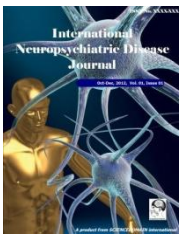

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Accuracy of Hyperintense Cerebrospinal Fluid Signals (CSF) on Inversion Recovery (IR) Images of Brain in the Diagnosis of Meningitis- a Cost Effective Experience from Third World Country

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Authors' contributions

This work was carried out in collaboration between both authors. Authors FM and SSMA designed the study and wrote the protocol. Author FM preformed the statistical analysis, managed the literature search, and wrote the first draft of the manuscript with assistance from author SSMA. Both authors read and approved the final manuscript.

Original Research Article

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ABSTRACT

Objective: To detect the diagnostic accuracy of inversion recovery sequence in detection of meningitis taking cerebrospinal fluid as the gold standard.
Material and Methods: This study was conducted in Aga Khan University Hospital (AKUH) Karachi. Retrospective data was reviewed from 1ST November 2010 to 31st November 2012.
All consecutive patients who came with clinical diagnosis of meningitis were included. Fifty patients were included in study on the basis of inclusion and exclusion criteria. Two independent neuroradiologists retrospectively reviewed FLAIR sequences blinded to CSF findings. Their findings were compared with cerebrospinal fluid results. Sensitivity, specificity, PPV, NPV and diagnostic accuracy were calculated.
Results: Hyperintense CSF signals on FLAIR sequence found to have 94.7% sensitivity, 83.3% specificity and accuracy of 92% in diagnosis of meningitis while PPV and NPV were 94.7% and 83.3% respectively.
Conclusion: We found that hyper intense CSF signals on FLAIR sequence has high accuracy in diagnosis of meningitis.

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Keywords: FLAIR; cerebrospinal fluid; meningitis.

1. INTRODUCTION

Now, there is established role of FLAIR sequence for leptomeningeal disease processes like subarachnoid haemorrhage, meningitis or metastases, cerebral venous sinus thrombosis with high-signal-intensity CSF mimicking subarachnoid haemorrhage on MR FLAIR images [1]. Actually FLAIR is an inversion recovery sequence in which inversion recovery pulse suppresses the signal intensity of CSF and allows detection of high protein or blood in subarachnoid space which appears as FLAIR hyper intensity [2].

Hyperintensity of subarcahnoid space on FLAIR depends on the amount of blood or protein and TE of sequence [3]. In many centers now post contrast FLAIR sequences are being acquired as there is mild T1W of FLAIR sequence [4]. Although enhanced study either FLAIR or T1W are most widely used sequence for detection of leptomeningeal process, however there are circumstances when patients cannot undertake gadolinium based imaging due to contraindications. In such instances unenhanced FLAIR can help in diagnosis of meningitis [5].

Hyperintense CSF on FLAIR imaging of the brain is a common clinical manifestation. There is a long list of differential diagnosis however correct diagnosis is possible with careful observation, distribution of hyper intensity, associated radiologic manifestations, clinical presentation and imaging parameters [6]. The rationale of our study is to use unenhanced FLAIR sequence as a cost effective tool in the diagnosis of meningitis in patients undergoing routine MRI without contrast. To our knowledge no such study has been conducted so far.

2. MATERIALS AND METHODS

We retrospectively reviewed the unenhnaced FLAIR sequence findings of 50 patients over a period of two years, who were admitted with clinical diagnosis of meningitis. Final diagnosis was based on patients past history, clinical examination and taking biochemical and bacteriological CSF results as gold standard.

Informed consent was waved off by the ethical review committee considering the retrospective nature of the study and the demographics were kept confidential.

All patients with clinical suspicion of meningitis were included. Patients with history trauma, subarachnoid haemorrhage, recent LP were excluded from the study. Patients with known malignancy, vasculitis, moya moya and CVST were also excluded.

