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ACCURACY OF MAGNETIC RESONANCE IMAGING IN THE DIAGNOSIS OF CENTRAL NERVOUS SYSTEM INFECTIONS IN CHILDREN AND ADOLESCENTS

Syeda Zakia Shah, Shahabuddin Siddiqui, Umair Ajmal

Pakistan Institute of Medical Sciences, Islamabad Pakistan

ABSTRACT

Objective: To determine the diagnostic accuracy of Magnetic Resonance Imaging in patients with suspicion of central nervous system infections keeping cerebrospinal fluid (lumbar puncture) findings as gold standard.

Study Design: Validity study.

Place and Duration of Study: Department of Radiology, Pakistan Institute of Medical Sciences Hospital, Islamabad, from Oct 2017 to Jul 2018.

Methodology: A total of 275 patients suspected for central nervous system infection of age 1 day-18 years presenting in children OPD and main OPD of PIMS hospital, of either gender were included. Patients with congenital anomalies e.g. Dandy Walker Malformations, Chiari Malformations, Anencephaly, Neural Tube defects and brain tumor were excluded. All the patients then underwent MRI and lumbar puncture as a routine protocol. Presence of central nervous system infections was checked in both. Data was analyzed using SPSS version 16.0.

Results: In magnetic resonance imaging positive patients, 160 (90.4%) were True Positive and 17 (9.6%) were False Positive. Among 98 Magnetic Resonance Imaging negative patients, 13 (13.3%) were False Negative whereas 85 (86.7%) were True Negative. Sensitivity of magnetic resonance imaging in the patients with suspicion of central nervous system infections keeping cerebrospinal fluid (lumbar puncture) findings as gold standard was found to be 92.49%, specificity 83.33%, positive predictive value 90.40%, negative predictive value 86.73 % and diagnostic accuracy of 89.09%.

Conclusion: Diagnostic accuracy of MRI for diagnosing central nervous system infections is quite high. The primary imaging modality in central nervous system infections is magnetic resonance imaging.

Keywords: Central nervous system infections, Encephalitis, Magnetic resonance imaging, Meningitis.

INTRODUCTION

Central nervous system infections are considered an important cause of morbidity and mortality worldwide[1]. Infections of central nervous system and adjacent structures are found to be life threatening with devastating consequences[2]. The most significant factor in prognosis of central nervous system infections is the identification of causative agents. This identification leads to specific therapeutic strategy and management[3]. Nervous system infections may be caused by bacteria, virus, and fungi. These agents are associated with typical clinical and imaging features[4]. A non-invasive imaging method is important for proper diagnosis. The primary imaging modality in central nervous system infections is Magnetic Resonance Imaging (MRI)[5].

Evidence exists that in neonatal brain infections, the preferred imaging modality over Computerized Tomography is MRI even in emergency situations. MRI techniques like diffusion weighted imaging (DWI) and MR spectroscopy provide valuable additional information regarding central nervous system lesions[6]. Central nervous system infection is found to be an emerging health problem with sustainable increase in number of cases every year. World Health Organization (WHO) had reported 350,000 deaths due to meningoencephalitis with an approximate incidence of 700,000 cases worldwide in 2004[7]. Prevalence of meningitis among children and young adults in Pakistanis is 1.57% with an estimated 23000 children die of central nervous system infection each year and a mortality rate of 34%[5].

Correspondence: Dr Syeda Zakia Shah, Senior Registrar, Department of Radiology, PIMS Islamabad Pakistan

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CNS infections may be classified in one of the following types depending on their T1, T2 and contrast enhancement characteristics; as ring enhancing lesions, enhancing nodules, space occupying lesions, grey matter hyperintensities and white matter hyperintensities.

Multiple MRI sequences are available which provide functional and molecular information. Imaging characteristics of CNS infections form a complex myriad. It is based on conventional magnetic resonance sequences, which narrow down the differential diagnosis. It is further differentiated into a single etiology using advanced MRI sequences and techniques[8].

To date, there is little data and very few studies have been carried out in Pakistan regarding accuracy of MRI in detecting CNS infection in children and adolescents. As different MRI patterns are also very important in diagnosis of disease, further studies may help understand and add to the knowledge of different patterns of central nervous system infections on MRI which may lead to prompt management and reduced morbidity and mortality in such patients.

