Turkish Journal of Cerebrovascular Diseases 2022; 28(3): 189-194 Türk Beyin Damar Hastalıkları Dergisi 2022; 28(3): 189-194
Turk J Cereb Vasc Dis
doi: 10.5505/tbdhd.2022.49002

CASE REPORT **OLGU SUNUMU**

POSTPARTUM REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME PRESENTING WITH REVERSIBLE SPLENIAL LESION

Doğan Dinç ÖGE[1], Ece GÖK DURSUN[1], Ethem Murat ARSAVA[1], Rahşan GÖÇMEN[2], İbrahim ESİNLER[3], Onur Can ZAİM[3], Mehmet Akif TOPÇUOĞLU[1]

[1]Hacettepe University Faculty of Medicine, Department of Neurology, Ankara, TÜRKİYE
[2]Hacettepe University Faculty of Medicine Department of Radiology, Ankara, TÜRKİYE
[3]Hacettepe University Faculty of Medicine, Department of Obstetrics and Gynecology, Ankara, TÜRKİYE

ABSTRACT

Co-occurrence of postpartum reversible cerebral vasoconstriction syndrome (RCVS) and reversible splenial lesion syndrome (RESLES) is highly rare, and may provide an opportunity in understanding the mechanism of these two rare entities. A 28-year-old female with postpartum psychosis in association with both RCVS and RESLES was reported. The worsening with antipsychotics and the dramatic response to oral nimodipine served as a clue to the diagnosis. RESLES and RCVS may have overlapping pathophysiology. It is possible that RESLES is one of the forms of cerebral edema resulting from RCVS.
Keywords: Reversible cerebral vasoconstriction syndrome, reversible splenial lesion, postpartum psychosis.

Address for Correspondence: Doğan Dinç Öge, M.D. Hacettepe University Faculty of Medicine, Department of Neurology, Sıhhiye, Ankara, Türkiye.
Phone: +90312 305 25 85 **E-mail:** dogandincoge@gmail.com
Received: 18.05.2022 **Accepted:** 27.07.2022
ORCID IDs: Doğan Dinç Öge 0000-0001-8103-4779, Ece Gök Dursun 0000-0001-7191-772X, Ethem Murat Arsava 0000-0002-6527-4139, Rahşan Göçmen 0000-0002-0223-9336, İbrahim Esinler 0000-0001-8117-0308, Onur Can Zaim 0000-0003-1825-8918, Mehmet Akif Topçuoğlu 0000-0002-7267-1431.
Please cite this article in press as: Öge DD, Gök Dursun E, Arsava EM, Göçmen R, Esinler İ, Zaim OC, Topçuoğlu MA. Postpartum reversible cerebral vasoconstriction syndrome presenting with reversible splenial lesion. Turkish Journal of Cerebrovascular Diseases 2022; 28(3): 189-194. doi: 10.5505/tbdhd.2022.49002

GEÇİCİ SPLENİAL LEZYON İLE PREZENTE POSTPARTUM REVERSİBL SEREBRAL VAZOKONSTRİKSİYON SENDROMU

ÖZ

Postpartum reversibl serebral vazoskonstriksiyon sendromu (RSVS) ile geçici splenial lezyon birlikteliği oldukça nadir bir durum olup, bu iki nadir hastalığın altında yatan mekanizmaların anlaşılabilmesi için bir fırsat doğurmaktadır. Bu çalışmada, 28 yaşında RSVS ve geçici splenial lezyon birlikteliği ile ilişkili bir postpartum psikoz olgusu tartışılmıştır. Hastnın antipsikotikler ile kötüleşmiş olması ve oral nimodipin'e dramatik yanıt vermis olması tanı için ipucu teşkil etmiştir. Geçici splenial lezyon ile RSVS'nin ortak patofizyolojik özellikleri olduğu düşünülebilir. Geçici splenial lezyonun RSVS sebebiyle gelişen serebral ödem tiplerinden birisi olması mümkündür.
Anahtar Sözcükler: Reversibl serebral vazokonstriksiyon sendromu, geçici splenial lezyon, postpartum psikoz.

INTRODUCTION

Reversible cerebral vasoconstriction syndrome (RCVS) comprises a group of disorders characterized by fully reversible narrowing of the cerebral arteries, usually presenting with acute-onset, severe and recurrent headaches, with or without additional neurologic signs and symptoms (1). It has been associated with several diverse conditions including pregnancy, vasoconstrictive drugs, and primary headache syndromes (2).

