

Reversible posterior encephalopathy syndrome induced by drug intoxication: A case report

Souad Maher, Kaoutar Imrani, Vladmir A Blata,
Khadija Belhoussni, Ittimade Nasser

ABSTRACT

Posterior reversible encephalopathy syndrome (PRES) is a rare complication of a sudden rise in blood pressure. It is seen in hypertensive patients. It is a clinical–radiological entity characterized by the association of neurological clinical signs and bilateral posterior cerebral edema usually reversible in neuroimaging. According to the literature, it is quite common in adults than in children. The most common causes are hypertensive encephalopathy, renal failure, central nervous system vasculitis, electrolyte disturbances, or when using cytotoxic or immunosuppressive therapies. It is clinically manifested as headache, seizures, coma, or visual disturbances. Imaging plays an undeniable role in the diagnosis and surveillance and cerebral magnetic resonance imaging (MRI) reveals bilateral and asymmetrical lesions affecting the basal ganglia, the left frontal lobe and the parietal lobes, in the form of hyperintensities in sequences. T2 and fluid-attenuated inversion recovery (FLAIR) imaging lead to vasogenic edema. The treatment of the basic pathology is the key to the reversibility of this syndrome. We report this article with the aim of retrieving and demonstrating the interest of imaging as part of a diagnostic approach and monitoring of PRES in

a 54-year-old subject followed for schizophrenia and arterial hypertension under neuroleptic treatment having presented seizures with high blood pressure after 10 days of this neuroleptic treatment. The clinical course is favorable without recurrence of crisis with disappearance of the lesions on the imaging of the control after the interruption of the neuroleptics and the normalization of the arterial tension, living and asymptomatic patient on a retreat of one year.

Keywords: Intoxication, Magnetic resonance imaging, Reversible posterior encephalopathy syndrome

How to cite this article

Maher S, Imrani K, Blata VA, Belhoussni K, Nasser I. Reversible posterior encephalopathy syndrome induced by drug intoxication: A case report. Int J Case Rep Images 2020;11:101082Z01SM2020.

Article ID: 101082Z01SM2020

doi: 10.5348/101082Z01SM2020CR

Souad Maher¹, Kaoutar Imrani¹, Vladmir A Blata¹, Khadija Belhoussni¹, Ittimade Nasser¹

Affiliation: ¹Radiology Department, Ibn Sina-Rabat CHU, Mohamed V University, Faculty of Medicine and Pharmacy, Rabat, Morocco.

Corresponding Author: Souad Maher, Radiology Department, Ibn Sina-Rabat CHU, Mohamed V University, Faculty of Medicine and Pharmacy, Rabat, Morocco; Email: souad-maher@hotmail.fr

Received: 04 October 2019

Accepted: 11 December 2019

Published: 06 January 2020

INTRODUCTION

Posterior reversible encephalopathy syndrome (PRES) is an entity described for about 20 years. This clinical and neuroradiological condition was first reported by Hinchey in 1996 [1]. This description has been facilitated by the increasing use of MRI imaging.

Its pathophysiology remains uncertain, even if endothelial function plays a major role, with loss of cerebrovascular autoregulation and rupture of the blood–brain barrier (BBB) leading to cerebral edema. This diagnosis is mainly evoked in patients with neurological symptoms, in the context of renal failure,

arterial hypertension, certain autoimmune diseases, pre-eclampsia, or eclampsia [2].

Clinically, the syndrome is manifested by neurological signs of acute or subacute onset, settling over a few hours or a few days, very heterogeneous presentation, nonspecific, and more or less severe [2]. There is great variability in the clinical presentation of this syndrome and imaging aspects that are sometimes atypical [3, 4].

Radiologically, the key examination for this diagnosis is brain MRI. Typically, MRI found cortical and subcortical abnormalities of vasogenic edema (hyper T2 signal and FLAIR) predominant in the parieto-occipital regions (Figure 1), regressing a few days or weeks [5].

The purpose of this article is to review and demonstrate the interest of imaging in the context of diagnostic procedures and monitoring of PRES.

