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Original Article

Susceptibility-weighted angiography and diffusion-weighted imaging in posterior reversible encephalopathy syndrome – Is there an association between hemorrhage, cytotoxic edema, blood pressure and imaging severity?

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ABSTRACT

Purpose. – To assess the significance of association and possible correlation between hemorrhage, cytotoxic edema, blood pressure and imaging severity in posterior reversible encephalopathy syndrome (PRES).

Materials and methods. – This retrospective study included the medical and imaging records of 35 consecutive patients with PRES. The clinical data analysis included the highest recorded blood pressure (BP) on the day of the ictus, MRI including spin-echo echo planar diffusion-weighted imaging (DWI), susceptibility weighted angiography (SWAN) and conventional sequences. The presence of hemorrhage and cytotoxic edema was evaluated for the significance of correlation and association with each other and with blood pressure and imaging severity.

Results. – On MR imaging, hemorrhage was found in 25.7%, and cytotoxic edema in 20% of patients. There was no statistically significant association of hemorrhage ($P = 0.403$) and cytotoxic edema ($P = 0.162$) with BP in contrast to significant association of hemorrhage ($P < 0.001$) and cytotoxic edema ($P = 0.011$) with imaging severity and with each other ($P = 0.002$). There was a significant correlation of hemorrhage (Cramer's V – 0.672) and cytotoxic edema (Cramer's V – 0.506) with imaging severity and with each other (Cramer's V – 0.523).

Conclusion. – The extent of imaging severity in PRES showed significant association and correlation with hemorrhage and cytotoxic edema. There was no statistically significant association of blood pressure with imaging severity, hemorrhage, and cytotoxic edema. Further prospective studies are needed to elucidate the pathophysiological mechanisms and their correlation with imaging findings in PRES.

Introduction

Posterior reversible encephalopathy syndrome (PRES) is an acute potentially reversible neurological disorder which presents with symptoms of neurotoxicity such as seizures, altered sensorium, headache and visual disturbances in a clinical setting of hypertension, uremia, chemotherapy, autoimmune disorders, preeclampsia or eclampsia and sepsis [1,2]. The typical neuroimaging feature is vasogenic edema in the bilateral parietooccipital region involving subcortical white matter [3]. Although the exact etiopathogenesis is unknown, the leading postulates include endothelial injury related to abrupt changes in blood pressure or effects of inflammatory mediators on the endothelium causing blood brain barrier breakdown and eventual brain edema [4,5]. Alternative hypotheses include vasospasm resulting in reversible edema progressing to cytotoxic edema in severe cases [6,7].

The atypical imaging findings in PRES include the involvement of deep white matter, basal ganglia, thalami, brain stem, cerebellum and spinal cord; the presence of hemorrhage i.e.

Abbreviations: DWI, Diffusion-weighted imaging; ESI, Enhanced susceptibility-weighted imaging; IPH, Intraparenchymal hematoma; MAP, Mean arterial pressure; MH, Microhemorrhage; PRES, Posterior reversible encephalopathy syndrome; SAH, Subarachnoid hemorrhage; SWAN, Susceptibility-weighted angiography; SWI, Susceptibility-weighted imaging.

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microhemorrhage (MH), intraparenchymal hematoma (IPH), and subarachnoid hemorrhage (SAH); foci of restricted diffusion and contrast enhancement [8,9]. The reported incidence of hemorrhage in PRES is variable, ranging from 15–17% of patients based on T2*GRE, FLAIR, CT and about 65% in studies based on susceptibility weighted imaging (SWI) [5,10,11]. Susceptibility-weighted angiography (SWAN) is an enhanced susceptibility imaging (ESI) technique which utilizes multi-echo gradient sequence and provides increased susceptibility weighting compared to T2* GRE. SWAN and SWI are different ESI techniques used to identify cerebral hemorrhage, the incidence of hemorrhage on SWAN has not yet been described in patients with PRES [12–14]. Diffusion-weighted imaging (DWI) is a sensitive tool to detect cytotoxic edema, seen in about 40% of children and 33% of adult patients with PRES as reported by Siebert et al. [15]. Previous studies report absence of significant association between imaging severity, hemorrhage, and restricted diffusion [9]. However, there is a lack of sufficient data regarding the correlation between imaging severity, hemorrhage and cytotoxic edema in PRES.