Mean age of patients were 5-80 years. Included patients were 29 males (58%) and 21 (42%) females. MRI examination was performed on 1.5 Tesla MR scanner. We read FLAIR sequence in coronol planes. Imaging parameter of FLAIR ; tr:9290ms, TE:116ms, TI:2500ms, field of view 23cm, matrix 256*256, no of sections 25, slict thickness 4mm. Two trained neuroradiologists interpreted the images blinded to CSF findings. In case of disagreement the readers met a consensus determination. Interobserver variability was not calculated. Positive cases have hyper intensity in sulci. The statistical analysis was performed on SPSS 16. Sensitivity, specificity, postive and negative predictive value and diagnsotic accuracy were calculated.

3. RESULTS

Out of fifty positive cases, thirty eight were read as positive and twelve as negative on unenhanced FLAIR sequence. On later correlation with CSF thirty six of the fifty cases were true positive while ten were true negatives. The age group of positive cases was from 5-80 years with mean age of 47.5 years. There were twenty seven males and nineteen females. Positive cases included twenty cases of tuberculous meningitis, twelve were viral and four were bacterial meningitis on CSF culture.

There were two false positive cases one of which has signals due to significant motion blur and other one turned out to have positive malignant cells on cytology.

Similarly there were two false negative cases of bacterial meningitis because these patients were already empirically treated outside (Table 1).

Table 1. CSF characteristics of patients

Groups	Number of patients	CSF characteristics
True positives	20	Tuberculous infection on CSF culture
True positives	12	Viral infection on CSF serology
True positives	4	Bacterial infection on CSF culture
False positive	1	Normal CSF detailed report (D/R) and culture (artifactual due to motion blur)
False positive	1	Malignant cells on cytology
False negative	2	Partially treated bacterial meningitis
True negatives	10	Normal CSF detailed report (D/R) and culture

Thus there were thirty six true positive, two false positive, ten true negative and two false negative results on unenhanced FLAIR.

Overall, FLAIR found to have 94.7% sensitivity, 83.3% specificity and accuracy of 92% in detecting meningitis. While positive predictive value and negative predictive value were 94.7% and 83.3% respectively.

4. DISCUSSION

Sulcal hyperintensity is a relative term technically used to describe the failure to suppress the CSF signals on FLAIR imaging. It has been labelled in the past as “hyperintense CSF,” “leptomeningeal hyperintensity,” or “hyperintensity within the subarachnoid space” [7]. Most commonly these findings are substantially reported in patients with subarachnoid hemorrhage, leptomeningeal deposits and meningitis, sub acute infarctions and moya moya disease [8]. We did retrospective analysis of sulcal hyperintensity on FLAIR imaging in several patients who had clinical question of meningitis. Our primary results suggest that the findings are reproducible in a larger group of patients. These findings confirm our opinion that sulcal hyperintensity on FLAIR imaging is one of the indicators of CSF abnormality such as meningitis and it can be confirmed in correlation with appropriate clinical history and CSF analysis.

The sulcal hyperintensity was frequently seen in our patients with clinical question of meningitis (Figs. 1, 2, 3). It has been speculated that the paramagnetic effect from the blood

product and high protein concentration in the CSF is responsible for the hyperintense signals within the subarachnoid space, secondary to failure of normal CSF suppression [8,9]. This is supposed to occur due to T1 shortening or T2 prolongation [6]. The mechanism causing changes in the sulcal signal on FLAIR images and unenhanced T1- and T2- weighted imaging (dirty CSF sign) may be similar in patients without CSF abnormality, such as those having mass lesion, dural venous sinus thrombosis and stroke [10].

Increase of blood pool in the sulcal space causing failure of CSF signal suppression may be a possible mechanism. The relative ratio of CSF to blood is reduced per voxel in case of blood pool expansion secondary to inflammatory changes [11].