CASE REPORT

A 54-year-old patient, without medical–surgical background, followed for schizophrenia and schizoaffective disorder treated by neuroleptic–haloperidol—at a dose of 10 mg/day per os. After 10 days of treatment, the patient was referred for seizures with arterial hypertension at 180/100 mmHg. The clinical examination was without particularity. The brain scan and lumbar puncture were normal. Cerebral MRI demonstrated T1 hypointensity and proton density hyperintensity in T2 and FLAIR in the subcortical white matter was reflected in bilateral and symmetrical hypersignals of interest to the left frontal lobe and posterior parietal lobes and basal ganglia, which led to vasogenic edema (Figure 1). The differential diagnosis of PRES is broad, and history may be limited. Venous sinus thrombosis or subdural, intracerebral, or subarachnoid hemorrhage can all present with headache, seizures, reduced consciousness, and focal neurologic signs. Infective encephalitis or meningitis, particularly herpes simplex encephalitis, should be considered, and rapid treatment with intravenous acyclovir and antibiotics may be lifesaving while a diagnosis is still being pursued. It is important to consider the diagnosis of posterior circulation stroke, because its treatment (which may include urgent thrombolysis) and prognosis both differ from those in PRES. Basilar artery thrombosis can present with progressive neurologic deficits and can result in tetraparesis, coma, or locked-in syndrome. Central nervous system vasculitis can present with symptoms similar to those in PRES, but the MRI findings are usually more diffuse, and many of the clinical features and MRI findings are irreversible. The diagnosis may be difficult because systemic signs of inflammation are often absent, but rapid treatment is vital to prevent further complications. Autoimmune encephalitis and metabolic encephalopathies, such as deranged serum glucose, sodium (including central pontine myelinolysis), uremia, or drug toxicity (e.g., cyclosporine) can also have similar

progressive symptoms.

Antiepileptic treatment was introduced (phenobarbital 50 mg of a dose of 3 mg/day) for 15 days with interruption of the neuroleptic drug in the strong presumption of its involvement in the occurrence of this PRES. The relay was provided by dopaminergic drugs (carbidopa–levodopa 200/20 mg). The clinical evolution was favorable without recurrence of crisis. A control of cerebral MRI after one month showed a disappearance of these subcortical hypersignals in T2 and FLAIR (Figure 2).

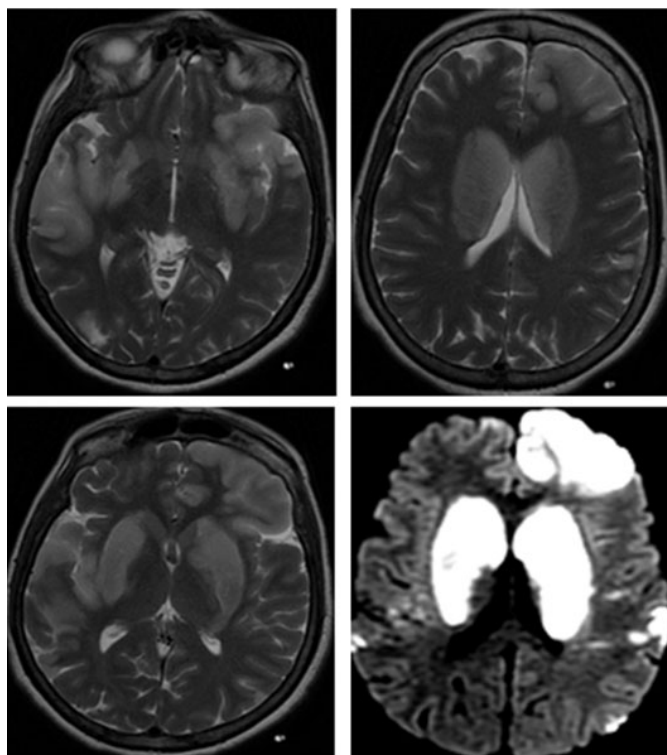


Figure 1: Initial brain MRI (T2 axial sections, diffusion) shows bilateral and asymmetric hyper signals affecting the basal ganglia, the left frontal lobe and the posterior parietal lobe regions.

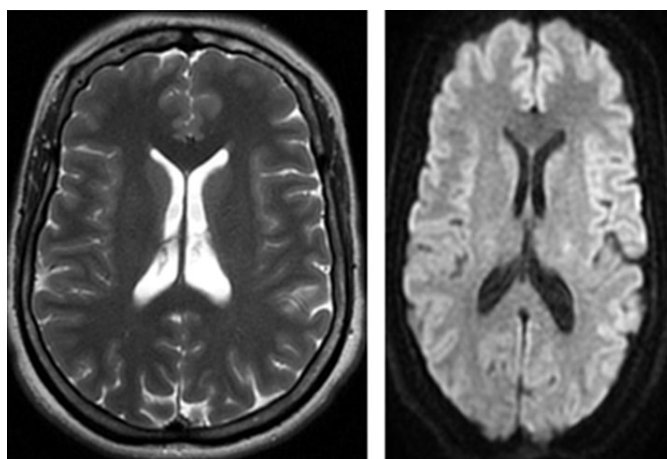


Figure 2: Control MRI in T2 and FLAIR axial sections at one month shows no signal abnormality on the FLAIR sequence.

