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ORIGINAL ARTICLE

Contrast-Enhanced Fluid Attenuated Recovery (FLAIR) Sequence of Magnetic Resonance Imaging for Tuberculous Meningitis in Paediatric Population

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ABSTRACT

Background: Tuberculous meningitis is a well known consequence of tuberculosis, related with top mortality and morbidity in emergent nations. Prompt recognition can play a noteworthy part in rewarding and treating patients of tuberculous meningitis.
Aim: To Ascertain the accuracy of contrast FLAIR MRI for diagnosis of tuberculous meningitis in children considering CSF culture as benchmark.
Setting: Radiology Department of AKUH.
Study Design: Cross-sectional study.
Place and Duration: This study was conducted at Department of Radiology, Aga Khan University Hospital, Karachi From January 2015 to December 2016
Sample Selection: A total of 148 paediatric patients with clinical impression of tuberculous meningitis for 6 months were incorporated in study. FLAIR images were carried out from skull base to vertex in coronal plane from nasion to occipital protuberance with interval of 1.5 mm and 5 mm sections were taken.
Data Analysis: Percentage were calculated for presentation of variables including FLAIR imaging findings, CSF Culture results and gender. Sensitivity, specificity, accuracy, positive and negative predictive values of FLAIR calculated and presented in percentages. Chi square test was applied taking P <0.05 as significant.
Results: 148 patients of which 67 were males (45.3%) and 81 were females (54.7%). Contrast enhanced FLAIR MRI test correctly identified 78.68 % of healthy individuals and labeled 76.68 % of the diseased correctly. Final stat showed 43 % of the people were correctly identified as true positive, 94 % of the people who were found negative were disease free in reality. The conclusive certainty for the imaging was found to be 78.37%.
Conclusion: MRI Contrast FLAIR imaging is a justifiable tool which can assist in before time identification of tuberculous infection of brain and primary start of antituberculous medications without waiting for CSF results which require up to weeks.
Keywords: Magnetic resonance imaging, Fluid attenuated inversion recovery, tuberculous meningitis.

INTRODUCTION

Meningitis can be explained as inflammation of the overlying membranes of the brain and spinal cord[1] . There are certain viruses, bacteria, or other microorganisms, and less commonly certain drugs can be resposible for this inflammation[2]. Tuberculosis shares 5.1 percent of the country's disease burden[3]. As stated in a survey of Pakistan demographics almost 50 million individuals are involved in this illness[4], of them 3-13 percent are children. The tuberculous meningitis infections derived from primary TB is found to be more in young population and intricates 0.3% of untreated primary disease. Tuberculousis involving meninges is a dominant, complicated sequelae of disease, with peak morbidity and mortality in under developing countries[5]. The comparative occurence of TBM is proportionately higher in first 5 years[6] has been described to be around 7-12% of all cases of tuberculosis. The ability of AFB culture for detecting Mycobacterium tuberculosis is far superior than PCR. A research proved that only 64% of culture-positive authenticated cases were found PCR positive[7] . A minimum of 10 to 100 organisms are required to detect M. tuberculosis in cultures. Because of this, the sensitivity of this investigation is outstanding and extends from 80% to 93%. Whereas, the specificity of culture is superior, around 98% [8], and for that reason it is benchmarked as gold standard. These investigations need sufficient amount of CSF along with painful lumbar punctures. Therefore, diagnosis of the disease remains a scareful question. Preliminary diagnostic imaging provides a central role in correct identification and prior management of tuberculous meningitis and can overcome morbidity and mortality[18]. Gadolinium enhanced MRI is usually identified as the best option for analysis of the disease including location of lesions and their demarcations, as well as areas of inflammation involved[10]. The gadolinium enhanced FLAIR imaging is proven to be beneficial in diagnosis of inflammatory brain diseases with sensitivity of 85% and specificity of 79%.[11] The visibility of enhancing meninges and tuberculomas are considered as two main suggestive findings for the diagnosis of TBM on this imaging technique. Non gadolinium MRI usually shows no signal abnormality. Combination of T1WI and FLAIR sequence has been used to assess the conspiquity and the count of lesions in individuals with brain tuberculomas[12]. T1WI with gadolinium are commonly performed. However, post gadolinium FLAIR sequence are found to be more reliable in appreciating leptomeningeal disease. Tuberculomas are identified as well defined lesions of variable sizes ranging from one to several centimeters. They can be solitary or multiple and can be found anywhere in brain parenchyma[13].

