Neurological Sciences (2019) 40:1873–1876
https://doi.org/10.1007/s10072-019-03914-3

ORIGINAL ARTICLE

A study on clinical characteristics and the causes of missed diagnosis of reversible posterior leukoencephalopathy syndrome in eclampsia

Tong Shen[1] · Hao Chen[1,2] · Jia Jing[3] · Hafiz Khuram Raza[1,4] · Zuozhui Zhang[1] · Lei Bao[1] · Su Zhou[1] · Shenyang Zhang[1] · Guiyun Cui[1,2]

Received: 7 November 2018 / Accepted: 24 April 2019 / Published online: 7 May 2019

Abstract

Purpose To explore the clinical and imaging characteristics and summarize the causes of missed diagnosis of reversible posterior leukoencephalopathy syndrome (RPLS) in eclampsia.

Methods We collected the data of a total of 45 patients with RPLS who were misdiagnosed initially (27 cases were confirmed and 18 cases were suspicious) out of 804 patients with severe eclampsia who had presented themselves to the Affiliated Hospital of Xuzhou Medical University from January 2014 to December 2016. We summarized the clinical and imaging characteristics of the patients and analyzed the possible causes of the misdiagnosis.

Results Among the 804 patients with eclampsia, 45 were misdiagnosed the first time. Their clinical manifestations included headache (20 cases), epilepsy (13 cases), blurred vision (11 cases), disturbance of consciousness (2 cases), and drowsiness (3 cases). The parietal lobe was involved in 22 cases, the occipital lobe in 15 cases, the frontal lobe in 20 cases, basal ganglia in 9 cases, and the temporal lobe in 8 cases. Low-density lesions were observed on computed tomography (CT) scans. Head magnetic resonance (MR) scans showed hypo-intense lesions on T1-weighted image (T1WI), hyper-intense lesions on the T2-weighted image (T2WI) and fluid-attenuated inversion recovery (FLAIR), iso-intense or slightly hyper-intense lesion on diffusion-weighted imaging (DWI), and slightly hyper-intense or hypo-intense lesion on apparent diffusion coefficient (ADC).

Conclusion The incidence of reversible posterior leukoencephalopathy syndrome is extremely high. The clinical features include headache, mental disturbance, seizures, blurred vision, and other neurological symptoms. The lesion area is mainly limited to the parietal and occipital lobes; however, the frontal lobe, basal ganglia, temporal lobe, corpus callosum, and cerebellum can also be involved. The prognosis is good with timely and appropriate treatments.

Keywords RPLS · Imaging features · Eclampsia · Hypertension · Headache · Misdiagnosis

Introduction

Posterior reversible encephalopathy syndrome (PRES), also called as reversible posterior leukoencephalopathy syndrome (RPLS), is characterized by clinical features of headache, mental disturbance, epilepsy, blurred vision, and other neurological symptoms. The patients with PRES may have abnormal results on CT and MR scans such as cerebral edema in the parietal, temporal, and occipital lobes. Both the clinical features and the abnormal neuroimage findings can be reversed by alleviating cerebral edema, controlling blood pressure, and managing epileptic seizures. In this study, we retrospectively analyzed the clinical and imaging characteristics of 45 patients with RPLS in our hospital and discussed the reasons for the missed diagnosis with the aim to improve the clinicians' understanding of the disease.

Tong Shen and Hao Chen contributed equally to this work.

✉ Hao Chen
haochen-2008@hotmail.com

✉ Guiyun Cui
cuiguiyun-js@hotmail.com

[1] Department of Neurology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou 221002, China

[2] Department of Neurology, The Affiliated Hospital of Xuzhou Medical University, Xuzhou 221006, China

[3] Department of Biology, Georgia State University, Atlanta, GA, USA

[4] School of International Education, Xuzhou Medical University, Xuzhou 221002, China

Material and methods

We investigated 804 female patients with eclampsia who had presented themselves to the Affiliated Hospital of Xuzhou Medical University from January 2014 to December 2016. Forty-five patients with RPLS were misdiagnosed (27 cases were confirmed and 18 cases were suspicious; there were 44 adults and 1 adolescent). Their age of onset ranged from 16 to 40 years with an average of 28 years. Among them, 40 cases were from the department of obstetrics, 3 cases were from the department of critical care medicine, and 1 case was from the neurology department. All patients underwent CT and MR scans (including T1WI, T2WI, FLAIR, DWI, and ADC). Magnetic resonance arterial angiography (MRA) (1 patient), craniocerebral CT angiography (CTA) (4 patients), and magnetic resonance venography (MRV) (4 patients) were also performed in some patients (Fig. 1).

