COMPUTED TOMOGRAPHIC EVALUATION OF POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME

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ABSTRACT

BACKGROUND AND PURPOSE

Posterior Reversible Encephalopathy Syndrome (PRES) is a neurotoxic state that occurs secondary to the inability of posterior circulation to autoregulate. The clinical spectrum and the underlying pathophysiology are still poorly defined. No conclusive evidence has been put forward regarding the relationship between clinical conditions and specific imaging findings of severity or location of oedema.

PURPOSE

To assess the role of computed tomography in evaluation of Posterior Reversible Encephalopathy Syndrome.

MATERIALS AND METHODS

55 patients referred to the Department of Radio-Diagnosis, with a history of neurological abnormalities, including altered mental function, visual loss, stupor with a predisposing history favouring PRES and followed up for a period of 10 – 30 days.

RESULTS

21 patients (38.2%) were females. 32 patients (58.1%) were in the age group between 21 to 30 years. Predisposing condition; 16 (29.1%) presented with pre-eclampsia, 12 (21.8%) with post-partum status in altered sensorium, 9 (16.4%) with seizures, 7 (12.7%) with hypertension, 6 (10.9%) with visual disturbances, 4 (7.3%) with eclampsia and 1 (1.8%) with uraemia.

20 cases (36.4%) showed findings suggestive of posterior reversible encephalopathy syndrome on initial computed tomography examination. 35 cases showed no initial radiological evidence suggestive of posterior reversible encephalopathy syndrome. Of the 20 cases which showed computed tomographic evidence of posterior reversible encephalopathy syndrome, recovery was noted in 5 cases (9.1%). Persistence of findings detected on first CT was noted in 13 patients (23.6%).

Regional predominance of the lesions was as follows. Frontal lobe (39%), Parietal lobe (32%), Temporal lobe (15%) and occipital lobe (15%).

CONCLUSION

Varied clinical manifestations are associated with anatomical findings recognisable by neuro-imaging as PRES. Prompt imaging is necessary for the recognition of the condition and appropriate therapy should be initiated as early as possible for better patient outcome. Further studies regarding this condition are needed to clearly identify clinical and neuro-radiologic correlates in patients with signs of PRES at the time of presentation and their long-term neurologic outcomes.

KEYWORDS

Computed Tomography, Posterior Reversible Encephalopathy Syndrome.

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INTRODUCTION: Posterior Reversible Encephalopathy Syndrome (PRES) is a neurotoxic state that occurs secondary to the inability of posterior circulation to autoregulate. The term was initially coined by Hinchey et al[1] in 1996. In spite of gaining substantial recognition since then, the clinical spectrum and the underlying pathophysiology are still poorly defined.

Global incidence of posterior reversible encephalopathy syndrome is less known. The only epidemiological data come from retrospective studies of patients seen between 1988 and 2013.[1-7] PRES has been reported in patients aged 4 to 90 years, although most cases occur in young to middle-aged adults, the mean age ranging across case series from 39 to 47 years. There is a marked female predominance that may reflect some of the causes. Many patients with PRES have comorbidities, which may be severe conditions, such as bone marrow or solid organ transplantation, chronic renal failure, and chronic hypertension.

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Clinical manifestations for diagnosis of PRES include the presence of headache, seizures, encephalopathy, and visual disturbances. These clinical manifestations appear to be the result of an acute encephalopathy that is probably related to oedema within the brain, usually in the cerebral white matter.

The newer neuro-imaging techniques are very much sensitive to changes in the distribution of water in the brain which makes it possible to detect white matter oedema even in its early phases. Imaging wise, findings of focal reversible vasogenic oedema suggests a diagnosis of posterior reversible encephalopathy syndrome.