To the best of my knowledge, no data on gadolinium enhanced FLAIR in diagnosis of tuberculous meningitis specially in pediatric population has been published from our part of the world where the disease is almost endemic, so this study aims to evaluate the clinical usefulness of post contrast FLAIR sequence for prompt diagnosis of tuberculous meningitis in children in our population, for early diagnosis of this morbid and mortal disease.

METHODS

Setting: Department of Radiology, Aga Khan University Hospital, Karachi. From March 2015 to Feb 2017.
Study Design: Cross-sectional study.
Duration of Study: 2 years
Sample Size: Sample size was calculated by using sample size calculation software and was calculated to be 146.It was calculated by keeping the prevalence of tuberculous meningitis at 12%, sensitivity of FLAIR at 85% and specificity at 79%. Precision is 0.14 and confidence 95%.
Sampling Technique: Non-proability consecutive sampling.
Sample Selection: Inclusion Criteria: Pediatric patients were selected from both genders from 1 day of life upto 14 years of age

having suspicion of inflamed meninges i.e having complaint of headache, pyrexia, TB contact, stiff neck, behavioral changes, seizures and altered sensorium.

All patients who will undergo FLAIR imaging and CSF AFB culture sampling.

Exclusion Criteria: Confirmed cases of meningitis.

Data Collection Procedure:

1 Consent was taken from the guardians of patient.

2 Image of FLAIR sequence were obtained from vertex to skull base in coronal plane from nasion to occipital protuberance. Slice thickness was kept at 5mm with interval of 1.5 mm. TE at 109, and TI at 2500. TR will be kept at 9000. Images were obtained on Seimens Machines 1.5 Tesla.

3 Gadolinium contrast was intravenously given to all patients as per body weight by a power injector at 0.2 ml / sec.

4 Imaging analysis and reporting of images was performed by radiologist having five years of experience.

5 Results of CSF culture were chased from hospital lab software.

6 All data was entered in a standard proforma (Annex 1).

Criteria of Diagnosis on Imaging: Enhancement of meninges or subarachnoid space or along cranial nerves was considered as positive. Wheare as negative findings were labeled if no enhancement or signal abnormality was noted in subarachnoid space, meninges or along cranial nerves. If any ring enhancing nodular lesions (tuberculomas) are seen in brain parenchyma ; images are also labeled as positive.

Ethics: As the population was Pediatric age group the consent form was signed by taking permission from their guardians. They were informed that their names will not be disclosed and questionnaires would be kept at a safe place to ensure confidentiality.

Statistics: Entry of data was done on SPSS 20 software. Percentage were calculated for presentation of qualitative variables including FLAIR imaging findings, gender and culture results. Mean+ SD was calculated for age.Sensitivity, specificity, PPV, NPV and Diagnosis accuracy of FLAIR sequence was checked by two by two table and presented in percentages. Stratification of results was performed against age and sex to analyze effect modification. Chi Square test was applied post stratification taking P value <0.05 as significant.