Postpartum reversible cerebral vasoconstriction syndrome (PPRCVS) is a distinct clinical entity comprising up to 10% of all RCVS cases (3-5). Even though the underlying mechanisms contributing to PPRCVS are not uncovered yet, alterations in female reproductive hormones and pregnancy-related changes in vascular physiology are thought to play a role in its pathophysiology (6).

Reversible splenial lesion syndrome (RESLES) is a rare benign clinic-radiological syndrome characterized by reversible, focal, and usually diffusion-restricted lesion in the central region of the splenium of corpus callosum (sCC) (7). It is associated with a plethora of diverse etiologies, yet the pathophysiological mechanisms are not completely understood (8). These two syndromes can rarely coexist. (9-11) We revisit the physiopathology of this association based on a new case reported herein and three other cases published in the germane literature.

CASE REPORT

A 28-year-old woman was consulted for acute onset disorientation and behavioral abnormalities that started two days after an uneventful delivery by cesarean section. Her relatives and physicians declared absence of significant medical issues and headache prior to her mental deterioration. We were informed that intramuscular methylergonovine was administered after the delivery to prevent postpartum bleeding. On examination, she was non-cooperative, disoriented and inattentive. Her speech was slow with perseverations. No other abnormality was detected in the neurological examination.

Since brain computed tomography showed no abnormal findings, a brain magnetic resonance imaging (MRI) study was scheduled. However, MRI was postponed due to her agitation, and a psychiatry consultation was obtained for alternating agitation episodes and an ongoing increase in her negativistic behaviors. Anti-psychotic treatment consisting of olanzapine 2.5 mg/day was initiated with a presumptive diagnosis of postpartum psychosis, which was followed by the further deterioration of the patient into a state of akinetic mutism. Olanzapine was then altered with risperidone 1 mg/day and lorazepam 3x1 mg/day was added but no clinical change was obtained. The MRI was then performed under sedation, and showed a nodular lesion in the center of the sCC characterized by restricted diffusion indicative of RESLES (Figure 1). The MR angiography (MRA) revealed segmental narrowing and dilatation of both anterior and posterior cerebral arteries, suggestive of postpartum angiopathy (also known as RCVS) (Figure 2). Oral nimodipine (6x30 mg/day) treatment was initiated, and clinical amelioration has observed on the second day of the treatment. The patient's mental status returned to normal and her speech became fluent without any pathological signs in several days.

Anti-psychotic treatments were discontinued, and the patient was discharged on the fourth day of nimodipine treatment with a normalized neurologic examination. After three weeks of nimodipine treatment, a follow-up MRI revealed resolution of the splenial lesion and the cerebral arteriopathy significantly. The treatment was subsequently stopped and she had no further health problems since then. Of note, consent was obtained for this paper from the patient.

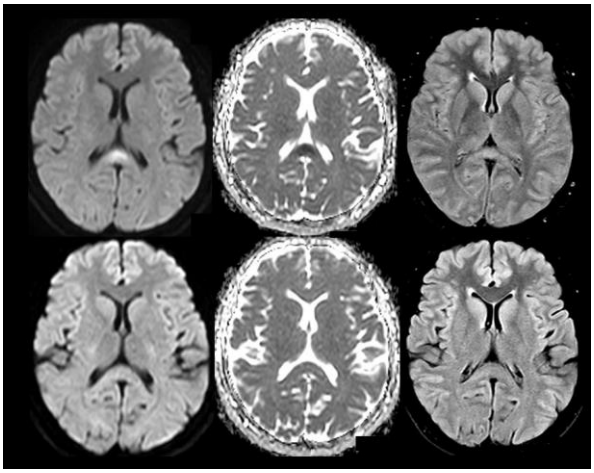

Figure 1. Resolution of DWI-bright; ADC-dark and FLAIR-hyperintense ovoid RESLES lesion. Magnetic resonance imaging, initial in upper bank and follow-up in lower bank. Diffusion-weighted imaging, apparent diffusion coefficient mapping and fluid-attenuated inversion recovery sequences, from right to left.

