Case Report

Synchronous reversible cerebral vasoconstriction syndrome following thyrotoxicosis in a postpartum woman

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Background: Reversible cerebral vasoconstriction syndrome (RCVS) typically manifests with acute-onset, recursive, severe headache that continues for a month; it rarely manifests as seizures. Development of RCVS following thyrotoxicosis has not been previously reported in detail.

Case Presentation: A 30-year-old postpartum woman with thyrotoxicosis developed a generalized seizure refractory to anticonvulsants. Magnetic resonance angiography demonstrated cerebral artery stenosis in the right anterior cerebral artery and the right middle cerebral artery. These findings were compatible with RCVS. Reversible cerebral vasoconstriction syndrome was treated successfully with i.v. nicardipine and conventional management was undertaken for thyrotoxicosis.

Conclusion: This is the first well-documented case of a postpartum woman with synchronous RCVS following thyrotoxicosis. Reversible cerebral vasoconstriction syndrome and thyrotoxicosis can coincidentally occur in postpartum women and manifest with postpartum seizures.

Key words: Postpartum, reversible cerebral vasoconstriction syndrome, seizure, thyrotoxicosis

INTRODUCTION

REVERSIBLE CEREBRAL VASOCONSTRICTION syndrome (RCVS) is not an uncommon clinical condition.[1] Reversible cerebral vasoconstriction syndrome typically manifests with acute-onset, recursive, severe headache that continues for a month; it rarely manifests as seizures.[1] Angiographic studies (e.g., cerebral angiography, computed tomographic angiography, or magnetic resonance angiography) typically show segmental or diffuse spasm in the cerebral artery, which resolves within 12 weeks.[1] We report a rare case of RCVS that manifested with convulsions in a postpartum woman with thyrotoxicosis.

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CASE REPORT

A 30 -YEAR-OLD WOMAN was transferred to the emergency department of our hospital from her local hospital because of a generalized seizure. At her 34th week of pregnancy, she noted increased appetite, weight loss, and sweating. She had been hypertensive, and 1 week before delivery, she had noted edema in the lower extremities. The day before she went to her local hospital, she visited the obstetrician's office for postpartum care, and she also noted hand tremor. She was admitted to the hospital because of thyrotoxicosis, according to her blood concentration of thyroid-stimulating hormone (<0.0025 μU/mL). She was treated with propranolol (30 mg/day orally) and propylthiouracil (300 mg/day orally). The next day, she developed a generalized seizure that was refractory to anticonvulsants, and she was transferred to our hospital. She denied drinking alcohol or smoking. She did not take any medications. Her medical history and family history were unremarkable.

At presentation, she was intubated, on a ventilator, and sedated with continuous propofol infusion. Her body temperature was 39.3°C, pulse rate 80 b.p.m., and blood pressure 160/80 mmHg. Physical examination revealed that her eyes were protruding mildly, and she showed facial edema

and thyroid enlargement. Except for hyperthyroidism, no other findings of the blood tests explained her convulsions (Table 1). Results of cerebrospinal fluid analysis ruled out meningitis. On the basis of her low blood level of thyroid-stimulating hormone, high free T4 level, and increased blood flow detected on thyroid ultrasonography, Graves' disease was diagnosed. Her head computed tomographic and magnetic resonance imaging showed no intracranial lesions. Magnetic resonance angiography (Fig. 1A) showed cerebral artery stenosis in the right anterior cerebral artery and the right middle cerebral artery; these findings were compatible with a diagnosis of RCVS.

The patient received i.v. magnesium for eclampsia and a combination of thiamazole, inorganic iodine, landiolol, and hydrocortisone for thyrotoxicosis. Reversible cerebral vasoconstriction syndrome was treated with a continuous infusion of nicardipine. On the third day, she was extubated but still disorientated and aphasic without sedatives, although electroencephalography demonstrated no remarkable findings. Although she showed improvement in aphasia on the following day, she demonstrated apraxia and agnosia. Additional brain imaging was not undertaken because her neurological symptoms were resolving gradually. On the 12th day, apraxia and agnosia completely resolved, and the Mini-Mental State Examination score reached a normal level. Follow-up magnetic resonance angiography on the 12th day was also normal (Fig. 1B), which confirmed the diagnosis of RCVS (Table 2). After discharge on the 20th day, she continued propylthiouracil therapy and has suffered no recurrence in the more than 2 years since.