RESULTS

148 patients were included in our study, 67 subjects were males (45.3%) and among them 81 were females (54.7%). The age ranges from birth upto 16 years having a mean value of 5 years +/_ 3 years. Cultures for AFB were affirmative in 26 patients (17.6%) and non detectable in 122 patients (82.4%). Contrast Enhanced MRI FLAIR findings supportive for tuberculosis were found in 46 cases (31.1%) and non supportive in 102 cases (68.9 %). (Table 1) Male and Female proportions were for total 26 positive AFB cultures were 11 (42.3%) for males and 15 (57.7 %) for females. There were 56 male patients found negative for AFB cultures (45.9%) and 66 (54.1%) were females. Similarly, 21 males (45.7%) were found positive on FLAIR imaging and 25 (54.3%) females. (Table 2) Cases which were positive on both cultures and FLAIR were 20. Six negative FLAIR cases were found positive on culture results. 74 patients appearing positive on FLAIR were found negative on cultures. 96 patients which were negative for imaging were also negative on CSF cultures. (Table 3.Therefore, considering these statistics 76.68 % of the diseased and 78.68 % of healthy individuals were correctly labeled by FLAIR MRI sequence. 94% of the people who tested negatve were not having tuberculous meningitis and 43% of the people who tested positive actually had tuberculous meningitis. The diagnostic accuracy for the contrast enhanced FLAIR sequence was found tobe 78.3%.

Table 1: Variables of the Pediatric study Population. n=148

Variables	n (%)
Age (years) Mean+- S.D	0.55+- 0.49
Minimum	0
Maximum	16
Gender	
Male	67 (45.3%)
Female	81 (54.7%)
AFB	
Positive	26 (17.6%)
Negative	122 (82.4%)
MRI	
Positive	46 (31.1%)
Negative	102(68.9%)

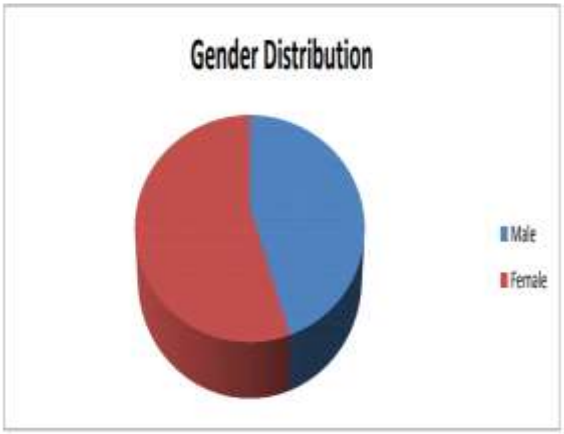

Figure 1: Pie chart showing gender distribution of the study population.

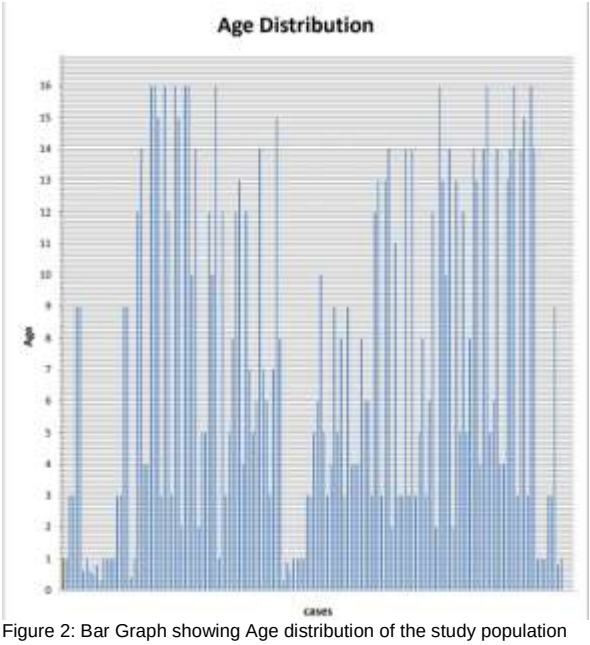

Figure 2: Bar Graph showing Age distribution of the study population

Table 2: Summary of investigations and results. n=148

Investigation	Male n %	Female n%	P-value
AFB			
Positive	11 (42.3%)	15 (57.7%)	0.45
Negative	56 (45.9%)	66 (54.1%)	
MRI			
Positive	21(45.7%)	25 (54.3%)	0.54
Negative	46 (45.1%)	56 (54.9%)	

Table 3: Chi-square test applied on results of MRI.

