

Simultaneous cerebral venous and arterial involvement in the postpartum period: Rare presentation of antiphospholipid syndrome

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Abstract

Reversible cerebral vasoconstriction syndrome (RCVS) and cerebral venous sinus thrombosis (CVST) are two causes of postpartum neurological complications and occurrence of concomitant RCVS and CVST is a rarity. Here, we report a rare case of postpartum stroke caused by concomitant RCVS and CVT triggered by catastrophic antiphospholipid syndrome. Our patient presented with postpartum seizure followed by prolonged unconsciousness with no prior history of headache. Her initial neuroimaging revealed extensive hemorrhagic infarcts involving brain, brainstem and cerebellum. Magnetic resonance angiography and venography revealed constriction of all large vessels of Circle of Willis with filling defects in superior sagittal sinus, junction of bilateral transverse and sigmoid sinus and complete non-visualization of left transverse sinus. Workup for vasculitis was negative but detailed evaluation of prothrombotic state was significant for presence of high titer of lupus anti-coagulant antibody and anti beta-2 glycoprotein antibody which continued to remain high at 3 months follow up. Patient was treated with intravenous methylprednisolone, heparin, nimodipine infusion and anticonvulsants. After 1 month, patient improved remarkably with radiological resolution of parenchymal lesions, arterial narrowing and filling defects of cerebral venous sinuses. Anti-phospholipid syndrome can trigger systemic prothrombotic state which involves both arterial and venous system; risk is even higher in peripartum period due to fluctuating estrogen levels. Even in cases with extensive central nervous system involvement like our patient, considerable recovery is possible with aggressive medical management.

INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) is an under-recognized but serious condition characterized by recurrent thunderclap headache, often associated with other neuro-deficit, and constriction of two or more large cerebral arteries, that resolve within 12 weeks. Though exact pathophysiological mechanisms are unclear, few triggers of RCVS are identified, pregnancy being one of them. Cerebral venous sinus thrombosis (CVST) is an infrequent disorder with wide clinical spectrum of clinical manifestation; headache and seizure being the commoner. Presence of concomitant RCVS and CVST is a rare, mostly found in association with pregnancy and ovarian tumour resection.^{1,2} We report here a patient who had catastrophic antiphospholipid syndrome (APS) resulting in

concomitant RCVS and CVST. Fortunately she recovered significantly with medical management and intensive care.

CASE REPORT

A 22-year-lady developed one episode of generalized tonic clonic convulsion of 15 mins duration after 24 hours of child birth by caesarean section and following that she became unconscious. There was no prior history of headache. She was admitted in our intensive care unit in comatose state after 2 days of seizure. She was intubated and remained unconscious for 8 days. Following improvement of consciousness, we documented complete left hemiparesis, anarthria and left third nerve palsy that involved the pupil. At presentation, her blood pressure was normal. She had no constitutional symptoms or

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history of foetal loss. Considering the catastrophic nature of the event our differentials were eclampsia and posterior reversible encephalopathy syndrome (PRES), CVST, RCVS and subarachnoid haemorrhage. We proceeded with neuroimaging. Computed Tomography (CT) and Magnetic Resonance (MR) imaging of brain were suggestive of ischemic and haemorrhagic lesions in all lobes, brainstem and cerebellum (Figure 1). Considering the multifocal pattern of the lesion we made the differential diagnosis of CVST, acute haemorrhagic leukoencephalopathy, catastrophic antiphospholipid syndrome (APS) and HELLP syndrome (Haemolysis, Elevated liver enzymes and Low platelet count) and its complications. MR angiography and venography revealed dual pathology in the form of irregular narrowing of all major intracranial arteries without any major vessel occlusion; and filling defects in superior

sagittal sinus along with right and left transverse-sigmoid junction. Her routine investigations including complete blood count, blood urea, liver function test, serum creatinine, electrolytes, chest X-ray, urinalysis were unremarkable. The cerebrospinal fluid (CSF) study was non-contributory. Workup for her prothrombotic state revealed elevated lupus anti-coagulant antibody and anti beta-2 glycoprotein antibody and it continued to remain high at 3 months follow up.