The purpose of this study was to determine the incidence of hemorrhage and cytotoxic edema by retrospective evaluation of the MR images of patients with clinically confirmed PRES. Second, was to look for the significance of association and any possible correlation between hemorrhage, cytotoxic edema, blood pressure and imaging severity in PRES.

Materials and methods

Study participants

The institute ethics committee of PIMS, Tiruvalla, India approved this retrospective study. The study group was comprised of 35 consecutive patients after exclusion of those with an alternate diagnosis on further work up or those who were at risk of bleeding (patients with low platelet count/elevated international normalised ratio or prothrombin time or partial thromboplastin time/those on oral or parenteral anticoagulants or antiplatelet drugs) or those who failed to improve with standard therapy for PRES from January 2010 to December 2016 as detailed in supplementary Table 1. The inclusion criteria were the same as in previous studies, i.e. patients with a diagnosis of PRES confirmed by classical MR imaging findings, in an appropriate setting followed by clinical resolution post therapy [5,8].

We reviewed the clinical records of the patients with an experienced clinical neurologist [RT] for symptoms of neurotoxicity at presentation, blood pressure at toxicity and known clinical associations such as autoimmune disease, cancer chemotherapy, sepsis, eclampsia and uremic encephalopathy. Blood pressures were acquired to calculate the mean arterial pressure (MAP) at toxicity to grade toxicity blood pressure as:

- normal (MAP < 105 mmHg);
- mild to moderately elevated (MAP = 106–115 mmHg);
- severely elevated (MAP > 116 mmHg).

The impact of imaging severity and complications on clinical outcome could not be evaluated as the modified Rankin scale at discharge was not assessed for many patients.

Image acquisition

All the subjects underwent MR imaging, i.e., DWI and SWAN with conventional sequences (T1W, T2W, and FLAIR) in a 1.5-T scanner (Signa HDxt, GE Healthcare). The parameters of single shot echo planar DWI were 5000/86.4/1 (TR/TE/excitations), b value of 0 and 1000, 5 mm/0.5 mm (Slice thickness/Interval) and 3D SWAN were 7.4/47.4/20° (TR/TE/Flip angle) with nine echoes centered on 47.4 ms with a slice thickness of 2.6 mm.

Image analysis

Two blinded radiologists ([AAG] and [SBH] with experience of > 5 years) independently assessed the MR imaging findings in PRES. Interrater differences were resolved through consensus.

Conventional imaging

The FLAIR images were evaluated for the imaging pattern and severity of PRES, modified from McKinney et al. [10]. Accordingly, PRES was classified into mild, moderate or severe (Fig. 1):

- mild PRES: cortical or subcortical hyperintensity without mass effect and with the absence of or mild cerebellar, brainstem or basal ganglia involvement;
- moderate PRES: confluent hyperintensities extending from the cortex to the deep white matter, not reaching the ventricular margin or with the involvement of any 2 following regions i.e. cerebellum, brainstem, or basal ganglia;
- severe PRES: confluent hyperintensities extending from the cortex to the ventricular margin, or edema causing a mass effect. The lesions involving all the 3 regions i.e. cerebellum, brainstem, and basal ganglia were also considered severe.

DWI

The DW images were visually assessed for cytotoxic edema, i.e. hyperintensity on trace images with low signal in the corresponding areas on ADC images (Fig. 2).

SWAN

The SWAN images were evaluated for hemorrhage, i.e. blooming in the hyperintense areas on FLAIR. The hemorrhagic complications were classified into MH, ICH, and SAH as described (Fig. 3):

- MH: foci of blooming in the regions involved measuring < 5 mm;
- ICH: foci of blooming in the areas involved measuring > 5 mm with or without associated mass effect;
- SAH: blooming on SWAN sequence involving the sulcal spaces or sulcal hyperintensity on FLAIR imaging.

Statistical analysis

Statistical analysis of all data sets was performed with SPSS, version 22 (IBM, Armonk, New York: IBM Corp). Chi square test was used to assess the significance of the association between hemorrhage, cytotoxic edema, blood pressure and imaging severity. The level of correlation between the nominal variables was determined using Phi and Cramer's V test. Both association and correlation between variables were assessed as association denotes a general relationship and correlation being more specific, denotes the strength of association between variables. A correlation co-efficient of > 0.5 on Phi and Cramer's test suggests that the two variables could measure the same concept. Cohen's kappa coefficient was used for interrater agreement of various imaging findings. A *P*-value of < 0.05 was considered statistically significant.

Results

Patients

Thirty-five patients with clinical history and imaging findings of PRES were identified. The average age of patients was