



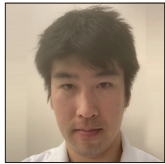
Case Report

Reversible cerebral vasoconstriction syndrome concomitant with cerebral venous sinus thrombosis following ovarian tumor resection: A report of two cases

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ABSTRACT

Background: Reversible cerebral vasoconstriction syndrome (RCVS) presents with characteristic clinical, brain imaging, and angiographic findings. The most common clinical feature of RCVS is a severe acute headache, which is often referred to as a thunderclap headache due to the nature of its presentation. It may occur spontaneously or may be provoked by various precipitating factors. We present a rare case of RCVS concomitant with cerebral venous sinus thrombosis (CVST) in a woman who underwent resection of an ovarian tumor.

Case Description: Case 1 – A 42-year-old woman was admitted to our hospital with severe headache radiating to the neck, with associated vomiting. She revealed a medical history of ovarian cancer and underwent an operation for the resection of the tumor, a month before presentation. After resection, her estradiol (E2) levels were reduced from 288 pg/ml to 31 pg/ml (normal range, 0–49 pg/ml). Initial imaging on admission to our hospital revealed the left posterior convexity subarachnoid hemorrhage. Magnetic resonance angiography (MRA) showed findings consistent with RCVS affecting the left posterior cerebral artery. Magnetic resonance venography (MRV) showed CVST of the left transverse and sigmoid sinuses. Single-photon emission computed tomography (SPECT) showed a left posterior ischemic lesion. These findings improved following treatment with nimodipine and anticoagulant. Case 2 – A 39-year-old woman presented with holocranial headache associated with vomiting. She was diagnosed with an ovarian tumor. She underwent an operation 3 months before presentation. After tumor resection, her E2 level decrease from 193 pg/ml to 19 pg/ml (normal range, 0–49 pg/ml). Magnetic resonance angiography (MRA) confirmed the presence of a vasospasm involving the right anterior cerebral artery. Magnetic resonance venography (MRV) confirmed the presence of thrombosis involving the superior sagittal sinus. She was discharged on postpartum day 31 without neurological deficits after treatment with anticoagulants. At her 3-month follow-up, both MRA and MRV were within the normal limits.

Conclusion: This is the first report of two women diagnosed with RCVS with concomitant CVST following ovarian tumor resection. Marked reductions in postoperative E2 levels could have contributed to the development of CVST and RCVS.

Keywords: Reversible cerebral vasoconstriction syndrome, Cerebral venous sinus thrombosis, Ovarian tumor, Single-photon emission computed tomography, Edoxaban

INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) is a unifying term used to describe a group of disorders sharing angiographic and clinical features, such as reversible segmental and

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multifocal vasoconstriction of cerebral arteries and severe headaches with or without focal neurological deficits or seizures.^[3,11] Patients presenting with these features were previously described using diverse terminology. The most common clinical feature of RCVS is a severe acute headache, which is often referred to as a thunderclap headache due to the nature of its presentation.^[5] RCVS has been reported in association with ischemic stroke and convexity subarachnoid hemorrhage (SAH);^[9] however, few reports have described RCVS concomitant with cerebral venous sinus thrombosis (CVST). This is the first case report that describes RCVS concomitant with CVST in a woman who underwent ovarian tumor resection and was followed-up with single-photon emission computed tomography (SPECT) and 3.0 T magnetic resonance imaging (MRI).

CASE DESCRIPTION

Case 1

A 42-year-old woman presented with a 3-week history of headache showing recent progression, as well as disorientation and reduced level of consciousness. She revealed a medical history of ovarian tumor resection [Figure 1a-c]. After resection, her estradiol (E2) level decreased from 288 pg/ml to 31 pg/ml (normal range, 0–49 pg/ml). Neurological examination revealed bilateral papilledema without focal neurological deficit. MRI (FLAIR and T2* images) revealed left occipital cortical SAH and dural venous sinus thrombosis involving the left transverse and sigmoid sinuses [Figure 2a]. MR angiography (MRA) revealed high-grade left posterior cerebral artery (PCA) stenosis [Figure 2b]. Notably, N-isopropyl-p-[123I] iodoamphetamine (IMP)-SPECT imaging performed on day 2 revealed left posterior ischemic lesions [Figure 2c]; however, these ischemic lesions disappeared on day 28 [Figure 2c]. The IMP-SPECT findings were correlated with vasoconstriction on cerebral angiography and MRA. Routine laboratory investigations revealed anemia (serum hemoglobin level 8.8 g/dL) without any other abnormality. All blood tests for thrombophilic conditions showed negative