DISCUSSION AND CONCLUSION

Postpartum cerebral angiopathy is a rare disease presenting with headache, seizures and focal neurological deficits, following labor. It occurs generally within the first 3 weeks of the postpartum period, but late onset presentations until 6 weeks postpartum have been reported (12). The most common symptom is thunderclap headache. Focal neurological deficits such as visual disturbances, dysarthria, aphasia, extremity paresis, dysesthesia, ataxia and epileptic seizures can also be present (2).

PPRCVS, as one of the severe forms of RCVS spectrum disorders, is characterized by a 75% incidence of neurological deficits or seizure, which is higher than other RCVS subtypes (3-6). Pregnancy is a known risk factor but the pathophysiological mechanisms are not yet fully elucidated. Pregnancy associated physiological changes, such as increased blood volume, systemic vasodilation, increased peripheral vascular resistance, increased arterial tonus, mild systemic inflammation and changes in the lipid profile are considered to alter the arterial wall functions, resulting in the observed diffuse cerebral arteriopathy (13). In addition, the use of vasoactive drugs such as methylergonovine during the peripartum period, which was the case in our patient, might also contribute to the pathophysiology (14).

Our detailed literature search revealed a total of 10 postpartum RESLES cases, 3 of which were associated with postpartum RCVS, making our case the fourth (Table) (9-11,15-20). The suggested etiologies included preeclampsia, eclampsia, postpartum psychosis and cerebral venous thrombosis in postpartum RESLES cases without RCVS in the literature. Overall, the imaging spectrum of RCVS includes cerebral infarction, convexity subarachnoid hemorrhage,

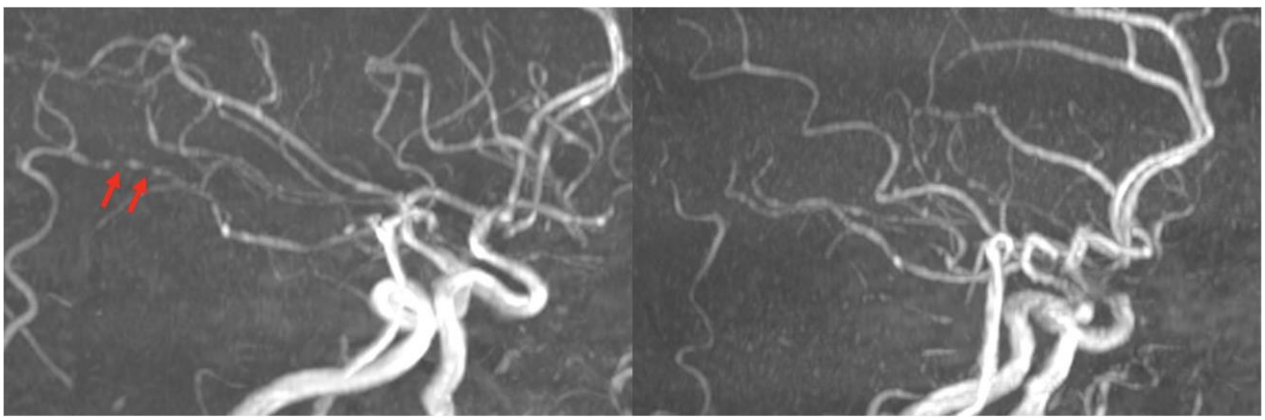

Figure 2. Resolution of multi-segmental cerebral vasoconstriction: time-of-flight magnetic resonance angiography (MRA), initial on the right and follow-up on the left. Red arrows show the constricted segments on the initial MRA.

lobar intracerebral hemorrhage and posterior reversible encephalopathy syndrome like (PRES-like) reversible cerebral edema (3). With other three previous cases, our experience adds typical RESLES lesion to the RCVS imaging spectrum. Other associations of RESLES include infections, seizures, anti-epileptic drug withdrawal and metabolic disorders (7). The presenting symptoms are varied, and include mental status changes, seizures, vertigo, visual and motor abnormalities, ataxia, tremor, psychosis and hallucinations (21).

Unlike three previous cases with postpartum RESLES with RCVS, where the initial symptom was thunderclap headache, our patient presented with postpartum psychosis without headache. A RESLES case presenting with only postpartum psychosis was published by Udaya et al; but in that case angiography was normal (15). Our case is the first in the literature, and thereby unique, as postpartum RCVS, RESLES and psychosis altogether co-exist. It should be noted that the psychosis of the patient worsened with anti-psychotics but improved with nimodipine.

