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KEYWORDS: CSF, MRI, Tuberculoma.

TO EVALUATE THE RELATIONSHIP OF MRI FINDINGS AND CSF ANALYSIS IN PATIENT DIAGNOSED WITH TUBERCULOMA.

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Abstract

BACKGROUND- CNS tuberculosis accounts for a high mortality and disability rate, representing the most severe form of tuberculosis. Early diagnosis and timely treatment are significantly critical to improve prognosis of these patients .

METHODS- It was a cross-sectional observational study conducted at Department of Radio-diagnosis, Geetanjali Medical College and Hospital, Udaipur.

RESULTS- MRI had a sensitivity of 87%, specificity of 92%, PPV and NPV of 83% and 94% respectively with a diagnostic accuracy of 90%. Three false negative cases were diagnosed as neurocysticercosis on MRI. One case of astrocytoma was falsely picked as tuberculoma on MRI. This patient had peripherally enhancing lesion on T1 contrast, hypointense lesion on T2, infratentorial lesion with perilesional edema.

CONCLUSION- MRI and CSF analysis are used for diagnosis of CNS infection. MRI has a huge potential superiority in the diagnosis of CNS infections. 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. CSF may provide with etiological basis of the disease, but may miss some diagnosis, as was in our study.

INTRODUCTION

Central nervous system (CNS) infections are a significant cause of mortality and morbidity world-wide. Today with the availability of excellent antimicrobials, many of these disorders are potentially treatable, making early recognition imperative. Like in other disorders of the CNS, non-invasive imaging-based diagnosis is the key as possibility of a tissue diagnosis by means of fine needle aspiration cytology (FNAC) or biopsy is difficult. Early diagnosis will also help to minimize long term complications related to the disease and its treatment.

Tuberculosis (TB), an infectious disease caused by the Mycobacterium tuberculosis, remains a major public health concern and ranks among the top ten causes of death worldwide. [1] Approximately 10 million people are infected with tuberculosis each year, especially those immunocompromised patients, such as HIV-infected individuals or people with risk factors like under-nutrition, diabetes, smoking and alcohol consumption. Tuberculosis typically affects the lungs (pulmonary TB) but can also spread to other sites (extrapulmonary TB) through lymphatic or hematogenous dissemination. Involvement of the central nerve system (CNS) occurs in 2e5% of patients with tuberculous infections and in up to 15% of cases of AIDSerelated tuberculosis [3,4] CNS tuberculosis accounts for a high mortality and disability rate, representing the most severe form of tuberculosis.[5] It mainly manifests as tuberculous meningitis, tuberculomas or tuberculous abscesses. Tuberculous meningitis is the most common form, followed by tuberculomas. Furthermore, tuberculomas represent 10%e30% of intracranial masses in tuberculosis endemic areas,[6] which may be indistinguishable from neoplasms. Early diagnosis and timely treatment are significantly critical to improve prognosis of these patients

MATERIAL AND METHODS

STUDY DESIGN- It was a cross-sectional observational study.

STUDY DURATION- It was 18 months (Feb 2019 to July 2020)

STUDY SITE -Department of Radio-diagnosis, Geetanjali Medical College and Hospital, Udaipur.

INCLUSION CRITERIA- All cases referred to department of radio diagnosis with suspected neuro-infections.

EXCLUSION CRITERIA –

1. All patients in whom MRI is contraindicated
2. Clinical conditions precluding the conductance of MRI.
3. Hypersensitivity to contrast media
4. Pregnant patients (use of contrast is contra indicated).

SAMPLING- Minimum sample size required was 71 or more. During the study period, we included 74 consecutive eligible patients.

DATA COLLECTION

Data were collected using a pre-designed semi-structured study proforma. We collected information regarding demography and presenting complaints from the medical records of the patients. The final diagnosis was made by the treating physician taking to account the imaging studies, CSF biochemical examination and clinical presentation. All patients underwent MRI brain and CSF biochemical analysis.

STATISTICAL ANALYSIS

The analysis included profiling of patients on different demographic, laboratory and clinical parameters. Descriptive analysis of quantitative parameters was expressed as means and standard deviation. Ordinal data were expressed as absolute number and percentage. Cross tables were generated for comparing MRI impression with CSF impression and MRI impression with the final clinical diagnosis of the patients. All analyses were done using SPSS software, version 24.0

RESULTS

In the present study, 74 patients were included. Mean age of the patients was 28.67 ± 16.21 years, ranging from 7 months to 77 years. It was observed that 14.9% of the patients were in aged less than 10 years and 11 to 20 years each, 27% were aged 21 to 30 years, 25.7% were 31 to 40 years of age, 8.1% were 41 to 50 years and rest of the 9.5% of the patients were aged more than 50 years of age. 36.5% of the patients were females (n=27) and rest being males (63.5%, n=47). The most common clinical presentation was headache, reported by 86.5% of the patients. Fever, seizures, vomiting, altered sensorium was observed in 79.7%, 62.2%, 60.81% and 56.8% of the patients respectively. Neck rigidity was reported by 40.5% of the patients.