Most common associations of the syndrome include acute hypertension, preeclampsia or eclampsia, renal disease, sepsis, and exposure to immunosuppressant's[2-5]. Less commonly, this condition has been described in the setting of autoimmune disease.[8-9]

Though the syndrome stresses on the posterior predominance of the lesions, the same on imaging are rarely isolated to the "posterior" parieto-occipital white matter and instead often involve the cortex, frontal lobes, basal ganglia, and brainstem.[6,7]

The underlying pathophysiology of PRES is yet to be clearly defined. Several theories have been proposed, the most widely accepted of which states that rapidly developing hypertension leads to a breakdown in cerebral autoregulation, particularly in the posterior cerebral region (where there is a relative lack of sympathetic innervation). Hyperperfusion ensues with protein and fluid extravasation, producing focal vasogenic oedema[9]. An alternative theory, which has been best characterised in pre-eclampsia, eclampsia, and sepsis, implicates endothelial dysfunction.[10,11] A third theory proposes that vasospasm with subsequent ischemia may be responsible.[12]

This condition is characterised by the rapid progress of symptoms and signs. Condition is reversible if detected in early stages and as such early recognition of PRES is important for timely institution of therapy, which typically consists of gradual blood pressure control and withdrawal of potentially offending agents.

Best modality for assessment of this condition is Magnetic Resonance Imaging. However, due to the disadvantages with the MRI like cost of the examination, duration for the same, non-availability in many places, CT can also be used as a useful adjunct and a valid modality for the initial detection and assessment of the same.

This study is to evaluate posterior reversible encephalopathy syndrome by computed tomography with clinical correlation and to detect the clinical associations and prevalence of this condition in the study group. Also, the helpfulness of the early detection and probable benefits of the same are discussed.

MATERIALS AND METHODS: Study population: 55 patients referred to the department of Radio-diagnosis from October 2013 to September 2015, with a history of neurological abnormalities, including altered mental function, visual loss, stupor with a predisposing history favouring PRES and followed up for a period of 10 – 30 days.

Study Design: Descriptive study.

Equipment: GE Healthcare BrightSpeed Elite - 16 slice CT scanner.

Inclusion Criteria:

1. Patients with clinical history of acute neurologic change including headache, encephalopathy, seizure, visual disturbance or focal deficit.
2. Brain imaging findings of focal vasogenic oedema.

Exclusion Criteria:

1. Patients who are unwilling to undergo computed tomography.
2. Patients with intracranial pathologies other than PRES and its associations on imaging.

Method of Data Collection: Brief clinical history, Consent for CT scan, CT brain – Non contrast.
Scan Range: Top of C1 lamina through top of calvarium,
Topogram: AP, Lateral; 120 kV, 10 mAs.
Scan Type: Axial. Detector configuration: 16 x 0.625.
SFOV: Head. kV: 120 mAs: 140.

RESULTS: Of these 55 patients, 21 patients (38.2%) were females. 32 patients were in the age group between 21 to 30 years accounting for 58.1%.

Of the 55 cases, 16 cases (29.1%) presented with pre-eclampsia, 12 cases (21.8%) with post-partum status in altered sensorium, 9 cases (16.4%) with seizures, 7 cases (12.7%) with hypertension, 6 cases (10.9%) with visual disturbances, 4 cases (7.3%) with eclampsia and 1 case (1.8%) with uraemia.

20 cases (36.4%) showed findings suggestive of posterior reversible encephalopathy syndrome on initial computed tomography examination. 35 cases showed no initial radiological evidence suggestive of posterior reversible encephalopathy syndrome. Of the 20 cases which showed computed tomographic evidence of posterior reversible encephalopathy syndrome, recovery was noted in 5 cases (9.1%). Persistence of findings detected on first CT was noted in 13 patients (23.6%).

Regional predominance of the lesions was as follows: Frontal lobe (39%), Parietal lobe (32%), Temporal lobe (15%) and occipital lobe (15%).

DISCUSSION: Posterior reversible encephalopathy syndrome (PRES) describes a usually reversible neurologic syndrome with a variety of presenting symptoms ranging from headache, altered mental status, seizures, and vision loss to loss of consciousness.

