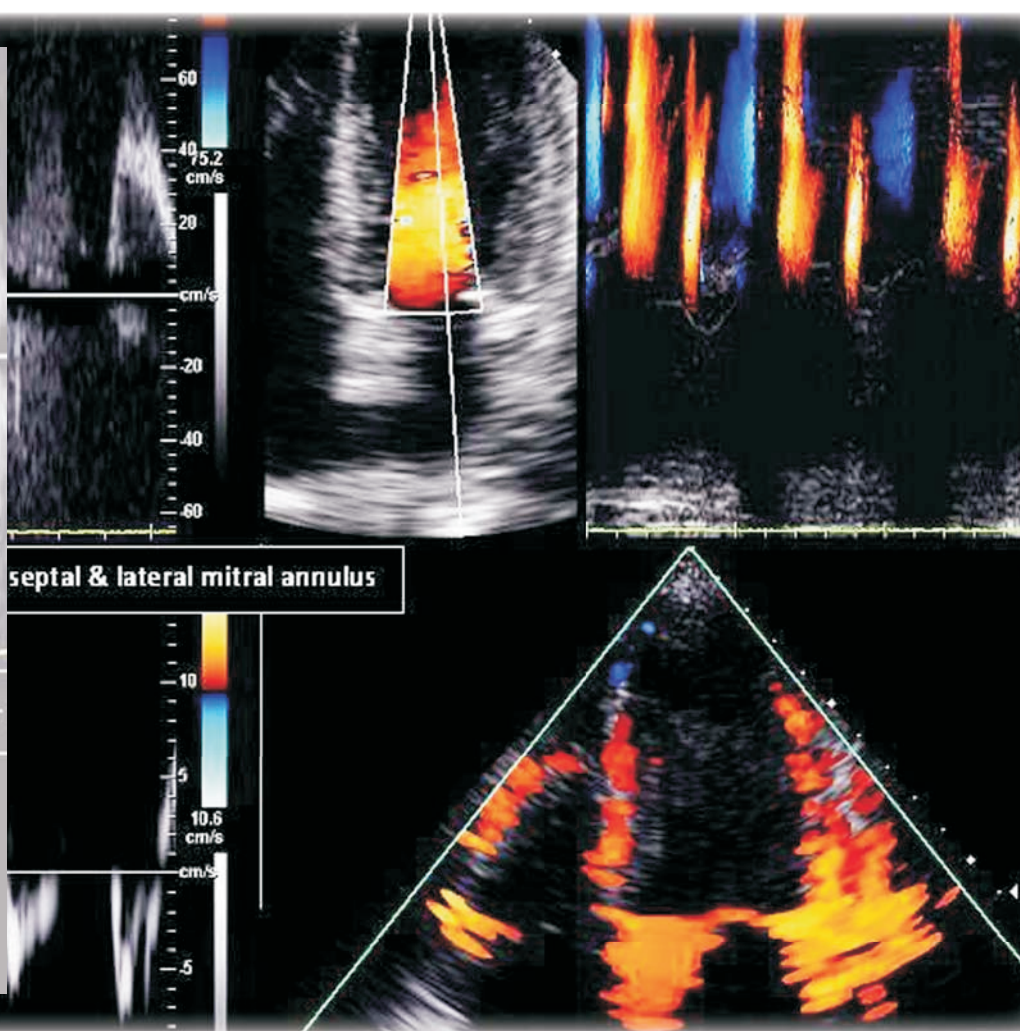
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Manuscript

A Fatal Case of Postpartum Cerebral Angiopathy with Concurrent Cardiomyopathy

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ABSTRACT

Reversible Cerebral Vasoconstriction Syndrome (RCVS) is a rare postpartum angiopathic syndrome which can cause ischemic or hemorrhagic stroke. Peripartum cardiomyopathy (PPCM) is a non-ischemic cardiomyopathy that also occurs postpartum. Here we report a case with concurrent of RCVS and PPCM. 32 years old female presented with worsening headache since her vaginal delivery six days ago. For a sudden onset left hemiplegia CT head showed a large right basal ganglia intracerebral hemorrhage causing midline shift leading to craniotomy. Cerebral angiogram done the next day showed diffuse intracranial vasoconstriction suggestive of RCVS and this persisted on angiogram a week later. Initial echocardiogram was normal with an ejection fraction (EF) of 60-65% that reduced to 15-20% a week later. Postpartum day 10 she had fixed, dilated pupils. CT brain showed tonsillar herniation with apnea test confirming brain death. This case is the first one to show the unique combination of two conditions, PPCM and RCVS and sheds more light into perhaps common pathophysiologic mechanisms.