Results

Clinical features

The patients with PRLS had the onset of their neurological symptoms during puerperium including. The symptom included headache (20 cases), epileptic seizures (13 cases), blurred vision (11 cases), disturbance of consciousness (2 cases), and drowsiness (3 cases). In our study, MRI lesion characteristics were as follows: the frequency of the parietal lobe was 49%, the frequency of the occipital lobe was 33%, the frequency of the frontal lobe was 44%, the frequency of basal ganglia was 20%, and the frequency for the temporal lobe was 18%. Their clinical manifestations included headache (20 cases, due to increased intracranial pressure), epilepsy (13 cases, due to involvement of the temporal lobe), blurred vision (11 cases, due to involvement of the occipital lobe), disturbance of consciousness (2 cases, due to involvement of the brain stem), and drowsiness (3 cases; due to involvement of the brain stem).

Neuroimaging features

A head CT scan results showed large symmetrical and hypodensity lesions of white matter in both cerebral hemispheres and the abnormal signals in the parietal, frontal, occipital, and temporal lobes, basal ganglia, cerebellum, and the radiate canal. The head MR scan findings revealed white matter lesions in the posterior cerebral hemisphere with hypo-intensity on T1WI, hyper-intensity on T2WI and FLAIR, iso-intensity or slight hyper-intensity on DWI, and iso-intensity or slightly hyper-intensity or hypo-intensity on ADC. Two out of three patients who were re-examined with head MR scans had a decrease in the extent of their lesions. Three out of the five patients who underwent MRA or CTA showed intracerebral arterial vasospasm. No obvious abnormality was revealed on MRV.

Misdiagnosis

Forty-five patients with RPLS were misdiagnosed from 804 patients with severe eclampsia.

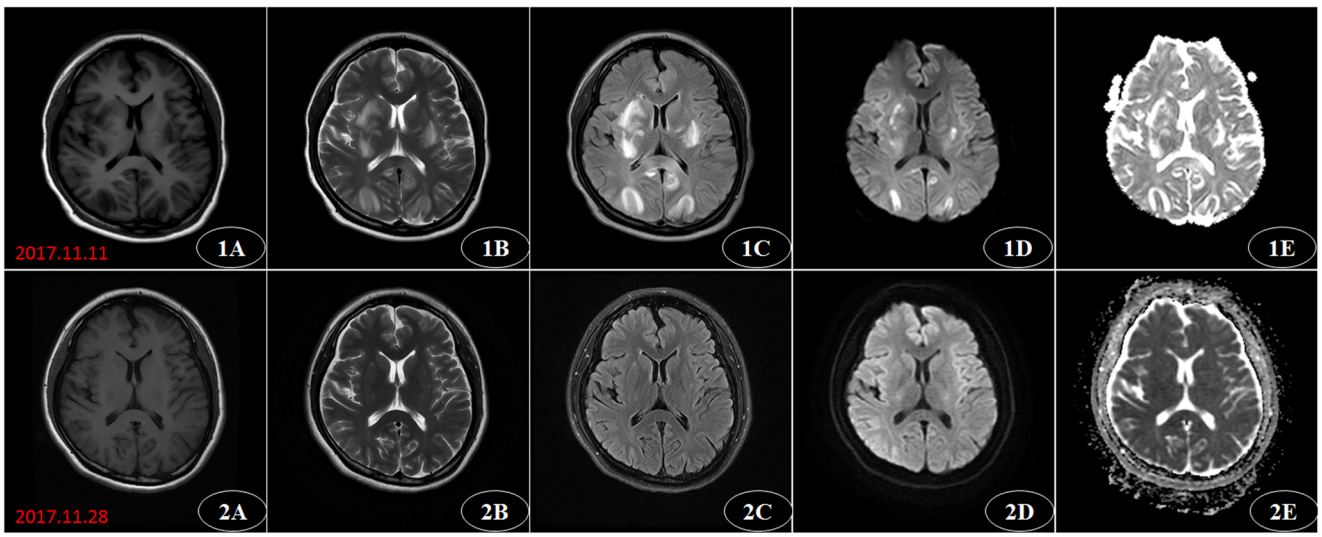

Fig. 1 The representative images are from a 30-year-old female with a 1 day history of loss of consciousness after cesarean section and a blood pressure of 166/100 mmHg. Figure 1A–E show multiple abnormal signals in the bilateral occipital lobe, basal ganglia, and corpus callosum with a low T1 signal and high T2, FLAIR, DWI, and ADC signals. Figure 2A–E show MRI scans performed after 17 days where lesions are no more visible

Treatment and prognosis

The clinical states of all the patients were improved after the reduction of cerebral edema, regulation of blood pressure, and controlling of seizures.