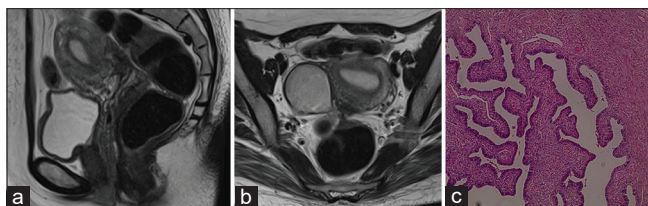


Figure 1: (a,b) Sagittal and axial T2-weighted MR image shows a large cystic ovarian tumor of 5cm at maximum diameter. The tumor had arisen from the right ovary, the margin was smooth and the uterus was normal size. (c) Ovarian endometrioid tumor of low malignant potential showing glands similar to the complex hyperplasia of the uterine endometrium.

or normal results, including tests for antinuclear antibodies, anti-DNA antibodies, antiphospholipid antibodies, C protein, S protein, and antithrombin-3. Moreover, genetic screening for mutation G1691A in the gene for Factor V, mutation G20210A in the gene for Factor II, mutation V617F in *JAK2*, and mutation in the *MTHFR* gene revealed no abnormalities. Cerebrospinal fluid (CSF) analysis revealed minor abnormalities including a marginally increased white blood cell count and mildly elevated protein levels. Therapy was initiated with nimodipine, magnesium sulfate, simvastatin, and unfractionated heparin (activated partial thromboplastin time: 2–2.5 times of the normal level).

Her MRV revealed no abnormalities a month later [Figure 2d]. Over the following 2 weeks, gradual improvement in the stenosis was observed on repeat ultrasonography and MRA [Figure 2e]. SPECT image showing absence of the ischemic lesion [Figure 2f]. Edoxaban was initiated, and following tapering of nimodipine, she was discharged on day 28 without neurological deficits.

Case 2

A 39-year-old female with a recent history of ovarian tumor resection developed holocranial headache associated with vomiting. After tumor resection, her E2 level decreased from 193 pg/ml to 19 pg/ml (normal range, 0–49 pg/ml). Neurological examination revealed no focal neurologic deficits. The next day she experienced repeat onset of severe headache followed by right lower limb paresis. On

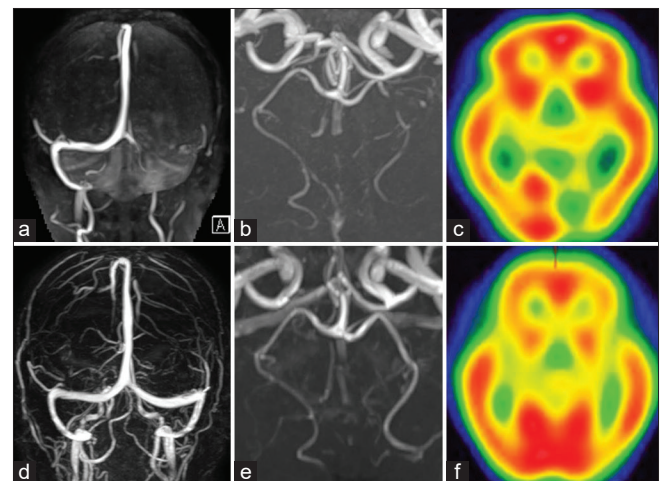


Figure 2: (a) Brain magnetic resonance venography image obtained on admission showing occlusion of the left transverse and sigmoid sinuses. Magnetic resonance venography image obtained 28 days after admission showing recanalization of the venous sinus (d). (b) 3D TOF MRA showing high-grade left PCA stenosis. Improvement in vasoconstriction is observed on day 14 from ictus (e). (c) SPECT images obtained on day 2 from ictus showing left posterior ischemic lesion. SPECT image obtained on day 28 from ictus showing absence of the ischemic lesion (f).

presentation to our department, she underwent a clinical examination which revealed all vital signs to be within the normal ranges. Magnetic resonance angiography (MRA) confirmed the presence of a vasospasm involving the right anterior cerebral artery [Figure 3a]. Magnetic resonance venography (MRV) confirmed the presence of a thrombosis involving the superior sagittal sinus [Figure 3b]. All blood tests for thrombophilic conditions were negative or normal. We subsequently initiated anticoagulation with low-molecular-weight heparin (enoxaparin) and nimodipine. Her subsequent clinical course was uneventful with slow recovery of the right limb paresis. Over the following weeks, there was a gradual improvement of the stenoses, as assessed by repeated MRI. She was started on a different anticoagulant (edoxaban) and discharged on postpartum day 31 without neurological deficits; we additionally tapered her nimodipine. At her 3-month follow-up, MRA and MRV were normal [Figure 3c and d]. She was ultimately diagnosed with postpartum stroke, wherein CVT was followed in quick succession by RCVS.