Key words: Postpartum Cerebral Angiopathy, Reversible Cerebral Vasoconstriction Syndrome, Peripartum cardiomyopathy, Subarachnoid hemorrhage.

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INTRODUCTION

Postpartum Cerebral Angiopathy (PCA) or Reversible Cerebral Vasoconstriction Syndrome (RCVS) is a rare but important postpartum syndrome characterized by severe headaches and vision abnormalities with complications including seizures, subarachnoid or parenchymal hemorrhage, ischemic stroke often presenting with neurological deficits. Usually complete recovery is expected within a few weeks however if there are ischemic or hemorrhagic manifestations and accompanying neurological deficits the prognosis can be grim.¹ The exact pathophysiologic mechanism and accordingly precise treatment options still need to be better understood.

Peripartum cardiomyopathy (PPCM) is also a known non-ischemic cardiomyopathy with left ventricular systolic dysfunction occurring mostly in the immediate postpartum period in the absence of another identifiable cause of heart failure where left ventricular dilatation is not necessary.² This is a unique postpartum case with the fatal combination of RCVS and PPCM that has rarely been reported in literature and sheds more light into perhaps common pathophysiologic mechanisms that the two entities might share.

CASE REPORT

32 years old Hispanic female with no past medical history presented with worsening headache since epidural anesthesia used for her uneventful spontaneous vaginal delivery six days ago which was not improving with over the counter medications. Initial examination was unrevealing, however, while in ED she suddenly developed left hemiplegia, dilated left pupil, altered sensorium and agonal breathing requiring endotracheal intubation. An immediate CT head showed large right basal ganglia intracerebral hemorrhage with intraventricular extension causing 10 mm right to left midline shift and downward herniation. An emergent frontotemporal craniotomy and evacuation of hemorrhage with drainage placement was done and patient remained intubated in ICU.

A cerebral angiogram done the next day showed diffuse vasoconstriction including the right and left MCA, ACA and vertebral arteries responding to intra-arterial verapamil suggestive of RCVS or vasculitis. (Figure 2A) An echocardiogram was completely normal with ejection fraction (EF) of 60-65%. MRI brain was also done to where other than edema around the craniotomy site there was no other area of restricted diffusion to suggest ischemia. Patient was initially started on nimodipine and then nicardipine drip which was continued for a week however, thereafter her blood pressure dropped below mean arterial pressure (MAP) of 60 and vasodilators had to be stopped. Norepinephrine as a vasopressor had to be started to maintain hemodynamic status that barely maintained her MAP in 70s and she remained difficult to wean off both vasopressors and the ventilator. Throughout this hemodynamic imbalance she was never tachycardic with average heart rate between 80 to 90. ANA, rheumatoid factor, CCP antibody and ANCA that were checked for vasculitis workup came out negative. Follow up repeat angiography after a week showed persistent diffuse vasospasm in the same distribution and intra arterial verapamil was again administered. (Figure 2B) A close follow up repeat angiography and verapamil administration was done the next day that showed improvement in the vasospasm compared to the day before. Subsequent echocardiogram, ten days later from the first one, done for lung congestion and hypotension showed dilated left and right ventricles with global impairment in systolic function leading to an EF of 15-20%. (Figure 1) Serial EKGs were also done and compared to ones on admission but there were no ST or T wave changes to suggest ischemia. The following day there was a change in her neurological status where she lost all brain and brainstem reflexes including no ocular calorics or oculocephalic reflexes, pupils fixed and dilated and was unresponsive despite all sedation being suspended. CT brain showed global edema and a later CTV demonstrated downward transtentorial herniation with concomitant findings of progressive tonsillar herniation and sulcal effacement. Also there was no contrast opacification of the distal left cervical and