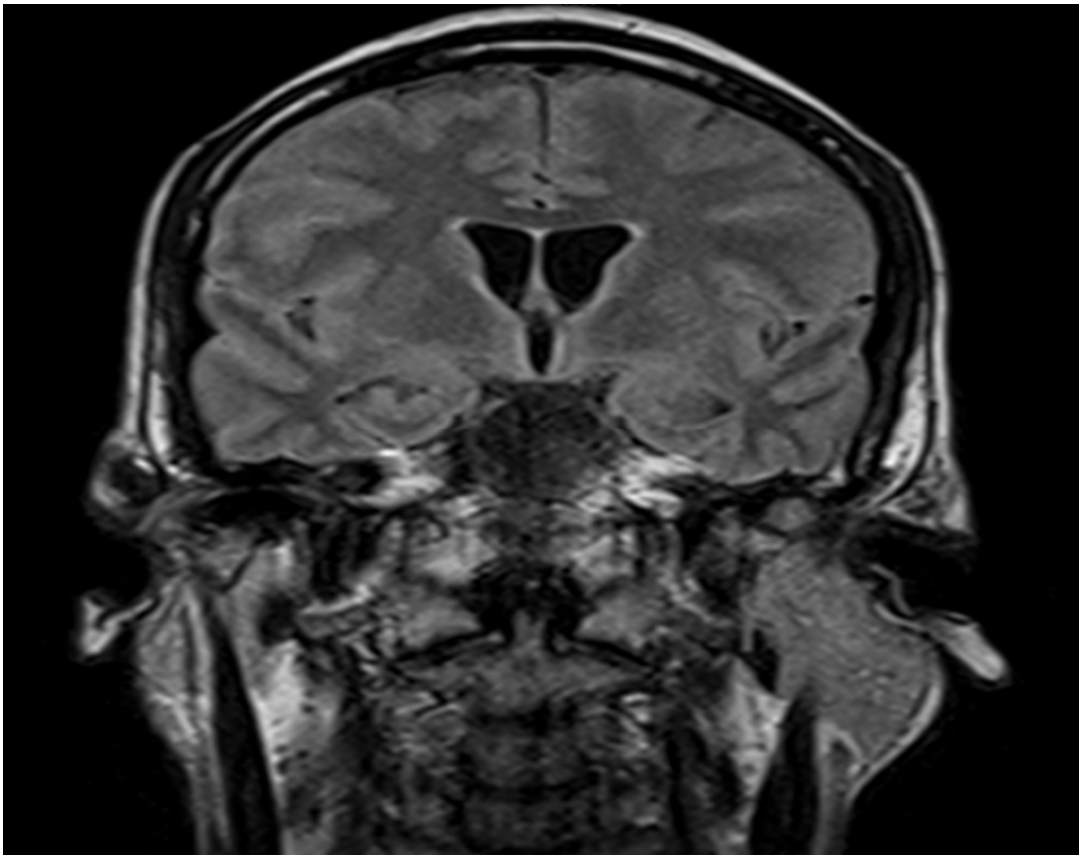

Fig. 1. 20 years old female admitted with diagnosis of meningits. Coronal
Unenhanced FLAIR image showing hyperitense signals in sulci and loss of normal CSF signals. Findings consistent with bacterial meningitis on Cerebrospinal fluid analysis

As specified by Taoka and Ercan et al. the sulcal space is composed predominantly of CSF and to lesser extent by arteries/capillaries (leptomeningeal) and venous network [12,18,19]. In normal subject the blood pool contributes less to the volume and it has oxygenated blood therefore the local magnetic field and signal intensity of CSF is not dramatically affected. This leads to satisfactory signal suppression [13]. Patients suffering from leptomeningeal disease has increased blood pool and in cases of venous congestion secondary to dural venous sinus thrombosis there is deoxthemoglobin which has paramagnetic effect causing

T2 shortening. This results in hyperintense signals within the sulci [14,15].