The patient was treated with intravenous methylprednisolone, low molecular unit heparin, nimodipine infusion and anticonvulsants. After her initial recovery we initiated vitamin K antagonist and achieved an INR of 2.3. Patient recovered significantly with medical management. She could walk on her own and did the basic activities of daily living with the mRS of 2. However, there was residual third nerve palsy. Subsequent

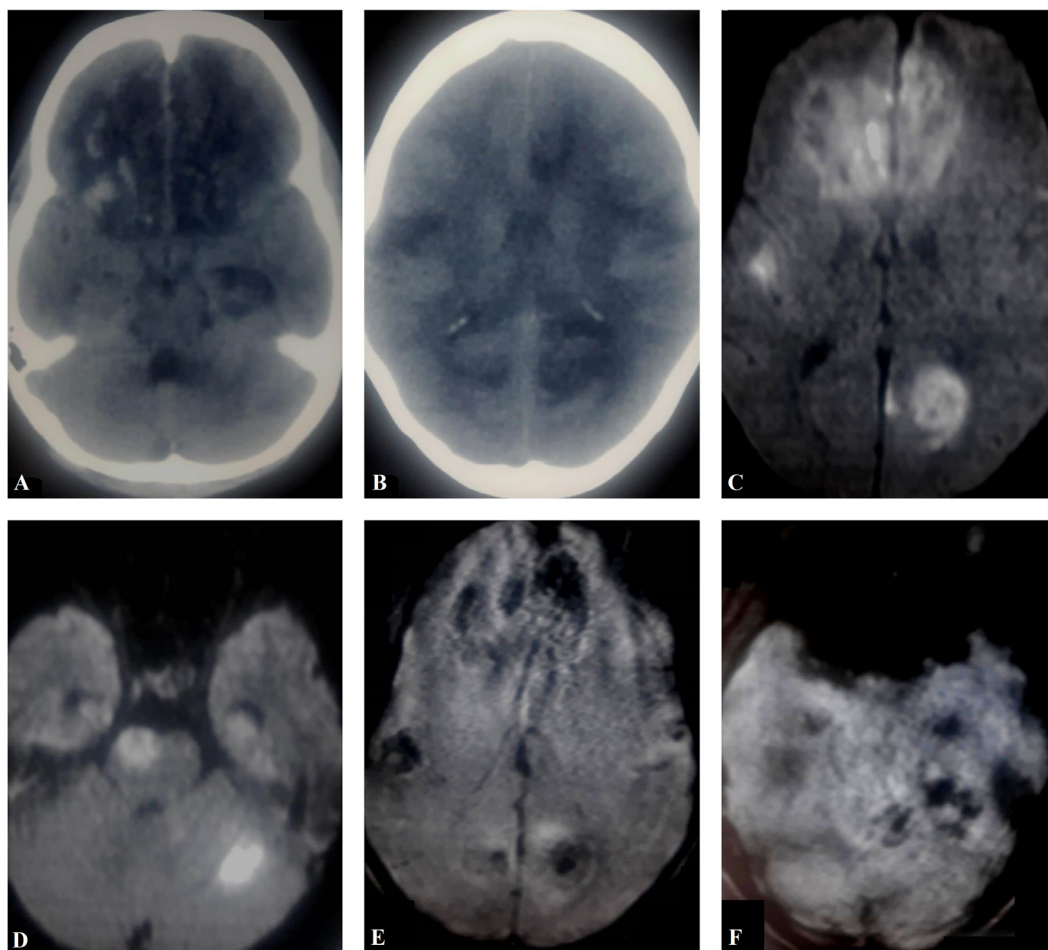


Figure 1. Computed tomography scan of brain showing bilateral frontal lobe haemorrhagic lesions, more on right side and subcortical white matter lesions (A & B). Magnetic resonance diffusion weighted imaging showing bilateral lobar, brainstem and cerebellar infarct (C & D). Susceptibility weighted imaging showing multiple supra and infratentorial bleeds (E & F)

imaging showed decrease in parenchymal lesions (Figure 2) and angiographic improvement of both her RCVS and CVST (Figure 3,4). Patient was discharged on vitamin K antagonist and flunarizine.

DISCUSSION

The combination of RCVS and CVST is a rare entity. In our search of literature, there were only few case reports of concomitant RCVS and CVST which is listed in Table 1 including our case.