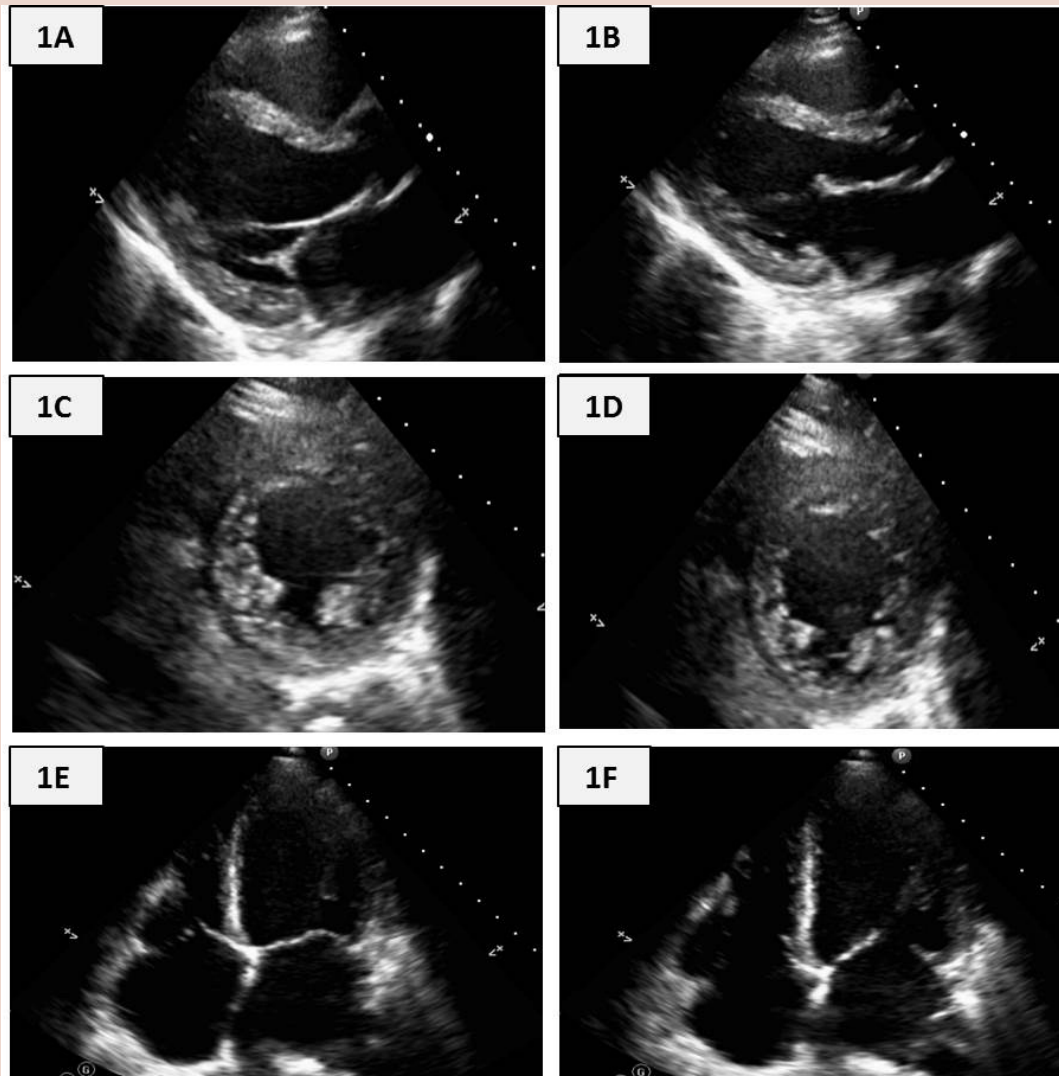


Figure 1: Echocardiogram with reduced systolic function (EF 15–20%): Parasternal long axis view of end systolic **1A** and end diastolic **1B**; Short axis view of end systolic **1C** and end diastolic **1D**; 4 chambers view of end systolic **1E** and end diastolic **1F**.