DISCUSSION

Posterior reversible encephalopathy (RPE) is a clinico-radiological entity associating a reversible damage of the central nervous system with a typical encephalic imaging [MRI or computed tomography (CT)]. There is great variability in the clinical presentation of this syndrome and imaging aspects that are sometimes atypical [6]. Several etiologies may be at the origin of this syndrome, they are dominated by hypertensive encephalopathy [7], pre-eclampsia, eclampsia [2], immunosuppressive therapies, and renal disorders [2].

The search for an underlying general pathology should be systematic, as well as the search for a triggering factor in case of occurrence of posterior reversible encephalopathy. This entity is well described in the literature, but still little known by the majority of clinicians, where we hope our article can help.

Posterior reversible encephalopathy occurs mainly in cases of severe arterial hypertension. Although rare, this condition must be evoked in the presence of any sign of encephalopathy occurring in the context of acute hypertension.

On the physiopathological approach, it is an arteriolar vasoconstriction with obstruction and permanent ischemia that was initially mentioned. However, the rapidly reversible character of clinical symptoms and CT and MRI abnormalities argued against the theory of permanent ischemia with cytotoxic edema and neuronal death. Since the use of diffusion imaging, the theory of vasogenic edema is confirmed, since there is no signal increase and no reduction of analog-to-digital converter (ADC) with, instead, an increase of ADC which confirms an increase in the diffusion of open water [2, 8].

Vasogenic edema results from an opening of the BBB. High blood pressure is theoretically enough to open the BBB. Some associated factors (toxins, antibodies, and toxic molecules) can promote the alteration of the BBB. The posterior predominance of vasogenic edema is explained by the peculiarities of autoregulation of the posterior circulation [2, 8, 9]. The self-regulation of the cerebral circulation rests at the level of the small vessels on a myogenic and neurogenic mechanism. Endothelial lesions decrease the myogenic response, which leads to compensate for it by the sympathetic system, but it is less developed in the vertebrobasilar system and posterior cerebral arteries; this will result in an increase in the infusion. Alteration of the BBB, hyperinfusion, and arterial hypertension lead to predominantly posterior vasogenic edema. Vasogenic edema is rapidly regressive, probably in less than 15 days, with normalization of imaging.

Clinically, the syndrome is manifested by neurological signs of acute or subacute onset, settling over a few hours or days, very heterogeneous presentation, nonspecific, and more or less serious. Symptoms may be limited to headache [10], confusion [1], visual disturbances [10], and/or isolated epileptic seizures. Classically, headaches

are not abrupt start, but settle on a few hours to last a few days. It is recognized that headaches are usually diffuse and progressive in place, although thunderclap headaches are also possible.

In the absence of management, the symptoms usually worsen gradually over several days to weeks, including encephalopathy, confusion, or coma. There are also severe forms with hemorrhage or massive edema of the posterior cerebral fossa resulting in hydrocephalus or compression of the brainstem. The onset of generalized tonic-clonic seizures occurs in more than one out of every two cases, before the other symptoms. A state of epilepticus is also possible; it is suspected before cerebral imaging in case of bilateral and occipital abnormalities on the electroencephalogram (EEG). Finally, focal deficit neurological signs may also exist in hemiparesis type.

Radiologically, PRE is manifested by abnormalities of the white matter and gray matter, with preferential posterior regions suggesting edema of the parieto-occipital posterior cerebral regions [4]. Imaging is essential and must be carried out as quickly as possible to allow early diagnosis in order to establish adequate treatment and limit the risk of irreversible damage.

Computed tomography is frequently abnormal, with diffuse posterior hypodensities not taking contrast. In the initial phase, the scanner is not a good diagnostic test because in the absence of hemorrhagic or ischemic parenchymal complications, it is falsely reassuring, being normal in 40% of cases.

Magnetic resonance imaging is often characteristic, which makes it possible to pose the diagnosis in an evocative clinical context, but can also be normal. Although posterior encephalopathy lesions can be detected by cerebral CT, MRI is considered the gold standard examination. The lesions appear in isosignal or hyposignal T1 and hypersignal T2 and FLAIR. There is usually no enhancement after injection of contrast medium. Magnetic resonance imaging in diffusion sequence is the best diagnostic tool allowing a suitable and rapid treatment in order to prevent the appearance of irreversible neurological lesions and permanent sequelae [11]. The lesions are often subcortical, bilateral, and symmetrical in the parieto-occipital regions. Cortical lesions are possible, but rare. Brainstem and cerebellar involvement is common [6], whereas frontal lobe involvement is rare and often associated with a poor prognosis. The typical appearance shows diffuse subcortical and deep lesions.

Angiography or cerebral arteriography can show the vascular irregularities with focal and diffuse vasoconstrictions and focal vasodilations often responsible for a "pearl collar" appearance even in the absence of significant arterial hypertension.