DISCUSSION

Cerebral venous thrombosis (CVT) is an uncommon form of stroke that presents with a wide range of clinical manifestations. Risk factors include ovarian tumor, iron deficiency anemia, pregnancy, intravenous drug abuse, infection, and dehydration.^[10] Headache is the predominant symptom reported in 90% of cases. Papilledema occurs in approximately 30% of cases and is attributed to elevated intracranial pressure. Focal neurological deficits occur in patients with CVT, primarily as a consequence of infarction and less commonly, secondary to hemorrhage.^[4] RCVS is a rare form of angiopathy, and childbirth is a known precipitating factor for this condition. RCVS is characterized by reversible segmental vasoconstriction of medium- and large-sized cerebral arteries.^[2,11] SAH is not a necessary criterion to diagnose RCVS, although approximately 22–34% of cases with RCVS are associated with convexity SAH.^[8] To the best of our knowledge, no reports have described IMP-SPECT findings in patients presenting with RCVS concomitant with CVT. In our patient (Case1), using IMP-SPECT imaging, we identified left posterior ischemic lesions on day 2, which disappeared on day 28.

The following pathomechanisms should be considered in the present case: RCVS and CVT coexisted in this woman or CVT resulted in RCVS. An association between CVT and RCVS has previously been reported in two women immediately postpartum.^[7] Another case report has described such an association between these two forms of angiopathy in a young woman who underwent stenting of the lateral venous sinus for the management of idiopathic intracranial hypertension [Table 1].^[1,6,7] In these

Table 1: Summary of patients with co-occurrence of RCVS and venous sinus thrombosis.

Case number	Author	Age/ Sex	Symptoms	Risk factor	Affected veins	Affected arteries	Associated condition	Therapy	mRS (admission)	mRS (discharge)
1	Katzin LW <i>et al.</i> .(2007)	37/F	Headache and vomiting	Pregnancy	Trolard	ACA, MCA, and PCA	Infarction	Warfarin	2	1
2	Markus <i>et al.</i> .(2011)	38/F	Headache	Pregnancy	SSS,TS,SS	PCA	None	Nimodipine, magnesium, statin, and warfarin	1	0
3	Bourvis N <i>et al.</i> (2016)	24/F	Headache and vomiting	Pregnancy	TS,SS	PCA and MCA	SAH and infarction	Nimodipine and warfarin	3	1
4	Our cases	42/F	Headache	Ovarian tumor, anemia	TS,SS	PCA	SAH	Nimodipine and edoxaban	2	0
5		39/F	Headache	Ovarian tumor	SSS	ACA	None	Nimodipine and edoxaban	1	0

RCVS: Reversible cerebral vasoconstriction syndrome, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, SAH: Subarachnoid hemorrhage, SSS: Superior sagittal sinus

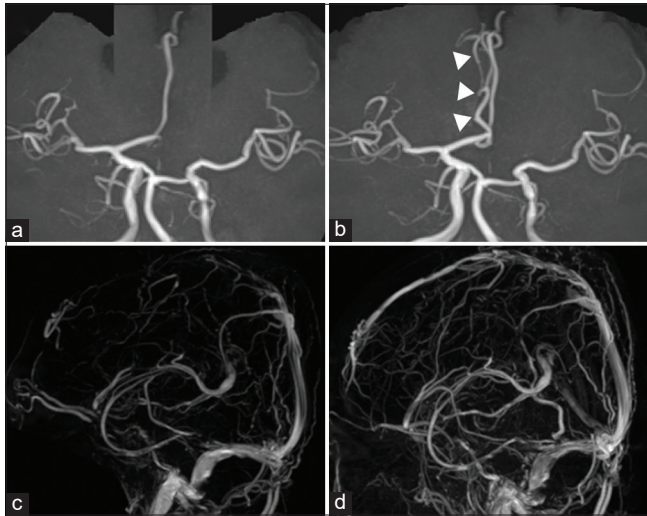


Figure 3: (a,c) Magnetic resonance angiography (MRA) confirmed the presence of a vasospasm involving the right anterior cerebral artery. On admission, MRA revealed vasoconstriction of the anterior cerebral artery. Vasoconstriction was normalized within 3 months. (b,d) Magnetic resonance venography (MRV) confirmed the presence of a thrombosis involving the superior sagittal sinus. On admission, MRV revealed thrombosis of the superior sagittal sinus, which normalized within 3 months.

cases, the authors concluded that CVT and RCVS were perhaps distinct pathophysiological entities. RCVS may have been triggered by reduced serum levels of estrogen, which is perhaps associated with loss of vasodilatation and other changes within the endothelium and the vessel wall.^[12] In our patients, resection of the ovarian tumor led to dramatically reduced estrogen levels (Case 1: 288–31 pg/ml, Case 2: 193–19 pg/ml), which could have contributed to the development of CVST and RCVS. Our patient showed concomitant venous thrombosis and arterial vasospasm in the setting of severe acute headache. This is the first report that describes RCVS concomitant with CVST followed by resection of ovarian tumor.

CONCLUSION

Our cases highlight that both RCVS and CVST should be considered perioperatively in women undergoing ovarian tumor resection. In our patients, resection of the ovarian tumor led to dramatically reduced E2 levels, which could have contributed to the development of CVST and RCVS.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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