Common conditions leading to both venous and arterial thrombosis are APS, pregnancy, hyper-homocysteinemia, cancer, certain infective pathologies and hormonal treatment.⁶ APS is a hypercoagulable state with tendency to develop both arterial and venous thrombosis. Pathophysiology of CNS manifestations include endothelial dysfunction, blood brain barrier disruption, increased entry of pro-inflammatory markers into the brain parenchyma, impairment of Gamma aminobutyric acid (GABA) receptor activity.⁷⁻¹⁰ The pathophysiology of enhanced thrombosis is complex and it involves endothelium, platelets, complement and innate

immune systems.¹¹ Raynaud's phenomenon in brain and other body parts is a result of inhibition of endothelial nitric oxide synthase (eNOS) which decreases nitric oxide production by endothelium which in turn leads to defective regulation of vascular tone and cell adhesion.¹²

Pregnancy is a state with very high estrogen level which increases the risk of hypercoagulability and in turn CVST. After child-birth estrogen rapidly declines and returns to almost pre-pregnancy level and thereby leads to widespread vasoconstriction which may act as a trigger to RCVS. The same phenomenon is also seen after ovarian tumor resection.^{5,13,14} In our patient, we believe that in the presence of a significant hypercoagulable milieu due to dual insult of APS and pregnancy, it resulted in the infarction of both the arterial and venous system, the RCVS and CVST. The known association of APS and Raynaud's phenomenon¹⁵ also give support to APS's effect on the arterial system. In addition, our patient had a good recovery with intensive medical management. She is advised to take warfarin lifelong as treatment of APS. To our delight her child is developing normally till date.

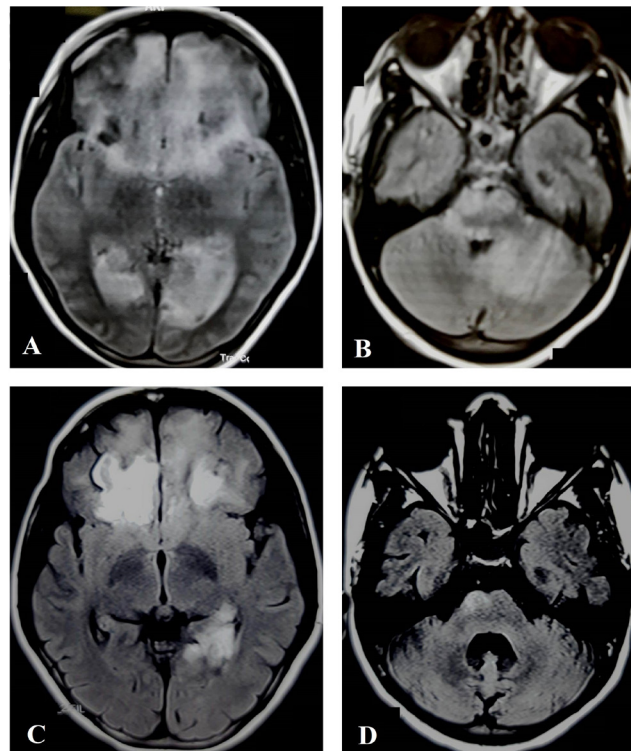


Figure 2. 1.5 T magnetic resonance imaging FLAIR sequence showing bilateral cortical, brainstem and cerebellar fluffy hyperintensities (A & B) and significant reduction of lesions on subsequent 3 T magnetic resonance imaging FLAIR sequence (C & D)

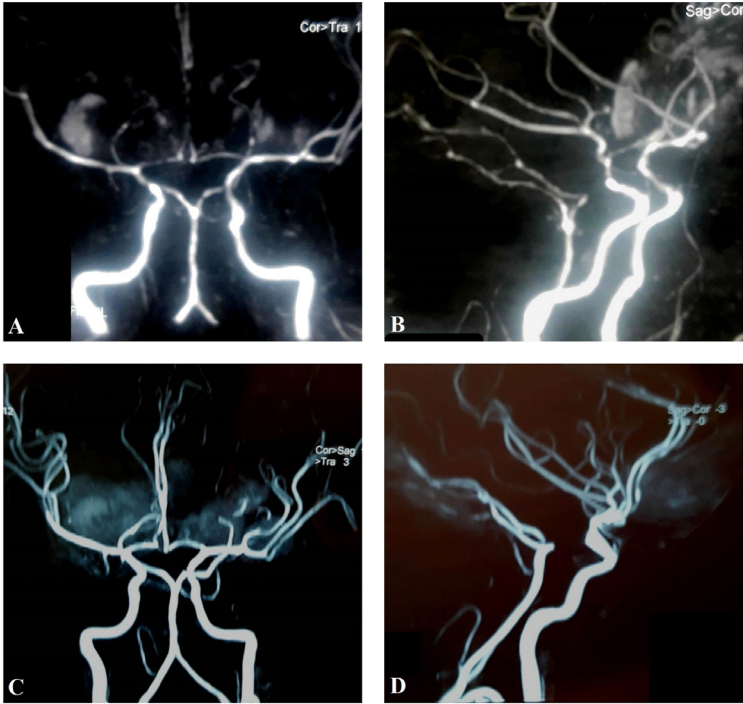


Figure 3. 1.5 T magnetic imaging time of flight arteriography sequence showing bilateral anterior, middle and posterior cerebral artery narrowing (A & B) and significant improvement on subsequent 3 T magnetic resonance time of flight arteriography sequence (C & D)