In the current study, a total of 55 patients with predisposing history or clinical condition suggestive of possibility of PRES were evaluated with computed tomography. Hinchey et al[1], opines that in their study in all

12 patients in whom the first imaging study done was CT, the radiologic diagnosis of white-matter disease was apparent on the scan. Although MRI yielded a higher-resolution image, it was not necessary for the diagnosis of reversible posterior leukoencephalopathy. The only advantage of MRI was its ability to show small, focal abnormalities beyond the limits of resolution of CT Various other studies by Schwartz et al,[13] Fisher et al,[14] Duncan R[15] have suggested that Computed tomography can be used satisfactorily to diagnose PRES.

In a study by Casey et al,[16] the author opines that PRES is usually diagnosed or ruled out by imaging. Typically, PRES may be suspected on the basis of history, but the clinical signs and symptoms are nonspecific. Imaging is thus an essential component of the diagnosis of PRES. When typical clinical risk factors are not present, or when the blood pressure is not dramatically elevated, improvement on follow-up studies may also be key in the diagnosis. Though the current study emphasises on imaging as the modality for detection of PRES, clinical diagnosis is equally important for better management of the patient. This typically holds good for the centres in rural and semi-urban areas of our country, where the availability of the imaging services are far from satisfactory.

In the current study, posterior reversible encephalopathy syndrome was predominantly seen in female patients. This is in keeping with the various other studies which show predominantly female preponderance.[1,5]

In the current study, the average age of presentation was 30.8 years (range, 1 – 63 years). The average age of presentation in the current study is relatively less, compared to other studies.[1,5,6] This may be due to the fact that more number of patients with pregnancy associated conditions were evaluated.

The main presenting features recognised in this study include: 1) Acute Hypertension, 2) Pre-eclampsia, Eclampsia, Post-partum status, 3) Seizures, 4) Visual disturbances.

The brain normally is protected from extremes of blood pressure by an autoregulation system that ensures constant perfusion over a wide range of systemic pressures. In response to systemic hypotension, cerebral arterioles dilate to maintain adequate perfusion, whereas vessels constrict in response to high pressures. Above the upper limit of autoregulation, hypertensive encephalopathy occurs.

Hypertension is one of the important causes of posterior reversible encephalopathy syndrome.[13,17]

In a study by Bartynski et al,[5] the authors found out that normotensive patients demonstrated the greatest degree of vasogenic oedema, whereas severely hypertensive patients demonstrated less brain oedema. This is in keeping with the present study, where degree of oedema was higher in normotensive patients.

Cases of eclampsia progressing to develop posterior reversible encephalopathy syndrome were noted in the study. Although, CT findings suggestive of posterior reversible encephalopathy was not present in these clinically suspected cases of posterior reversible encephalopathy syndrome, clinical evidence of recovery were documented in all the cases following appropriate and prompt institution of therapeutic measures. This can be attributed to the modality that was used for the diagnosis of the same. Computed tomography, although being the most common modality used and having advantages of easy availability and less time taken for evaluation of a patient, fails miserably in detection of the subtle early changes of posterior reversible encephalopathy syndrome. As demonstrated by this study, computed tomography can be normal in many cases in which clinical features of posterior reversible encephalopathy syndrome are present. In these types of clinical situations, appropriate therapy should be started and further imaging by MRI may be advocated.

This study raises an important question as to whether all patients with a classical clinical presentation of eclampsia routinely undergo imaging studies, given that the results may or may not affect their treatment. We are of the opinion that the current practice of confirming the diagnosis of eclampsia on the basis of the clinical presentation is sufficient and imaging to be reserved for patients with atypical presentations, such as those who develop seizures after delivery. In addition, the reversibility of clinical signs and radiologic abnormalities may argue against neuro-imaging of patients at risk of PRES. Thus it can be concluded that imaging is crucial for patients with an uncertain diagnosis, in whom timely imaging and a diagnosis of PRES may lead to more appropriate decisions regarding treatment of hypertension, thus preventing the possible development of permanent neurologic deficits.