The mechanism underlying RESLES has not been unveiled yet. It is speculated that due to the high density of crossing fibers, the myelin sheaths of splenial fibers are prone to water and electrolyte deposition. It has been suggested that ion transfer mechanisms of these axon bundles, which are very tightly arranged in the central region of the sCC, are insufficient to pump intracellular fluid into the extracellular space in the setting of pre-eclampsia. This relative insufficiency may result in intra-myelin edema and myelin vacuolization (21). Another suggested mechanism is cytokine induced glutamate excitotoxicity associated cytotoxic edema formation (22). Hiraga et al, on the other hand, proposed a simpler mechanism linking arterial tonus changes originating from pregnancy-related hormonal and metabolic alterations to both RCVS and RESLES (10,13).

In conclusion, we present a rare case with combination of postpartum psychosis, RESLES and RCVS. This case adds RCVS-induced arteriopathy among the causes of postpartum RESLES.

REFERENCES

1. Calabrese LH, Dodick DW, Schwedt TJ, et al. Narrative review: Reversible cerebral vasoconstriction syndromes. Ann Intern Med 2007; 146(1): 34-44.
2. Ducros A. Reversible cerebral vasoconstriction syndrome. Lancet Neurol 2012; 11(10): 906-917.
3. Ducros A, Boukobza M, Porcher R, et al. The clinical and radiological spectrum of reversible cerebral vasoconstriction syndrome. A prospective series of 67 patients. Brain 2007; 130(Pt 12): 3091-3101.
4. Singhal AB, Hajj-Ali RA, Topcuoglu MA, et al. Reversible cerebral vasoconstriction syndromes: Analysis of 139 cases. Arch Neurol 2011; 68(8): 1005-1012.
5. Ducros A, Fiedler U, Porcher R, et al. Hemorrhagic manifestations of reversible cerebral vasoconstriction syndrome: Frequency, features, and risk factors. Stroke 2010; 41(11): 2505-2511.
6. Skeik N, Porten BR, Kadkhodayan Y, et al. Postpartum reversible cerebral vasoconstriction syndrome: Review and analysis of the current data. Vasc Med 2015; 20(3): 256-265.
7. Garcia-Monco JC, Cortina IE, Ferreira E, et al. Reversible splenial lesion syndrome (resles): What's in a name? J Neuroimaging 2011; 21(2): e1-14.
8. Blaauw J, Meiners LC. The splenium of the corpus callosum: Embryology, anatomy, function and imaging with pathophysiological hypothesis. Neuroradiology 2020; 62(5): 563-585.
9. Sekine T, Ikeda K, Hirayama T, et al. Transient splenial lesion after recovery of cerebral vasoconstriction and posterior reversible encephalopathy syndrome: A case report of eclampsia. Intern Med 2012; 51(11): 1407-1411.
10. Hiraga A, Koide K, Aotsuka Y, et al. Reversible cerebral vasoconstriction syndrome with transient splenial lesions after delivery. Intern Med 2016; 55(22): 3357-3359.
11. Takahashi Y, Hashimoto N, Tokoroyama H, et al. Reversible splenial lesion in postpartum cerebral angiopathy: A case report. J Neuroimaging 2014; 24(3): 292-294.
12. Singhal AB, Bernstein RA. Postpartum angiopathy and other cerebral vasoconstriction syndromes. Neurocrit Care 2005; 3(1): 91-97.
13. Topcuoglu MA, McKee KE, Singhal AB. Gender and hormonal influences in reversible cerebral vasoconstriction syndrome. Eur Stroke J 2016; 1(3): 199-204.
14. Cappelen-Smith C, Calic Z, Cordato D. Reversible cerebral vasoconstriction syndrome: Recognition and treatment. Curr Treat Options Neurol 2017; 19(6): 21.
15. Udaya SC, Chauhan BN, Philip VJ. Bright splenium of a psychotic mind. Ann Indian Acad Neurol 2015; 18(1): 80-83.
16. Chen Z, Xu M, Shang D, et al. A case of reversible splenial lesions in late postpartum preeclampsia. Intern Med 2012; 51(7): 787-790.
17. Curtis R, Winder T, Scott J, et al. Benign post-partum reversible restricted diffusion lesion of the splenium. Can J Neurol Sci 2013; 40(1): 89-90.
18. Altunkas A, Aktas F, Ozmen Z, et al. Mri findings of a postpartum patient with reversible splenial lesion syndrome (resles). Acta Neurol Belg 2016; 116(3): 347-349.
19. Liu J, Liu D, Yang B, et al. Reversible splenial lesion syndrome (resles) coinciding with cerebral venous thrombosis: A report of two cases. Ther Adv Neurol Disord 2017; 10(12): 375-379.
20. Yang Q, Chang CC, Liu M, et al. Sequential occurrence of eclampsia-associated posterior reversible encephalopathy syndrome and reversible splenial lesion syndrome (a case report): Proposal of a novel pathogenesis for reversible splenial lesion syndrome. BMC Med Imaging 2019; 19(1): 35.