Follow-up

On follow-up after 6 months, 40 patients had recovered completely while 5 patients could not be contacted.

Discussion

An association between eclampsia and RPLS was first proposed and named by Hinchey et al. in 1996 [1]. Due to numerous causes and complex clinical and imaging features, this disease is easy to be misdiagnosed which lead to a delay in the treatment and subsequent irreversible neuronal cell death. The common causes include hypertensive encephalopathy, eclampsia or pre-eclampsia, renal failure, and the use of immune-suppressants [2]. The incidence and rate of misdiagnosis in patients with RPLS are very high so it is important for clinicians to improve their understanding of this disease.

Pregnancy era, pre-existent hypertension, influence on birth or fetus were low birth weight and stillbirths. In our study, there were 45 patients with high blood pressure before and during pregnancy era. Unfortunately, no attention was paid to its impact on the fetus. The precise pathogenesis responsible for RPLS is still not clear. A dysfunction of cerebral blood flow autoregulation due to an abrupt elevated blood pressure resulting in blood–brain barrier breakdown and subsequent vasogenic edema is the most frequently proposed mechanism [3]. Due to the richness of the capillaries in the white matter and its loose structure, the extracellular fluid tends to remain in the white matter. Thus, the lesions are more often found in the loose white matter and less in the structurally dense cortex. All the patients in this study were derived from eclampsia patients and support this theory. A possible role of endothelial dysfunction has also been argued. Immunosuppressive or cytotoxic drugs can damage the vascular endothelial cells, leading to the release of proinflammatory cytokines, adhesion factors, and VEGF, which may cause blood–brain barrier breakdown. Vasoactive substances can make cerebral arteries spasm and induce cerebral edema.

Understanding the various clinical manifestations of RPLS is crucial for early diagnosis. Headache, disturbance of consciousness, seizures, and visual disturbances are considered to be common tetralogy of RPLS [4]. In this study, there were 20 cases of a severe headache, 11 cases of blurred vision, 13 cases of seizures, 3 cases of drowsiness, and 2 cases of disturbance of consciousness. Forty-five patients in this study showed a dramatic reversal of clinical symptoms and imaging changes within a short time after prompt treatment, and the prognosis was relatively good.

The imaging features of RPLS have been reported in many studies [5–7]. It is called “brain posterior” because the parietal and occipital lobes are most frequently affected. However, with the deepening of research on this disease, neuroimaging findings are not only limited to parietal and occipital lobes but also the frontal lobe, temporal lobe, cerebellum, brainstem, and basal ganglia can be affected [2]. Both CT and MRI examinations can show lesions of RPLS. On account of the higher sensitivity to soft tissue edema, MRI can find early lesions and small local abnormalities. Therefore, MRI is the preferred method for finding RPLS lesions [8]. DWI and ADC map contribute to the diagnosis of patients with RPLS and can also distinguish between cytotoxic brain edema and vasogenic brain edema in ischemic brain injury. In this study, no abnormalities were found in the CT scans of 20 patients. Low-density lesions on bilateral hemispheres, which were difficult to be detected, were visible in the remaining 25 cases. This was the main cause of missed diagnosis in some patients. The reasons for the high positive rate of cranial MRI in some patients are as follows: First, a patient may have the typical clinical symptoms. Second, if a patient undergoes the cranial MRI examination as soon as possible at the beginning of the disease, the diagnostic rate should be higher. In addition, MRA and MRV examinations can further exclude cerebral infarction, cerebral venous sinus thrombosis, and other cerebrovascular complications.

