IMAGING CHARACTERISTICS OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME (PRES)

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Posterior reversible encephalopathy syndrome (PRES) is a neuroradiological entity characterized by hypertension, altered mental status, visual disturbances, headache and generalized seizures associated with white matter changes predominantly affecting the posterior occipital and parietal lobes of the brain. Since Magnetic Resonance Imaging (MRI) is more sensitive and specific imaging technique than Computed Tomography (CT), establishing the diagnosis and follow-up in patients with PRES is based mainly on MRI findings. The typical imaging appearance of PRES most commonly includes hyperintensity on T2-weighted (T2W) and Fluid Attenuated Inversion Recovery (FLAIR) images seen in the parieto-occipital, posterior frontal, cortical and subcortical white matter. In addition to the typical MRI images, PRES may also have an atypical presentation, which is highly important to be recognized on time, in order to apply the timely and appropriate treatment. Acta Medica Medianae 2016;55(1):64-69.

Key words: Posterior Reversible Encephalopathy Syndrome, Magnetic Resonance, Computed Tomography, Brain

Introduction

Posterior reversible encephalopathy syndrome (PRES), or reversible posterior leukoencephalopathy syndrome (RPLS), which was first described by Hinchey in 1996, is a reversible syndrome with typical symptoms including an acute headache, seizures and visual disturbances. The PRES is primarily associated with white matter changes which predominantly affect the posterior occipital and parietal lobes of the brain, but may also spread to the brainstem, cerebellum, and other cerebral areas (1-3).

Since the precise pathogenesis still remains uncertain several different theories have been proposed as an explanation for the occurrence of this syndrome.

The exact pathogenesis of the condition is still unclear and remains a controversial issue, but there have been suggestions about the association with a dysfunction of autoregulation in the central nervous system vasculature. The increased blood flow and breakdown of the blood brain barrier are caused by the loss of autoregulation mechanism, resulting in the occurrence of a vasogenic edema during the conditions with elevated blood pressure. Due to the lack of sympathetic tone in vasculature arising from the basilar artery, there is a predisposition of the occipito-parietal areas to this condition (4-6).

However, a positive correlation between the extensiveness of cerebral edema and the level of blood pressure is not shown in this theory.

Another theory proposes that a vasospasm following a vasoconstriction resulting from a severe hypertension causes a local ischemia, arteriolar necrosis, and blood-brain barrier disruption, thus leading to a cerebral edema (5,7).

Several clinical conditions such as hypertensive encephalopathy, renal failure, acute intermittent porphyria, thrombotic thrombocytopenic purpura, preeclampsia, eclampsia etc. are commonly associated with this syndrome (8-11).

PRES has also been previously reported in some cases of patients having certain systemic conditions such as Systemic lupus erythematosus (SLE), Wegener granulomatosis, nonspecific renal inflammatory conditions (glomerulonephritis, hepatorenal syndrome), hypertension, and postchemotherapy (3,12-18).

This condition is normally completely reversible if it is diagnosed early and its underlying causes consequently treated.

The cases of the syndrome resulting in a fatal outcome are very rare. However, a fatal outcome can occur due to an increased intracranial pressure which is usually caused by a progressive cerebral edema, intracerebral haemorrhage or certain underlying pathology and complications (19).
Diagnosis of PRES

A typical clinical picture and the findings on magnetic resonance imaging (MRI) of the brain are used for the diagnosis of PRES.

The clinical diagnosis of PRES is established on the presence of certain conditions such as hypertension, headache, visual disturbances, altered consciousness and generalized seizures with characteristic MRI findings (1,2,9,20).

Imaging findings are of a primary importance for PRES diagnostics.

Imaging characteristics of PRES

Since MRI is more sensitive and specific imaging technique than Computerized Tomography (CT), establishing the diagnosis and follow-up in patients with PRES is based mainly on MRI findings.

The typical imaging appearance of PRESS most commonly includes hyperintensity on T2-weighted (T2W) and Fluid Attenuated Inversion Recovery (FLAIR) images seen in the parieto-occipital and posterior frontal cortical and subcortical white matter. In addition to the typical MRI images, PRES may also have an atypical presentation, which is highly important to be recognized on time, in order to apply the timely and appropriate treatment (7).

Less typical is the involvement of the brainstem, cerebellum and basal ganglia. Atypical MRI image findings include a restricted diffusion, contrast enhancement and hemorrhage (7,8, 21).

Since it is possible to reverse PRES, an adequate treatment usually completely resolves the deficits in a few days to weeks (Figure 1 a,b). However, as there have been reports of only partial resolution, the condition may result in a fatal outcome (22).

Figure 1. The first and a control brain MRI examination of the brain: a) FLAIR image shows typical cortical and subcortical hyperintensity lesions, b) after a few weeks there is a complete reversal of lesions on FLAIR sequence.