Most cases with visual disturbances having spontaneous recovery may in fact be cases of PRES.[1,18]

Posterior reversible encephalopathy syndrome can also be seen in the setting of uraemia.[19]

The regional predominance of the lesions was varied and was noted most commonly in frontal lobes followed by parietal, occipital and temporal lobe. In the present study, the predominance of the lesion was in anterior circulation.[16]

The predilection for involvement of posterior circulation territories is generally accepted to result from the relatively sparse sympathetic innervation of the vertebrobasilar circulation.[20] In a healthy subject, cerebral autoregulatory mechanisms that have both myogenic and neurogenic components maintain constant brain perfusion. The effectiveness of the neurologic component of autoregulation is directly proportional to the degree of sympathetic innervation.[21] In patients with PRES, the myogenic response is blunted by either passive over distention of the vessel due to elevations in blood pressure[22,23] or direct toxic effects on the endothelium.[24] Because autoregulatory mechanisms are thus more dependent on the neurogenic response, the more poorly innervated areas in the posterior circulation are most vulnerable. The result is the leakage of fluid into the interstitium and vasogenic oedema.

In the current study, no overall difference in location of the lesion based on suspected aetiology was noted. This is in keeping with a study done by Fugate et al,[25] who also

found no difference in location based on suspected aetiology was noted.

In a study by Stott VL,[26] the findings of the focal parenchymal changes were not completely reversible in 3 of the cases their study. This is in keeping with the current study, wherein 13 patients failed to show reversibility of the lesions and were found to develop permanent neurological deficit. This could likely be to the delay in diagnosis as well as delayed commencement of the treatment for the same.

Reversibility is rarely the spontaneous evolution of PRES. However, if this is true for most patients, it is not a rule and some patients have an unfavourable outcome, in spite of a prompt correct therapy.[27]

Sparing of the calcarine fissure and paramedian occipital lobe structures helps differentiate PRES from bilateral infarction of the posterior cerebral artery territory.

LIMITATIONS:

1. Limited experience from a single tertiary centre.
2. The sample size.
3. Modality chosen for the evaluation of the condition. CT although is cost effective and affordable radiological investigation in an urban area, is still an expensive modality in rural and semi-urban areas. This is particularly applicable to the current study, as the same was performed in a tertiary centre located in rural area. Although, MRI is a standard and confirmatory radiological investigation for the evaluation of posterior reversible encephalopathy syndrome, CT can step in as an alternative modality for the evaluation of the same.
4. In addition, the patients who underwent imaging, majority were the ones presenting with pre-eclampsia, eclampsia and post-partum patients. This clearly represents a selection bias, likely introduced by the fact that the incidence of the condition is more commonly seen in this subset of the patients. Another selection bias stems from the fact that more female patients were imaged, possibly resulting in the gender predominance for presence of this condition in the current study.
5. Transplant and chemotherapy patient population is not represented as a result of the organisation of our medical centre.
6. Also, there may be a bias toward more benign cases because patients who died of acute critical illness had to be excluded to ensure reversibility.

However, requiring proof of reversibility is actually a strength of the study because it preserves the homogeneity of the population.

Despite these limitations, the current study suggests that the varied clinical manifestations as described earlier are associated with anatomical findings recognisable by neuro-imaging as PRES. The current study aims to shine some light on the varied manifestation of the condition and also stresses on the need for prompt imaging for the recognition of the same and instillation of appropriate therapy for better patient care.

Also the current study clearly identifies the need and sets the stage for a prospective study of clinical and neuro-radiologic correlates in patients with clinical signs of PRES at the time of presentation and their long-term neurologic outcomes.

CONCLUSION: Varied clinical manifestations are associated with anatomical findings recognisable by neuro-imaging as PRES. Prompt imaging is necessary for the recognition of the condition and appropriate therapy should be initiated as early as possible for better patient outcome. Further studies regarding this condition are needed to clearly identify clinical and neuro-radiologic correlates in patients with signs of PRES at the time of presentation and their long-term neurologic outcomes.

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