METHODOLOGY

This validation study was conducted from October 2017 to July 2018 in the department of Radiology, Pakistan Institute of Medical Sciences, Islamabad. Two hundered and seventy five patients suspected for central nervous system infection from 1 day age till 18 years of age, of either gender were included. Patients with congenital anomalies e.g. Dandy Walker Malformations, Chiari Malformations, Anencephaly, Neural tube defects and brain tumor were excluded. Sample size was calculated by using WHO sensitivity & specificity calculator using 95% confidence intervals, 5% significance level, sensitivity of 96%, specificity of 85.71% and prevalence of 87.71%[5]. The sampling technique used was non-probability, consecutive sampling.

Study was conducted after taking approval from the department as this study was carried out to test the accuracy of a modality and there was no compromise in the patient's dignity, rights, safety and well-being. Confidentiality of data was however ensured. All the suspected patients of CNS infection presented in the children and main emergency/OPD of the hospital who were referred to the Radiology department for MRI, were included in the study. MRI was performed on 1.5 Tesla Phillips, Super conducting machine. Coronal, axial, and sagittal images were taken after proper positioning of the patient. The sequence in axial plane included; turbo spin echo (SE) T2-weighted sequence, SE T1-weighted pre and post contrast sequence and Fluid-Attenuated Inversion Recovery (FLAIR) sequence.

The MRI images of post contrast T1 WI sequences were examined by a qualified radiologist who determined the presence or absence and the location of abnormal enhancement in sulci, cisterns, ventricles, or any combination of these in cases of meningitis, heterogeneous post-contrast enhancement of T1 hypointense cerebral/cerebellar regions in cases of cerebritis, ring enhancing lesions in case of abscesses or subdural empyemas, nodular enhancement or ring enhancement of tuberculomas, irregular gyral enhancement of temporal lobes in cases of viral encephalitis, etc. The data was recorded on a proforma as positive or negative.

Lumbar puncture for cerebrospinal fluid (CSF) analysis was done by skilled senior doctors under strict aseptic conditions and CSF analysis was reported by a senior qualified pathologist. The outcome variable was measured as CNS infection existence or absence using MRI parameters.

Data was analyzed using SPSS version 16.0. Quantitative variable like age was calculated using mean and standard deviation. Qualitative variables like gender, positive CSF findings, and positive MRI findings were measured using frequencies and percentage. Diagnostic accuracy was measured to find the relationship between MRI patterns and cerebrospinal fluid. Inferential results were reported using 95% confidence interval and 5% significance level. Sensitivity, specificity, positive predictive value and negative

predictive value were calculated using 2x2 contingency table.

RESULTS

Out of 275 patients, 194 (70.55%) were between 1 day to 12 year of age (table-I). Out of these 275 patients, 196 (71.27%) were male and 79 (28.73%) were females with a ratio of 2.5:1.

MRI brain was performed on all patients who fulfilled the criteria. MRI findings were in favor of central nervous system infections in 177 (64.36%) patients. CSF findings confirmed central nervous system infection in 173 (62.91%) cases. In MRI positive patients, 160 were true positive and 17 were false positive. Among 98 MRI negative patients, 13 were false negative whereas 85 were true negative as shown in table-II. Sensitivity of MRI in the patients with suspicion of central nervous system infections keeping cerebrospinal fluid (lumbar puncture) findings as gold standard was found to be 92.49%, specificity 83.33%, positive predictive value 90.40%, negative predictive value 86.73% and diagnostic accuracy of 89.09%.

Table-I: Distribution of patients according to age.

Age (years)	No. of Patients (%)
1 day - 12 year	194 (70.55)
13-18 year	81 (29.45)

Mean ± SD = 10.36 ± 5.23 years

Table-II: Diagnostic accuracy of MRI in patients with suspicion of central nervous system infections keeping cerebrospinal fluid (lumbar puncture) findings as gold standard.