	+VE	-VE	
MRI	20	26	+VE
MRI	6	96	-VE

$$\text{Positive Predictive Value} = \frac{\text{True positive}}{\text{True positive + False positive}} \times 100$$

$$\text{Positive Predictive Value} = \frac{20}{46} \times 100 = 43\ \%$$

$$\text{Negative Predictive Value} = \frac{\text{True negative}}{\text{False negative + True negative}} \times 100$$

$$\text{Negative Predictive Value} = \frac{96}{102} \times 100 = 94.1\ \%$$

$$\text{Diagnostic accuracy} = \frac{\text{True positive + True negative}}{\text{True positive + False positive + False negative + True negative}} \times 100$$

$$\text{Diagnostic accuracy} = \frac{20+96}{20+26+6+96} \times 100 = 78.37\ \%$$

DISCUSSION

The most common route of spread of Tuberculous meningitis haematogenous spread from some other culprit organ. Histologically a tuberculoma consist of a caseous necrotic centre which is surrounded by a epithiloid cell capsule also containing collagen, lymphocytes and Langerhans giant cells. Its central necrotic part contains Tuberculous bacilli and ocassionally begins to form tuberculous abscess[14, 1]

There is usually a normal CSF study in most cases of tuberculous meningitis with clinical symptomatology and final reports of CSF cultures takes weeks. In our study we find a fair PPV of FLAIR contrast images of MRI which is about 43% likely due to diversity in tuberculoma appearance. Previous literature witnesses Tuberculomas to be an isointense centre with a hypointense rim on non gadolinium T1 weighted images, and a hypintense centre with hyperintense rim on T2 weighted images. Reduced lesions show isointense appearance on T1WI and hyperintense on T2W and FLAIR sequences with limited cases appearing hypointense on T2WI. Appearance of core hypointensity correlates with necrosis and hypercellularity. Liquifactive necrosis mostly shows T2 hyperintensity and T1 hypointensity likely due to free water within the lesion. Caseous necrosis in Tuberculomas is a different form of necrosis with large amount of fat contents[15, 16]. In our study we only detected FLAIR contrast sequences as criteria for being positive or negative MRI. This single sequence finding of MRI could be the reason for low PPV in our study. Tuberculous meningitis and viral encephalitis are the two vulnerable brain diseases where MRI can predict the diagnosis well before CSF culture results in hand. Here in our study we used gadolinium as contrast agent which is most widely used contrast agent for MRI. It helps to assess integrity of blood brain barrier in different intracranial diseases and infections including meningitis. The agent is paramagnetic and gets accumulated in infected areas causing shortening of T1 and T2 relaxation times. This study only observed Contrast FLAIR images sequence. The addition of widely used contrast T1 images could increase the PPV of MRI imaging. T1 contrast images with gadolinium are considered as standard for imaging of nearly all brain infections. However, the drawback of such images comes with detection of leptomeningeal disease which is often difficult because normal meninges also enhance to some extent and reduced T1 relaxation times due to gadolinium in normal vessels may create confusion[17, 18].

A good negative predictive value of our study i.e 94% is worthy enough to label as disease free. This is also in consistence with previous studies using gadolium enhanced FLAIR sequences for leptomeningeal infections. In our thought the cause behind this is suppression of CSF signals on FLAIR images resulting in better visualization of Tuberculomas and meningeal disease abutting CSF borders[19]

Also, slow flowing blood in not as hyperintense on post gadolinium FLAIR images as on T1 weighted post gadolinium images making better distinction between enhancing meninges and enhancing cortical vessels.

CONCLUSION

To conclude our study, contrast enhanced FLAIR sequence of MRI is anappropriate imaging which can aid in the primary identification of tuberculous meningitis. Our calculations and statistics showed values which are analogous with the forgoing available literature.

REFERENCES

1 Dastur HM, Desai AD. A comparative study of brain tuberculomas and gliomas based upon 107 case records of each. Brain 1965;88:375-86.