Biological examinations are not contributory in the positive diagnosis of PRE. The lumbar puncture is almost systematic to eliminate meningeal hemorrhage if the brain scanner is normal.

One of the major criteria of this syndrome is that it is reversible, clinically and radiologically, at the origin of its classically favorable reputation. Thus, typically, the diagnosis of PRES must be evoked on a clinical and radiological basis in an evocative context to be posed wisely. Regression of the signs clinically and radiologically confirms the diagnosis a posteriori. In fact, the repetition of cerebral imageries is essential in this syndrome, especially since the differential diagnoses are numerous (stroke, thrombophlebitis, dissection, encephalitis, and migraine).

Regarding its treatment, the PRES has no specific support, knowing that it usually regresses when the precipitating or promoting factor can be controlled or eliminated. Overall, full recovery takes place over a few days to a week in more than three quarters of cases. The prognosis is even better if the diagnosis was established early with appropriate treatment [12]. An antiepileptic treatment can be justified in association with the strict control of the arterial hypertension if it exists (of at least 25% from the first hours, by preferring infusions in the antihypertensive treatment in order to avoid fluctuations its situations).

CONCLUSION

Posterior reversible encephalopathy is a rare, uncommon, and exceptional complication induced by intoxication by certain neuroleptics. Magnetic resonance imaging is the key test for diagnosis and monitoring. Early and appropriate management usually prevents the occurrence of irreversible sequelae.

REFERENCES

1. Hinchey J, Chaves C, Appignani B, et al. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334(8):494–500.
2. Cozzolino M, Bianchi C, Mariani G, Marchi L, Fambrini M, Mecacci F. Therapy and differential diagnosis of posterior reversible encephalopathy syndrome (PRES) during pregnancy and postpartum. *Arch Gynecol Obstet* 2015;292(6):1217–23.
3. Hugonnet E, Da Ines D, Boby H, et al. Posterior reversible encephalopathy syndrome (PRES): Features on CT and MR imaging. *Diagn Interv Imaging* 2013;94(1):45–52.
4. Papoutsis D, El-Attabi N, Sizer A. Postpartum posterior reversible encephalopathy syndrome (PRES) in a twin pregnancy complicated by preeclampsia-eclampsia: Case report. *Clin Exp Obstet Gynecol* 2014;41(3):351–3.
5. Dietemann JL, Jacques C, Schneider F, et al. L'encéphalopathie postérieure réversible. *Feuilles de Radiologie* 2001;41(5):397–405.
6. Ahn KJ, You WJ, Jeong SL, et al. Atypical manifestations of reversible posterior leukoencephalopathy syndrome: Findings on

diffusion imaging and ADC mapping. *Neuroradiology* 2004;46(12):978–83.

7. Bell MJ. A historical overview of preeclampsia-eclampsia. *J Obstet Gynecol Neonatal Nurs* 2010;39(5):510–8.
8. Bartynski WS, Boardman JF. Distinct imaging patterns and lesion distribution in posterior reversible encephalopathy syndrome. *AJNR Am J Neuroradiol* 2007;28(7):1320–7.
9. Bartynski WS. Posterior reversible encephalopathy syndrome, part 2: Controversies surrounding pathophysiology of vasogenic edema. *AJNR Am J Neuroradiol* 2008;29(6):1043–9.
10. Fisher N, Saraf S, Egbert N, Homel P, Stein EG, Minkoff H. Clinical correlates of posterior reversible encephalopathy syndrome in pregnancy. *J Clin Hypertens (Greenwich)* 2016;18(6):522–7.
11. Furukawa M, Terae S, Chu BC, Kaneko K, Kamada H, Miyasaka K. MRI in seven cases of tacrolimus (FK-506) encephalopathy: Utility of FLAIR and diffusion-weighted imaging. *Neuroradiology* 2001;43(8):615–21.
12. Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: Clinical and radiological manifestations, pathophysiology, and outstanding questions. *Lancet Neurol* 2015;14(9):914–25.

Author Contributions

Souad Maher – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Kaoutar Imrani – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Vladimir A Blata – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Khadija Belhoussni – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Ittimade Nasser – Conception of the work, Acquisition of data, Drafting the work, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy

or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission

The corresponding author is the guarantor of submission.

Source of Support

None.

Consent Statement

Written informed consent was obtained from the patient for publication of this article.

Conflict of Interest

Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

Copyright

© 2020 Souad Maher et al. This article is distributed under the terms of Creative Commons Attribution License which permits unrestricted use, distribution and reproduction in any medium provided the original author(s) and original publisher are properly credited. Please see the copyright policy on the journal website for more information.

Access full text article on
other devices



Access PDF of article on
other devices





Submit your manuscripts at
www.edoriumjournals.com