PRES had no clear diagnostic criteria. Diagnosis of PRES should be considered in all patients with acute neurologic symptoms (for example, seizure, encephalopathy or confusion, headache, visual disturbances) who are at risk to develop PRES (2). Patients with acute and subacute onset of neurological symptoms accompanied by specific clinical conditions (such as rapid increase in blood pressure, severe fluctuations in blood pressure, immunosuppression, autoimmune diseases, renal failure, pre-eclampsia, or eclampsia) need to consider PRES. The clinical symptoms and signs of PRES (such as blurred consciousness, seizures, headaches, and visual impairment) are not specific and can also be seen in other neurological diseases, so other white matter lesions need to be eliminated, like venous sinus thrombosis. The diagnostic workup was combined with clinical symptoms with neuroradiologic presentation. However, an atypical imaging presentation should not reject the diagnosis of PRES in a compatible clinical situation. In this study, the patients mainly suffered from severe eclampsia, which is an important factor in the pathogenesis of RPLS. We believe that the following are the main reasons for the misdiagnosis of RPLS: (1) There are no specific clinical and imaging characteristics associated with RPLS. (2) Most of the patients were pregnant women who

can undergo only a limited number of imaging studies due to concerns about radiation damage to the fetus; it is the main reason for the decrease of lesion extension in only 1 out of 3 patients who were followed up by MR scans. (3) A CT scan has a low positive rate, and the characteristics of MRI signals are similar to those of other diseases. (4) Obstetrics is the main first-diagnosis department for PRLS patients, and obstetricians lack awareness of this disease. The differential diagnosis of RPLS includes cerebral venous sinus thrombosis, venous cerebral infarction, top of the basilar artery syndrome, mitochondrial encephalopathy, etc. However, these disorders do not have the course reversibility typically seen in RPLS. Cerebral venous sinus thrombosis and venous infarction, which can be identified on MRI and MRV, are also the common complications of pregnancy. The treatment of RPLS mainly includes the elimination of the cause, control of blood pressure, termination of pregnancy, rehydration, discontinuation of cytotoxic drugs, and hyperbaric oxygen therapy. After proper and prompt treatments, the clinical state of the patients improves in a relatively short time. Lesions may not be visible on imaging examinations anymore. The imaging examination is particularly crucial for the diagnosis of RPLS. For patients with postpartum headaches and repeated seizures, RPLS should be considered. Cranial MRI, MRA, and MRV should be performed in a timely manner for early detection. As the initial symptoms are reversible, the clinical state of the patients gradually improves with the elimination of the cause. The early targeted treatment is important to avoid neurological deficits [9].

Funding This paper was supported by the National Natural Science Foundation of China (Grant No. 81271268).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Hinchey J, Chaves C, Appignani B, Breen J, Pao L, Wang A, Pessin MS, Lamy C, Mas JL, Caplan LR (1996) A reversible posterior leukoencephalopathy syndrome. N Engl J Med 334(8):494–500
2. Porcello Marrone LC, Gadonski G, de Oliveira Laguna G, Poli-de-Figueiredo CE, Pinheiro da Costa BE, Lopes MF (2014) Blood-brain barrier breakdown in reduced uterine perfusion pressure: a possible model of posterior reversible encephalopathy syndrome. J Stroke Cerebrovasc Dis 23(8):2075–2079
3. Fugate JE, Rabinstein AA (2015) Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol 14(9):914–925
4. Yiş U, Karaoğlu P, Kurul SH, Soylu A, Çakmakçi H, Kavukçu S (2016) Posterior reversible leukoencephalopathy syndrome with spinal cord involvement in a 9-year-old girl. Brain and Development 38(1):154–157
5. Rykken JB, McKinney AM (2014) Posterior reversible encephalopathy syndrome. Semin Ultrasound CT MR 35(2):118–135
6. Siebert E, Bohner G, Endres M, Liman TG (2014) Clinical and radiological spectrum of posterior reversible encephalopathy syndrome: does age make a difference?—a retrospective comparison between adult and pediatric patients. PLoS One 9(12):e115073
7. Singh RR, Ozyilmaz N, Waller S, U-King-Im JM, Lim M, Siddiqui A, Sinha MD (2014) A study on clinical and radiological features and outcome in patients with posterior reversible encephalopathy syndrome (PRES). Eur J Pediatr 173(9):1225–1231
8. Chen S, Hu J, Xu L, Brandon D, Yu J, Zhang J (2016) Posterior reversible encephalopathy syndrome after transplantation: a review. Mol Neurobiol 53(10):6897–6909
9. Gao B, Lv C (2014) Posterior reversible encephalopathy syndrome in 46 of 47 patients with eclampsia: beyond it. Am J Obstet Gynecol 211(1):83–84