2 Splendiani A, Puglielli E, Amicis R, Necozione S. Contrastenhanced FLAIR in the early diagnosis of infectious meningitis. J Neuroradiol 2005;47(8):591-8.

3 ShamsiTs, Hashmi K, Adil S, Ahmad P, Irfan M, Raza S et al. The stem cell transplant program in Pakistan — the first decade. Bone Marrow Transplant. 2008 Aug;42(1):114-17

4 Iqbal J, Jamil A, Malik AH. Latent tuberculosis; jail as a risk factor.Professional Med J 2012;19(1):59-62.

5 Kalita J, Misra UK. Outcome of tuberculous meningitis at 6 and 12months: a multiple regression analysis. Int J Tuberc Lung Dis 1999;3(3):261-5

6 Rock BR, Olin M, Cristina A, Baker A, Molitor WT and Peterson K P. Central Nervous system Tuberculosis, pathogenesis and clinical aspects. ClinMicrobiol Rev 2008;21(2): 243-61

7 MafijUddin K, Hossain A, Ahmed T, Talukder AH, Barua PC, AwalMiah A etal. Comparison of Acid Fast Bacilli Microscopy, Culture, and Polymerase Chain Reaction for Detection of Mycobacterium tuberculosis in Clinical Specimens. JID 2009;180(183):191.

8 Daniel Brodie, MD, Neil W. Schluger. The Diagnosis of Tuberculosis. Clin Chest Med 2005;26:247-71.

9 Qamar FN, Rehman AJ, Iqbal S, Hymayun K. Comparison of clinical and CSF profiles in children with tuberculous and pyogenic meningitis; role of CSF protein: glucose ratio as diagnostic marker of tuberculous meningitis. J Pak Med Assoc 2013;63(2):206-210

10 Wasay M, Kheleani BA, Moolani MK, Zaheer J, Pui M, Hasan S et al. Brain CT and MRI findings in 100 consecutive patients with intracranial tuberculoma. J Neuroimaging. 2003;13:240–247
11 Parmar H, Sitoh Y, Anand P, Chua V, Hui F. Contrast enhanced flair imaging in the evaluation of infectious leptomeningeal diseases. Eur J Radiol 2006;58:89-95
12 Trivedi R, Saksena S, Gupta RK. Magnetic Rasonance Imaging in Central Nervous System Tuberculosis. Indian J Radiol Imaging 2009;19(4):256-64.
13 Gothwal SK, Khurana N, Khosya S, Gharpure N. Multiple Tuberculoma in Brain Presented with isolated ocular abnormality. J NeurolDisord 2013; 1:1 Definitions, and Descriptions: A Review. Radiology. 1999;213(3):647-62.
14 Whitener DR. Tuberculous brain abscess: report of a case and review of literature. Arch Neurol 1978;35:148-155.
15 Gupta RK, Pandey R, Khan EM, Mittal P, Gujral RB, Chhabra DK. Intracranial tuberculomas:MRI signal intensity correlation with histopathology and localized proton spectroscopy. Magn Reson Imaging. 1993;11:443-449.
16 Gupta RK, Jena A, Sharma A, Guha DK, Khushu S, Gupta AK. MR Imaging of intracranial Tuberculoma. J ComputAssist Tomogr. 1988;12:280-285.
17 Husstedt HW, Sickert M, Kostler H,Haubitz B, Becker H. Diagnostic value of the fast-FLAIR sequence in MR imaging intracranial tumors. Eur Radiol. 2000;10(5):745–752
18 Brant-Zawadzki M, Atkinson D, Detrick M, Bradley WG, Scidmore G. Fluid attenuated inversion recovery (FLAIR) for assessment of cerebral infarction. Initial clinical experience in 50 patients. Stroke.1996;27:1189–219.
19 Ginsberg LE. Contrast enhancement in meningeal and extra-axial disease. Neuroimaging ClinN Am. 1994; 4(1):133–152.