	CSF Positive Findings	CSF Negative Findings
MRI positive findings	160 (TP)	17 (FP)
MRI negative findings	13 (FN)	85 (TN)

TP: True positive, FP: False positive FN: False negative TN: True negative

DISCUSSION

In meningitis, only a minority of patients present with the classic triad of fever, neck stiffness, and altered mental status. Classic physical examination maneuvers, such as Brudzinski and Kernig signs are relatively insensitive although specific for predicting cerebrospinal fluid pleocytosis. Patients with parenchymal involvement, as occurs with encephalitis and brain abscess, may also have focal neurologic deficits or seizures. Early in the course of meningitis and encephalitis, MRI and CSF examination could appear benign, and clinicians should not be falsely reassured. Delaying antibiotic and anti viral therapies negatively impacts outcomes, in particular, with bacterial meningitis and herpes simplex virus encephalitis. As with other rare, life-threatening diagnoses encountered in emergency medicine, the diagnosis and treatment of brain infections needs proper history and physical examination, which should be further confirmed with relevant imaging and laboratory tests[9].

The introduction of MRI has created an important place for itself in the detection and further characterization of brain lesions. The detection rate of most CNS lesions by MRI exceeds 90%, in comparison to 77% for CT scan, without the need to invasively inject iodinated intravenous contrast agents or the hazardous radiation effects of x-rays. These safety measures of MRI are particularly advantageous to pediatric and elderly patients[10]. This study was conducted to assess the diagnostic accuracy of MRI in patients with suspicion of central nervous system infections, keeping cerebrospinal fluid (lumbar puncture) findings as gold standard. MRI supported the diagnosis of central nervous system infection in 177 (64.36%) patients. CSF findings confirmed central nervous system infection in 173 (62. 91%) cases. In patients with positive findings on MRI, 160 were true positive and 17 were false positive. Among 98 MRI negative patients, 13 were false negative whereas 85 were true negative. Overall sensitivity of MRI in detecting central nervous system infections was found to be 92.49%, specificity 83.33%, positive predictive value 90.40%, negative predictive value 86.73% and diagnostic accuracy of 89.09%, which is comparable to a study conducted by Vaswani *et al* showing sensitivity of 96% and specificity of 85.71% in patients with positive cerebrospinal fluid analysis findings[5].

According to Azad *et al*, who detected CNS infection in all of the CSF positive cases on CE-FLAIR sequence with sensitivity of 100% but with sensitivity of only 72% on CE T1WI[8]. In our study the sensitivity is high (92.49%), as Vascular and meningeal enhancements on T1-weighted sequence is quantitatively proven to be significantly greater than that for FLAIR sequence due to T1 shortening effect.

The limitations of FLAIR sequence are related to slight increase in duration of the MR study by about one minute. Longer effective TE and CSF flow artifacts can sometimes lead to hyperintense sulci especially in children on pre-contrast FLAIR and may make distinction of post contrast meningeal enhancement difficult[11].

Timely diagnosis of infectious meningitis is critical. A proper MRI protocol is essential in demonstrating unequivocal meningeal enhancement, as previously contrast-enhanced FLAIR sequence remained a subject of debate because of artifactual hyperintensities in the posterior fossa due to CSF pulsations and a lower relaxivity[11-14].

Nowadays, both MRI and CSF analysis are used for diagnosis of CNS infections[15]. MRI has a huge potential superiority in the diagnosis of CNS infections[16]. MRI can provide the images in 3D planes and various oblique planes, without causing artifacts, and it has no side effect on human body as there is no ionizing radiation. Nowadays, MRI has been used in the diagnosis of pathologies all over the body from head to toe. CSF in normal individuals has certain pressure and chemical components that maintain the relative stability of intracranial pressure. Central nervous system diseases result in pathological changes in the metabolism of neurons, which can change the property and components of CSF. If there is obstruction to flow of CSF, it will result in increased intracranial pressure. Therefore, the evaluation of CSF is one of the important diagnostic tools for central nervous system diseases. Both MRI and cerebrospinal fluid can detect pathological changes in human body, which makes contributions to the detection of diseases[17].

Cheng *et al*, found that both MRI and CT scan could be used to accurately diagnose lesions in the brain[18], but according to Dorsett & Liang, MRI detects abnormalities in 90% patients with viral encephalitis while CT scan was abnormal in about quarter of patients[19].

Spudich *et al*, found that Magnetic Resonance Imaging is superior in evaluating tissues within the lesion as well as tissue around the lesion. It is also very sensitive in identifying the size, number and distribution of lesions[20].

CONCLUSION

This study concluded that diagnostic accuracy of MRI for diagnosing central nervous system infections is quite high. The primary imaging modality in central nervous system infections is magnetic resonance imaging.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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