DISCUSSION

REVERSIBLE CEREBRAL VASOCONSTRICTION syndrome typically manifests with headache; in rare, severe cases, like that of our postpartum patient, convulsions or impaired consciousness can be the first obvious manifestation. Whether affected patients lack headache is unclear because they are unconscious.[2]

The majority of the reported RCVS cases have developed in patients taking medications such as vasoactive stimulants, antidepressants, ephedrine, triptans, or ergotamine, and in

Table 1. Laboratory data of a 30-year-old woman with postpartum synchronous reversible cerebral vasoconstriction syndrome following thyrotoxicosis

Complete blood count			Biochemistry			Immunoserological		
WBC	15,500	/μL	Total protein	6.4	g/dL	CRP	5.85	mg/dL
Hb	12.2	g/dL	Albumin	3	g/dL	TP antibody	Negative	
Plt	31.6×10^4	/μL	BUN	8.8	mg/dL	TSH receptor antibody	10.4	U/mL
Coagulation			Cr	0.33	mg/dL	Thyroglobulin antibody	1,628	IU/mL
PT	73	%	AST	19	IU/L	Antithyroid peroxidase	335	IU/mL
PT-INR	1.18		ALT	18	IU/L	Antinuclear antibody	Positive	
APTT	27	s	ALP	269	IU/L	Homogeneous	80	fold
D-dimer	1	ng/mL	LDH	212	IU/L	PR3-ANCA	Negative	
Endocrine			γ-GTP	16	IU/L	MPO-ANCA	Negative	
Glucose	117	mg/dL	T-Bil	1	mg/dL	Anti-CL βPI antibody	Negative	
HbA1c	5.1	%	CK	36	IU/mL	Anti-CL antibody	Negative	
Lactate	9.7	mg/dL	AMY	48	IU/mL	Lupus anticoagulant	1.22	
VitaminB1	39	ng/mL	Na	132	mEq/L	RF	<15	U/mL
Cortisol	25.2	μg/dL	K	3.9	mEq/L	Spinal fluid analysis		
Ammonia	66	μg/dL	Cl	99	mEq/L	WBC	2	/μL
TSH	<0.0025	μU/mL	Mg	1.7	mg/dL	Mono	1	/μL
FT3	6.01	pg/mL	Ca	9.6	mg/dl	Poly	1	/μL
FT4	2.76	ng/dL				Protein	40	mg/dL
						Glucose	56	mg/dL

γ-GTP, γ-glutamyl transferase; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AMY, amylase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CK, creatine kinase; CL, cardiolipin; CL βPI, cardiolipin beta 2-glycoprotein 1; Cr, creatinine; CRP, C-reactive protein; FT3, free triiodothyronine; FT4, free thyroxine; Hb, hemoglobin; HbA1c, glycated hemoglobin; LDH, lactate dehydrogenase; MPO-ANCA, myeloperoxidase-antineutrophil cytoplasmic antibody; Plt, platelets; PR3-ANCA, serine proteinase3-antineutrophil cytoplasmic antibody; PT, prothrombin time; PT-INR, prothrombin time – international normalized ratio; RF, rheumatoid factor; T-Bil, total bilirubin; TP, total protein; TSH, thyroid stimulating hormone; WBC, white blood cells.