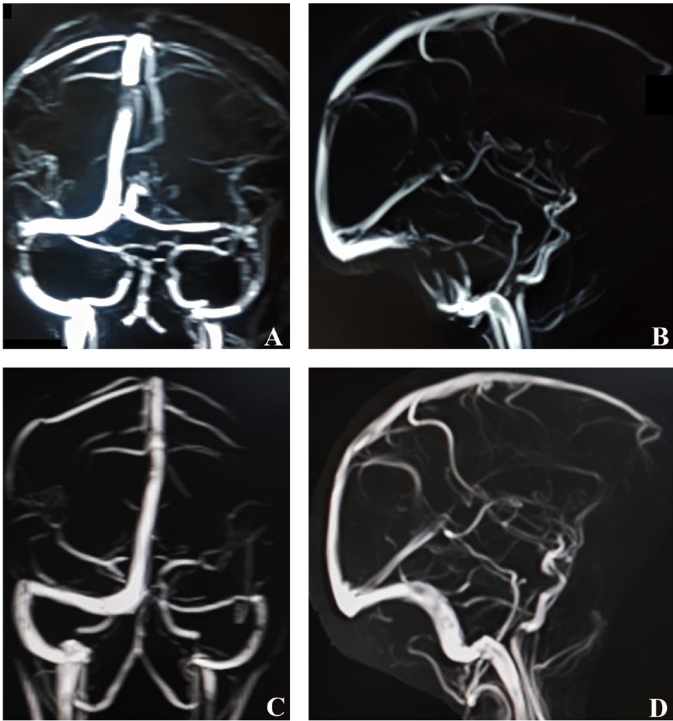


Figure 4. 3 T magnetic imaging contrast venography sequence showing superior sagittal sinus and bilateral transverse and sigmoid sinus filling defects (A & B) and significant improvement on subsequent 3 T magnetic resonance contrast venography sequence (C & D)

Table 1: Reported cases of concomitant reversible cerebral vasoconstriction syndrome and cerebral venous sinus thrombosis

Author, Year	Age/Sex	Presentation	Risk factor	Affected veins	Affected arteries	Related condition	Therapy	Improvement in modified Rankin Scale
Katzin <i>et al.</i> 2007 ¹	37/F	Headache and vomiting	Pregnancy	Vein of Trolard	Anterior Cerebral Artery, Middle Cerebral Artery, Posterior Cerebral Artery	Infarction	Warfarin	1
Markus <i>et al.</i> 2011 ³	38/F	Headache	Pregnancy	Superior Sagittal Sinus, Transverse Sinus, Sigmoid Sinus	Posterior Cerebral Artery	None	Nimodipine, magnesium, statin, and warfarin	1
Bourvis <i>et al.</i> 2016 ⁴	24/F	Headache and vomiting	Pregnancy	Transverse Sinus, Sigmoid Sinus	Middle Cerebral Artery, Posterior Cerebral Artery	Infarction and Subarachnoid Haemorrhage	Nimodipine and warfarin	2
Lahiri <i>et al.</i> 2018 ⁵	24/F	Headache, seizure		Superior Sagittal Sinus, Transverse Sinus	Middle Cerebral Artery	Parenchymal bleed with intraventricular extension	Nimodipine and enoxaparin	1
Shimi <i>et al.</i> 2020 ²	42/F	Headache	Ovarian tumor resection, anemia	Transverse Sinus, Sigmoid Sinus	Posterior Cerebral Artery	SAH	Nimodipine and edoxaban	2
Same	39/F	Headache	Ovarian tumor resection,	Superior Sagittal Sinus	Anterior Cerebral Artery	None	Nimodipine and edoxaban	1
Present Case	22/F	Headache, seizure, hemiparesis, cranial nerve palsy, prolonged unconsciousness	Pregnancy	Superior Sagittal Sinus, Transverse Sinus, Sigmoid Sinus	Anterior Cerebral Artery, Middle Cerebral Artery, Posterior Cerebral Artery	Infarction and parenchymal haemorrhage	Nimodipine, magnesium, enoxaparin, warfarin, flunarizine	3

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