Our study had several limitations. Our elementary data cannot justify the mechanism explaining the sulcal hyperintensity on FLAIR imaging in patients with apparent CSF abnormality [16]. In addition, we only did retrospective review of subjects with clinical diagnosis of meningitis. Therefore, incidence and sensitivity of detecting sulcal hyperintensity and its associated pathophysiology and other MR findings were biased. Lastly, the hypothesized mechanisms in this study are unsubstantiated and are based indirectly on clinical and laboratory findings.

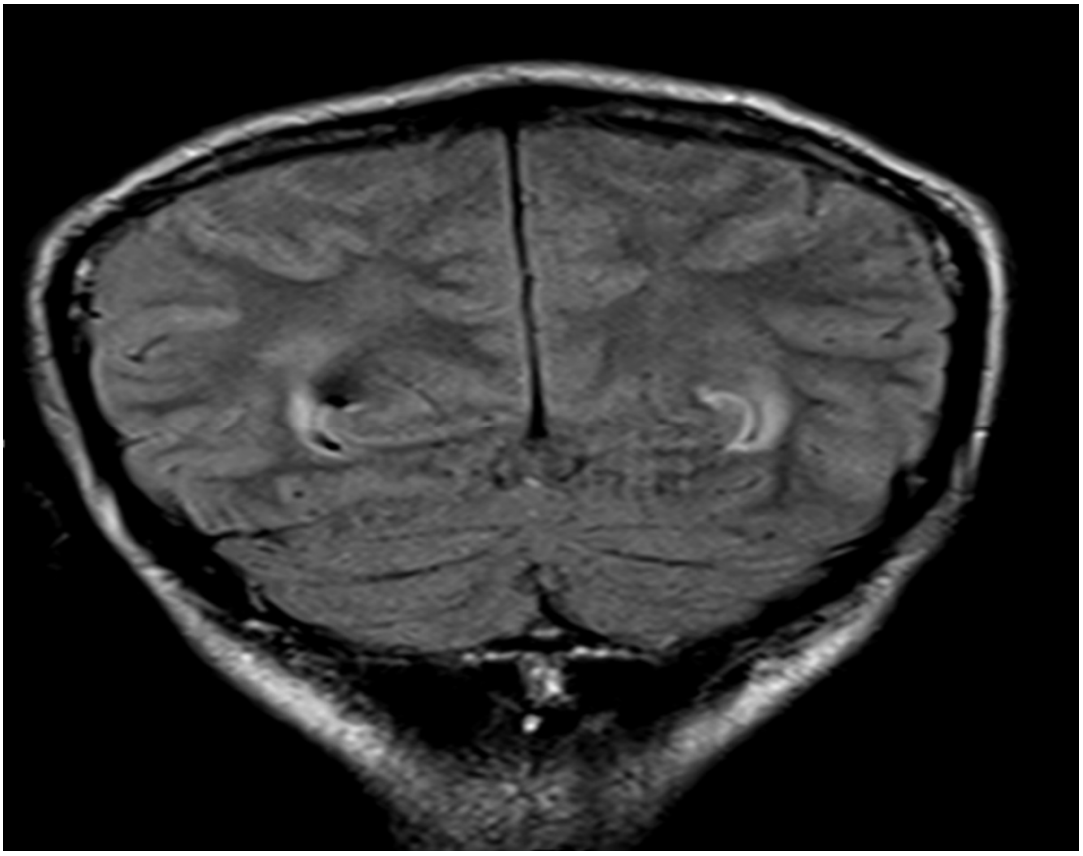

Fig. 2. 40 years old male admitted with diagnosis of meningitis. Hyperintense signals are seen in sulci with loss of CSF signals.Cerebrospinal fluid analysis was consistent with viral meningitis

Sulcal hyperintensity on FLAIR is a non-specific finding and occurs frequently in patients with or without CSF abnormality [17,18]. Therefore, patients coming to emergency department with signs of meningism may be suffering from the sinister diagnosis of subarachnoid haemorrhage which needs prompt recognition and treatment [19]. Careful triage and clinical correlation is of utmost significance.

However, this sign is very reliable if interpretated in proper clinical settings.