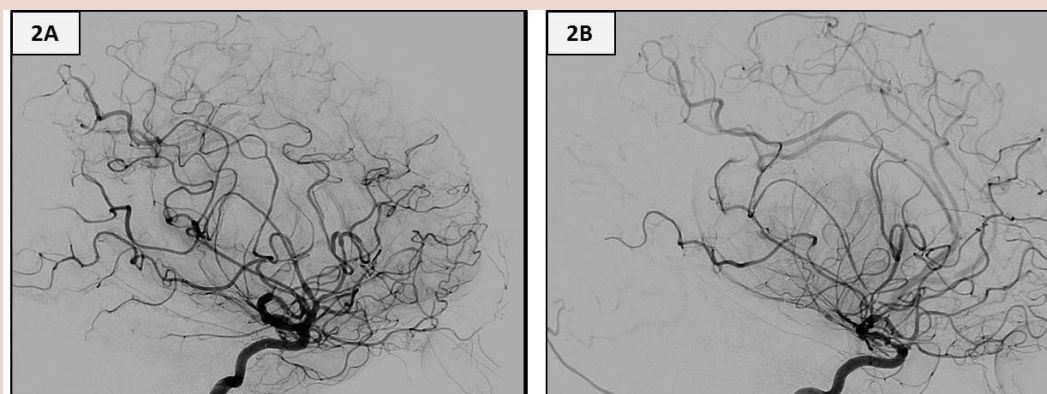


Figure 2: Cerebral angiogram. **2A**, Initial cerebral angiogram with diffuse vasospasm; **2B**, Subsequent cerebral angiogram with persistent vasospasm.

intracranial ICA. ICP was measured at 10 mmHg for which mannitol was given without any improvement. Nuclear medicine SPECT and apnea test were then done which were consistent with the diagnosis of brain death.

DISCUSSION

The pathophysiologic mechanism of RCVS is considered to consist of altered cerebral autoregulation in response to endothelial injury, which impairs the sympathetic perivascular network located in cerebral arterial adventitia and usually resolves in 3 months.¹ It is thought that the postpartum period is a trigger for RCVS due to the levels of antiangiogenic and proangiogenic factors, including growth factors that have been correlated with eclampsia such as placental growth factor (PIGF). There may also be a role for the soluble PIGF receptor.³ The diagnosis can be confirmed by cerebral angiography which shows multifocal segmental arterial constrictive lesions. However MRI, CTA and transcranial Doppler are other modalities that can be utilized. Contrast enhanced MRI shows continuous thickening with moderate degrees of contrast enhancement throughout the arterial wall unlike dense, eccentric wall enhancement seen with vasculitis.^{1,4} As the name suggests RCVS is usually reversible with complete recovery in 3 months or so after close monitoring of patients however patients with intracranial hemorrhage compared to ischemia have shown to have worse outcomes including residual neurological or cardiologic deficits and maternal death.^{5,7} On the other hand PPCM is thought to be caused by angiogenic imbalance, genetic, inflammatory, hormonal, hemodynamic and autoimmune factors. Of these pre-eclampsia, eclampsia were thought to be important predisposing factors but were lacking in our patient.¹⁰ Given the rapid decline of EF from normal to 15–20% within ten days in the immediate postpartum period and in the absence of any other identifiable cause confirms the diagnosis of PPCM.

Although there has been a reported case of takotsubo cardiomyopathy with RCVS, this case is the first one to show the unique combination of two rare conditions, peripartum cardiomyopathy and RCVS.⁵ Despite that increased body stress response such as even stroke was thought to associate takotsubo cardiomyopathy with RCVS, this does not entirely hold true for this case.^{5,6} Takotsubo cardiomyopathy usually presents as ST elevation on EKG with characteristic apical ballooning on echocardiogram, these findings were not present in our patient. This might just be an association but it does shed light into a possible causation and further case reports are needed to prove common underlying pathophysiologic mechanisms between these two cardiovascular conditions. Possible common mechanism is likely angiogenic imbalance; both RCVS and PPCM have been seen to be contributed by placental

angiogenic regulators like PIGF in RCVS and soluble fms-like tryptophan kinase (sFlt1) a VEGF inhibitor in PPCM.^{10–13} Mice studies have shown that mice that lack PFC-1a, a regulator or pro-angiogenic factor like VEGF, develop severe PPCM.^{10–13} Also it is important to acknowledge that this is likely PPCM and not stroke associated cardiomyopathy because of the fact that the mechanism of this stroke was due to angiopathy and that the hemorrhage was drained by craniotomy immediately after the occurrence thereby reducing the stress response burden on the cardiovascular system. Due to the risk of recurrence of RCVS and concomitant likelihood of postpartum cardiomyopathy it is important that patients are counseled and monitored accordingly.^{5,8} It is likely that a combination of diffuse persistent cerebral vasospasm accompanied by poor cardiac function necessary to maintain cerebral perfusion culminated in eventual brain death of this otherwise healthy, postpartum patient.

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