Typical presentation of PRES

The subcortical white matter of the occipital and parietal lobes of the brain predominantly affected by a widespread vasogenic edema, which is commonly reversible, is a typical radiological presentation of PRES. The distributions of vasogenic edema in PRES are usually seen as symmetrical and bilateral. However, they can also appear as asymmetrical or unilateral. (23).

The affected regions as seen on CT are indicated by areas of a diffuse white matter hypodensity (Figure 2 a,b,c). Isointense or low signal intensity on T1-weighted images, and high signal intensity on T2-weighted images indicate the lesions, on MRI (Figure 3 a,b,c).

Figure 2. Cranial CT shows areas of a diffuse white matter hypodensity affecting symmetrically: a) frontal lobes, b) parieto-occipital lobes, and c) left cerebellar hemisphere.

Figure 3. Brain MRI: a,b,c) axial T2W tomograms, d,e,f) axial FLAIR tomograms show typical presentation of areas with increased signal intensities in parieto-occipital and frontal region symmetrically bilaterally.

The changes in PRES are best seen on FLAIR images as cortical and/or subcortical hyperintensities (Figure 3 d,e,f). After an injection of a contrast agent there is usually no enhancement.

The lesions most frequently affect the parietal and occipital lobes, followed by the frontal lobes, the inferior temporal-occipital junction, and the cerebellum, in descending order. Bartynski et al. (7) noted three major patterns of distribution: holoispheric involvement in 23% of cases, involvement predominantly along the superior frontal sulcus in 27% of cases, and mainly a parietal and occipital involvement in 22% of cases. Despite the lesions appearing asymmetrically in 28% of cases, a highly typical appearance is that of bilateral and symmetrical lesions. A fact distinguishing PRES from bilateral infarct in posterior cerebral artery territory is that PRES commonly spares the calcarine and occipital lobe structure.
A reduced cerebral blood volume was revealed by perfusion imaging, which indicates a mechanism which involves cerebral hypoperfusion.

A mild damage of brain tracts which can be reversible is indicated by fractional isotrophy showing the zones of decrease and it is in accordance with a mild decrease N-acetylaspartate (NAA) values obtained by MR spectroscopy (24,25).

MR spectroscopy is not considered superior to conventional MR sequences. However, it can be very useful for ruling out other etiologies of changes. In approximately a half of the cases, an increased signal intensity is seen following the application of contrast agents (24).

Susceptibility-weighted imaging (SWI) is a technique used in recent years for the detection of microhemorrhagies. A higher occurrence rate of microhemorrhage in PRES, associated with vasculopathy has been revealed by this sequence (26).

Atypical presentation of PRES

Clinicians should be aware of several other radiological features detected by neuroimaging that are atypical such as anterior, cortical, brainstem lesions, foci of permanent injury, hemorrhage into lesions, and unilaterality (27).

Early imaging characteristics of PRES, that precede the more classic clinical presentation, including mild sulcal hyperintensity on FLAIR and leptomeningeal enhancement on postgadolinium T1W sequences in the posterior parietal, temporal, and occipital lobes, have been described by Nakagawa et al. (21).

Rarely, the lesions can spread to the basal ganglia (14%), the brain stem (13%) and the deep white matter, particularly involving the splenium of the corpus callosum (Figure 4 a,b,c) (7). Despite this involvement being unilateral it does not necessarily indicate incorrect diagnosis.

Figure 4. Atypical presentation of PRES: a) axial CT, and b) axial MRI tomograms show a hypodense (hyperintense) lesion in left basal ganglia, b) axial MR tomogram also shows atypical presentation of areas with increased signal intensities in the brain stem.

The blood-brain barrier can be damaged by a progressive disorder of the cerebrovascular regulation mechanisms, in some severe forms, whereby an enhanced signal in T1-weighted images is shown in MRI with gadolinium injection (28). As described by Benziada-Boudour et al. (29) the appearance of a cytotoxic edema which would be shown as a decrease in diffusion coefficient is equally possible. Haemorrhage can occur in such cases that have progressed further. Haemorrhage is now becoming more recognized as an atypical manifestation in PRES and does not exclude the diagnosis (33). Depending on the study, it occurs in between 5 and 30% of cases. Its possible anatomical locations with a similar incidence include the brain parenchyma, occurring as a focal haematoma or petechial gyral pattern, or the subarachnoid space (Figure 5 a,b) (30-32).

Figure 5. Brain CT revealed a global brain edema with a subarachnoid hemorrhage: a) a large left parietal hematoma with a displacement of mediosagittal structures; b) compression with hemorrhage in the brainstem.

The exact pathological mechanism involved in PRES is still not clear. However, it is thought to be associated with hypertension and hyperperfusion or vasculopathy with resulting hypoperfusion (32).