Another limitation of this study was that we have not calculated interobserver variability.

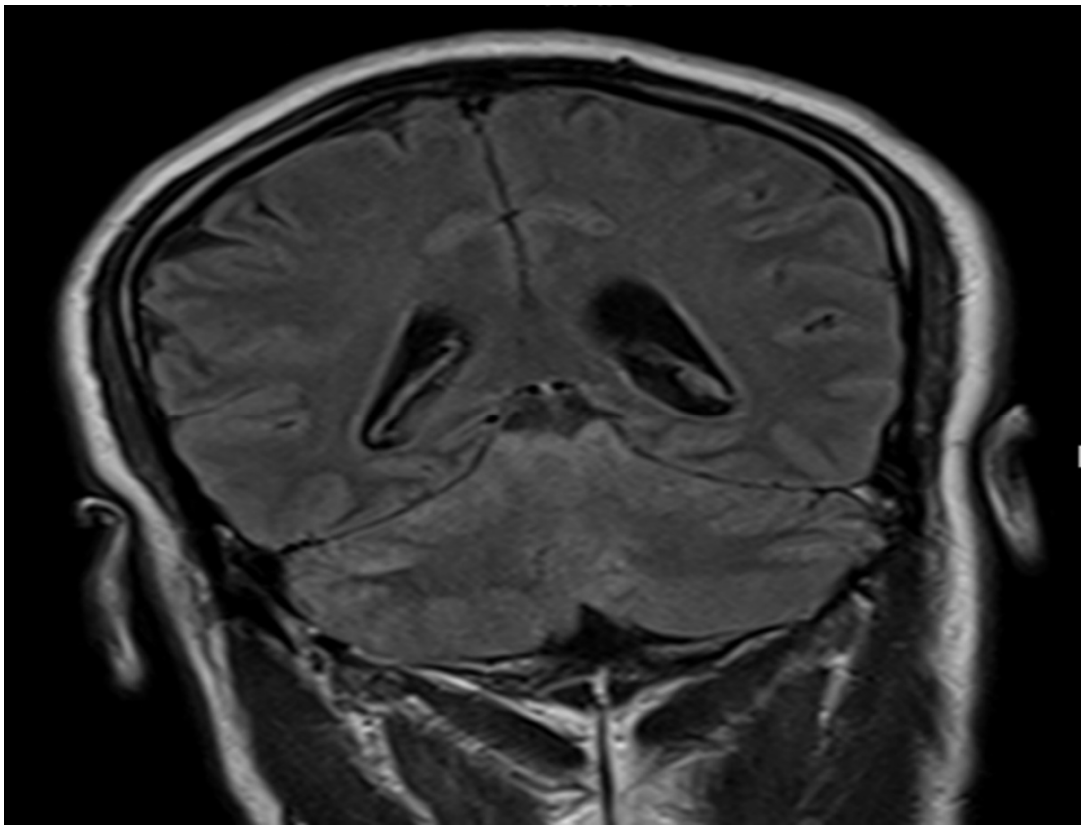

Fig. 3. 80 years old male admitted with diagnosis of meningitis. Unenhanced FLAIR shows hyperintense signals on FLAIR sequence with loss of CSF signals. Cerebrospinal fluid analysis shows high protein without any organism on culture and sensitivity. Subsequent cytology was positive for malignant cells

5. CONCLUSION

Hyperintense CSF on unenhanced FLAIR imaging of the brain is commonly seen in patients with meningitis. The differential diagnosis extends from conditions of high to little clinical significance. Correct diagnosis is possible with careful observation of distribution of hyperintensity, associated radiological manifestations, clinical presentation and knowledge of imaging parameters. We found that hyper intense CSF signals on unenhanced FLAIR sequence has high accuracy in diagnosis of meningitis, making it cost effective tool in our part of the world. Further confirmation of our findings with a large cohort and prospective study design can be a breakthrough.

CONSENT

Not applicable.

ETHICAL APPROVAL

Not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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