21. Tada H, Takanashi J, Barkovich AJ, et al. Clinically mild encephalitis/encephalopathy with a reversible splenial lesion. Neurology 2004; 63(10): 1854-1858.
22. Starkey J, Kobayashi N, Numaguchi Y, et al. Cytotoxic lesions of the corpus callosum that show restricted diffusion: Mechanisms, causes, and manifestations. Radiographics 2017; 37(2): 562-576.

Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

Peer-review: Internally peer-reviewed.

Authorship Contributions: Surgical and Medical Practices: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Concept: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Design: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Data Collection or Processing: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Analysis or Interpretation: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Literature Search: DDÖ, EGD, EMA, RG, İE, OCZ, MAT. Writing: DDÖ, EGD, EMA, RG, İE, OCZ, MAT.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

Table. Literature review of postpartum RESLES cases.

Authors	Year	Age	Comorbidities	Symptom onset	Symptoms	MRI findings	Predisposing condition	Treatment	Radiographic Outcome
Chen et al. [16]	2012	27	None	3 weeks postpartum	Recurrent headache, nausea and bilateral transient visual impairment	RESLES, normal MRA	Late postpartum preeclampsia	N/A	Complete resolution
Sekine et al. [9]	2012	34	Migraine, hypertension	Immediately after spontaneous vaginal delivery	Thunderclap headache, seizure	T2 hyperintensities including the cerebellum, left thalamus, basal ganglia, bilateral posterior subcortical white matter with accompanying RESLES. Follow-up MRA showed segmental vasoconstriction in the proximal PCA, MCA and intracranial ICA segments	Eclampsia	Olmesartan, magnesium sulfate, glycerol	Complete resolution
Takahashi et al. [11]	2012	33	None	17 days postpartum	Thunderclap headache, transient speech disturbance	RESLES; severe bilateral proximal narrowing of anterior, middle and posterior cerebral arteries on MRA	None	Intravenous steroid treatment	Complete resolution
Curtis et al. [17]	2013	28	None	9 days postpartum	Recurrent bilateral transient visual impairment	RESLES; normal MRA and MRV findings	Possible subclinical postpartum preeclampsia	N/A	Complete resolution
Udaya et al. [15]	2014	21	None	2 weeks postpartum	Behavioral abnormalities, mutism, psychosis	RESLES; normal arteriograms and venograms	None	Lorazepam, Escitalopram, Olanzapine	Complete resolution
Altunkas et al. [18]	2015	19	None	20 days postpartum	Headache, nausea, vomiting	RESLES	None	N/A	Complete resolution
Hiraga et al. [10]	2016	28	None	Immediately after spontaneous vaginal delivery	Intermittent Thunderclap headache	RESLES; segmental constriction of the left MCA and bilateral PCAs on MRA	None	None	Complete resolution
Liu et al. [19]	2017	29	None	42 days postpartum	Persistent right temporal headache	RESLES	None	Warfarin, mannitol, anti-epileptics	Complete resolution
		27	None	7 days postpartum	Parieto-occipital headache, increased perspiration, left sided numbness	RESLES	None	Interventional thrombolytic therapy, heparin, warfarin	Complete resolution
Yang et al. [20]	2019	23	None	10 days postpartum	Thunderclap headache, dizziness, blurred vision	PRES on the initial MRI, RESLES on the follow up MRI 10 days later (while asymptomatic)	Eclampsia-associated PRES	None	Complete resolution