Controversies about PRES

There is a controversy related to the term PRES or PRLS. First, the confusion may be caused by the term leukoencephalopathy, since it suggests that white matter is exclusively involved. However, in up to 94% of the cases, the presence of the lesions has been detected in gray matter as well. Second, the posterior cerebral hemispheres are not the only locations that show image changes and clinical features. Therefore, the term “posterior reversible encephalopathy syndrome” may be misleading. Third, a chronic seizure or death may occur caused by certain complications such as ischaemic or haemorrhagic stroke. In such cases the term “reversible” is inadequate due to the clinically and radiologically incomplete reversibility.

An early diagnosis of PRES as well as its proper management are of an essential importance in order to avoid irreversible ischemic damage or death (20,35).

Differential diagnosis

The differential diagnosis of the T2W confluent white matter hyperintensities, includes a large number of conditions as well as other causes of vascular and inflammatory diseases.

The conditions such as acute cerebral ischemia, infarcts including “top of basilar syndrome”, cerebral venous thrombosis, transient cerebral hyperaemia, Creutzfeldt-Jakob disease, gliomatosis cerebri, infections-meningitis encephalitis, post infectious encephalomyelitis, vasculitis, epinephrine induced, toxic or metabolic encephalopathy, and
demyelinating disorders, are considered in differential diagnosis (36).

Making a distinction between PRES and acute ischemic stroke is very important since there should be no aggressive management of hypertension in ischemic stroke, whereas in PRES hypertension should be controlled and managed actively.

DWI and ADC map are very useful for distinguishing between a vasogenic and a cytotoxic edema, which represents foci of irreversible ischemia. Both of these MR techniques are sensitive to molecular diffusion of water molecules. A decrease in Na+, K+-ATPase activity with a consequent decrease in water molecule transport results in cytotoxic edema showing a bright signal on DWI, whereas, caused by a T2 shine-through effect, on DWI, a vasogenic edema can show an increase of a signal intensity, but is commonly iso- or hypointense. Due to highly mobile water in regions of vasogenic edema, the ADC values are high, unlike in cytotoxic edema, which enables the precise differentiation. Since the signal abnormalities on DWI are not accompanied with a decrease in ADC values, the edema in cases of PRES, is of a vasogenic (Figure 6 a,b,c,d,e,f) (37-39).

A catheter angiography findings on PRES typically involve focal or diffuse vasoconstriction, vasodilation or a ‘string-of-beads’ appearance. CT angiography or MR angiography can also reveal these irregularities of vessels (7). Such findings may be confused with other medical conditions, such as vasospasm or vasculitis (40).

**Figure 6.** Brain MRI: a) DWI shows characteristic iso to hyperintensities due to T2 shine-through effects with b) high ADC values.

**Conclusion**

MRI findings are mainly used as a basis for establishing the diagnosis and follow-up in patients with PRES. The typical appearance of PRES includes hyperintense zones in the parieto-occipital and posterior frontal cortical and subcortical white matter revealed by neuroimaging. The recognition of atypical locations of lesions as part of PRES is very important in cases of the incomplete traditional expression patterns. The uncommon locations involve brain stem and deep white matter, whereas focal hemorrhage or subtle subarachnoid blood can complicate the lesions.

**References**

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Revijalni rad

IMIDŽING KARAKTERISTIKE SINDROMA POSTERIORNE REVERZIBILNE ENCEFALOPATIJE (PRES)

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Sindrom posteriorne reverzibilne encefalopatije (PRES) predstavlja neuroradiološki poremećaj koji se karakteriše hipertenzijom, izmenjenim mentalnim statusom, poremećajima vida, kao i generalizovanim napadima, uz prisustvo promena bele mase, dominantno zahvatajući posteriorne segmente okcipitalnih i parijetalnih lobusa. S obzirom da je magnetno-rezonantna imidžing (MRI) tehnika pregleda intrakranijalnih struktura senzitivnija i specifičnija u poređenju sa kompjuterizovanom tomografijom (CT), postavljanje dijagnoze i praćenje bolesnika sa PRES-om bazira se na osnovu MRI nalaza. Tipična imidžing prezentacija PRES-a najčešće se odnosi na hipersignalne promene na T2-weighted (T2W) i Fluid Attenuated Inversion Recovery (FLAIR) sekvencama, koje zahvataju kortikalnu i subkortikalnu belu masu parijeto-okcipitalnog i posteriornog frontalnog režnja. Pored tipične slike, PRES može dati i atipičnu prezentaciju, što je izuzetno bitno prepoznati na vreme, kako bi se primentila pravovremena i adekvatna terapija. Acta Medica Medianae 2016;55(1):64-69.

Ključne reči: sindrom posteriorne reverzibilne encefalopatije, magnetna rezonanca, kompjuterizovana tomografija, mozek