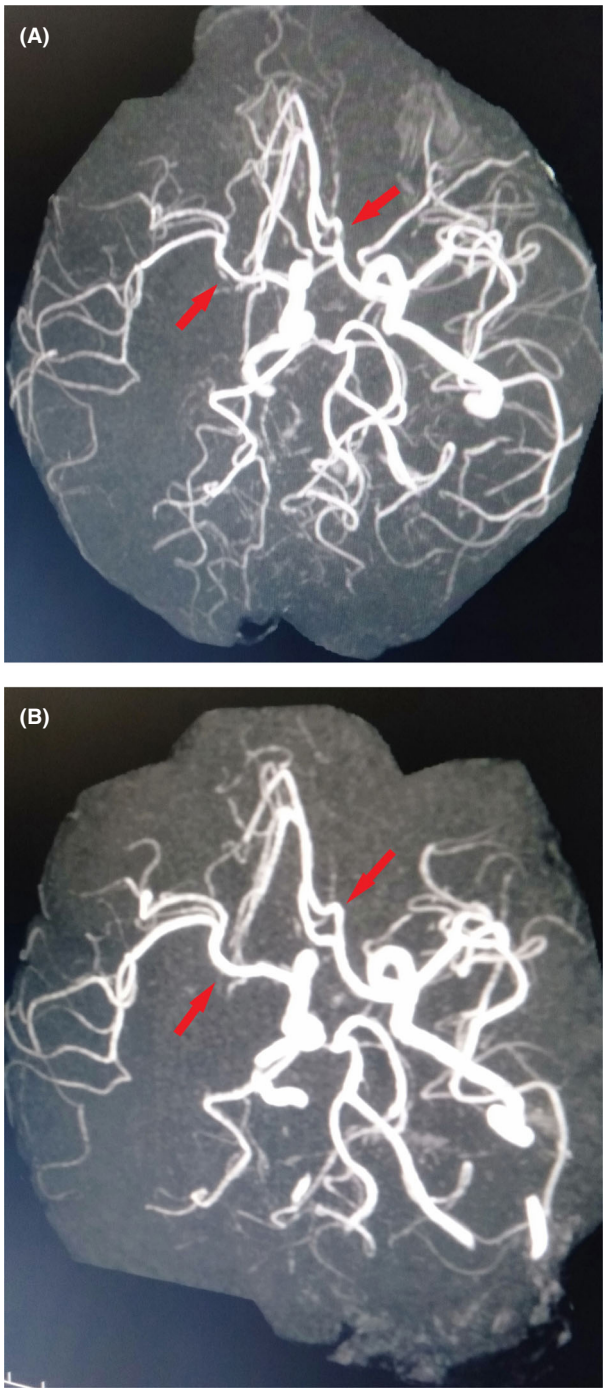

Fig. 1. Initial and follow-up magnetic resonance angiography of a 30-year-old woman with postpartum synchronous reversible cerebral vasoconstriction syndrome following thyrotoxicosis. Cerebral artery stenosis was apparent in the right anterior cerebral artery and the right middle cerebral artery on admission (A, arrows), and it disappeared on the 12th day (B, arrows).

Table 2. Diagnostic criteria of reversible cerebral vasoconstriction syndrome (excerpt from Ducros 2012)[1]

Acute and severe headache (often thunderclap) with or without focal deficits or seizures
Uniphasic course without new symptoms more than 1 month after clinical onset
Segmental vasoconstriction of cerebral arteries shown by indirect (e.g., magnetic resonance angiography or computed tomography) or direct catheter angiography
No evidence of aneurysmal subarachnoid hemorrhage
Normal or near-normal cerebrospinal fluid (protein concentrations <100 mg/dL, <15 white blood cells per μL)
Complete or substantial normalization of arteries shown by follow-up indirect or direct angiography within 12 weeks of clinical onset

postpartum women.[3] Transient sympathetic overactivity, which can result with these drugs and after parturition, diminishes the vascular tone in the cerebral artery, which is the proposed mechanism for RCVS.[3] Abrupt decreases in estrogen and progesterone levels, which can induce vasoconstriction, is another putative mechanism for the development of RCVS in postpartum women.[4] Skeik *et al*. reported 98 cases of postpartum RCVS, all of which developed within 30 days of delivery and 71% of which developed within 1 week. Most of the patients had no hypertension or proteinuria during the perinatal period; however, RCVS can occur without warning. Of Skeik *et al*.'s 98 patients, 43 (44%) had convulsions, and intracranial lesions – hemorrhage in 38 (39%) and infarction in 32 (33%) – were also common.[5] Our patient had earlier thyrotoxicosis, which could theoretically induce sympathetic hyperactivity, and thus could also have affected the development of RCVS. However, this was only speculative because we did not directly investigate sympathetic hyperactivity or the relationship between sympathetic hyperactivity and development of RCVS in this case. Nevertheless, because the development of RCVS after thyrotoxicosis was reported in only a single conference abstract,[6] our patient should represent the first well-documented case of postpartum RCVS diagnosed concurrently with thyrotoxicosis.

Early use of nimodipine, a calcium-channel antagonist, is proposed for the management of RCVS on the basis of findings of a prospective study in which early termination of headache was associated with this therapy, although its long-term outcomes are unclear.[7] Our patient was treated successfully with i.v. infusion of nicardipine, another calcium-channel antagonist, coupled with the standard, conventional management for thyrotoxicosis.

This case study has several limitations. First, a new-onset generalized seizure in a postpartum woman with hypertension can be a manifestation of eclampsia; that is, any one of three clinically defined syndromes (eclampsia, RCVS, and thyrotoxicosis) can manifest with generalized seizures alone, as in our patient. Because we treated all three clinical conditions simultaneously, we can neither specify which treatment had a direct effect on each of the three conditions nor determine a single pathology that could have triggered generalized seizure among the three conditions. Second, the causal relationship between thyrotoxicosis and RCVS is only a conjecture from the patient's clinical history, not based on objective data, as already mentioned. Finally, we did not undertake a follow-up computed tomography or magnetic resonance imaging on the third day when she developed apraxia and agnosia despite the improvement in aphasia. Although these symptoms spontaneously regressed without neurological sequelae in our case, an investigation for brain parenchymal lesions is encouraged in the presence of focal neurologic signs such as aphasia, apraxia, and agnosia.

CONCLUSION

THIS WAS THE first well-documented case of a postpartum woman with synchronous RCVS following thyrotoxicosis. Reversible cerebral vasoconstriction syndrome and thyrotoxicosis can coincidentally occur in postpartum women and manifest with postpartum seizures.

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DISCLOSURE

Approval of the research protocol: N/A.
Informed consent: The patient provided informed consent for the publication of this case report.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None.

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