Table 1. Distribution of patients according to their final diagnosis

Final diagnosis	Frequency	Percent
Meningitis	24	32%
Tuberculoma	23	31%
Neurocysticercosis	10	14%
HS encephalitis	6	8%
HIV encephalitis	4	5%
Abscess	3	4%
Creutzfeldt Jacob disease	2	3%
Astrocytoma	1	1%
Normal brain	1	1%
Total	74	100%

The most common diagnosis was that of meningitis, observed in 32% of the patients. Among these 24 cases of meningitis, 13 were that of tubercular meningitis, 8 were viral and 3 were bacterial meningitis. Tuberculoma was diagnosed in 31% of the patients. One patient who had findings of tuberculoma on MRI was diagnosed as low-grade Astrocytoma on follow up and biopsy. Neurocysticercosis was diagnosed in 14% of the patients and HS encephalitis was observed in 8% of the patients. Four patients had HIV infection. Three patients were diagnosed with abscess, two had CJD, and there was one case of astrocytoma. One patient who was suspected of meningitis was clinically and biochemically was found to be normal with no brain infection.

Table 2. Distribution of Tuberculoma patients according to their MRI findings

MRI findings	Frequency	Percent
T1+C		
Ring enhancing lesion	18	78%
Conglomerated lesions	5	22%
T2		
Central hypointensity with peripheral hyperintensity	11	48%
Hypointensity	11	48%
Isointensity	1	4%
LOCATION		
Infratentorial	3	13%
Supratentorial	20	87%
NUMBER		
Multiple	16	70%
Single	7	30%
PERILESIONAL EDEMA		
No	1	4%
Yes	22	96%
Total	23	100%

On T1 with contrast, 78% had ring enhancing lesion and rest had conglomerated peripherally lesions. On T2 imaging, 48% of the patients had central hypointensity with peripheral hyperintensity and hypointensity each, while one case had isointensity. Supratentorial location was observed in 87%, while rest of the lesions were infratentorial. Multiple lesions were observed in 70% and rest were single. Perilesional edema was observed in 96%.

Table 3. Distribution of Tuberculoma patients according to their laboratory findings

Lab investigations	Frequency	Percent
Blood WBC		
Increase	23	100
Blood ADA		
Borderline	1	4.3
Normal	1	4.3
Raised	21	91.3
CSF appearance		
Clear	11	47.8
Turbid	12	52.2
CSF protein		
Normal	5	21.7
Raised	18	78.3
CSF glucose		
Decreased	17	73.9
Normal	6	26.1
CSF lymphocytes		
Increase	18	78.3
Normal	5	21.7
CSF raised neutrophils		
No	21	91.3
Yes	2	8.7
CSF total WBC		
Increase	19	82.6
Normal	4	17.4
CSF culture		
Acid fast bacilli	10	43.5
Negative	13	56.5
Total	23	100

All the cases had an increase of blood WBC count and raised ADA was observed in 91%. CSF had turbid appearance in 52.2%, raised protein in 78.3%, decreased glucose in 73.9%, increased lymphocytes in 78.3%, raised neutrophils in 8.7%, increased total WBC in 82.9% and acid fast bacilli positive culture in 43.5%.

Table 4. Diagnostic performance of MRI as compared to CSF examination/clinical follow up

MRI	CSF	
	Positive	Negeative
Positive	20	4
Negative	3	47
Total	23	51

MRI had a sensitivity of 87%, specificity of 92%, PPV and NPV of 83% and 94% respectively with a diagnostic accuracy of 90%. Three false negative cases were diagnosed as neurocysticercosis on MRI. One case of astrocytoma was falsely picked as tuberculoma on MRI. This patient had peripherally enhancing lesion on T1 contrast, hypointense lesion on T2, infratentorial lesion with perilesional edema.

DISCUSSION

We observed that on T1 with contrast, 78% had ring enhancing lesion and rest had conglomerated lesions. On T2 imaging, 48% of the patients had central hypointensity with peripheral hyperintensity and hypointensity each, while one case had isointensity. Supratentorial location was observed in 87%, while rest of the lesions were infratentorial. This is in accordance with the statement of previous literatures.[7] Multiple lesions were observed in 70% and rest were single. Perilesional oedema was observed in 96%. MR Imaging findings of tuberculomas are varied depending on its three stages of maturation: noncaseating, caseating with a solid centre and caseating with a liquefied centre. Noncaseating tuberculomas generally exhibit hypointense signal on T1-weighted images and are hyperintense on T2-weighted and FLAIR images. They generally demonstrate homogeneous nodular enhancement on contrast- enhanced T1- weighted images. Caseating lesions with a solid centre appear relatively iso- to hypointense on both T1-weighted and T2-weighted images with an isointense to hyperintense rim on T2-weighted images, and with ring-like gadolinium enhancement. The rim may be inseparable on T2-weighted images with the presence of peripheral oedema. Caseating lesions with liquefied centres are hypointense on T1-weighted images and hyperintense with a hypointense rim on T2-weighted images, and show ring-like enhancement as well.

Ma et al reported that 60% patients had both supra- and infra-tentorial tuberculomas (brain stem and cerebellum), while four

(40%) had lesions located supratentorial (cerebral hemispheres, basal ganglia and thalamus). Tuberculoma was solitary in one (10%) patient, and multiple lesions were seen in nine (90%).[8] 122 tuberculomas were detected totally in all patients on contrast-enhanced T1-weighted images, of which 92 (75.4%) were dispersed in the cerebral hemispheres, 25 (20.5%) in the cerebellum, and five (4.1%) in the brain stem, with predominant distribution in the corticomedullary junction. The lesions were between 0.2 cm and 4.5 cm in size. One hundred ten of the tuberculomas were smaller than 1 cm, six lesions ranged from 1 to 3 cm, and the rest exceeded 3 cm in diameter. On T1-weighted images, 115 tuberculomas were mildly hypo- intense and almost indistinguishable from the normal cerebral gray matter, while 7 demonstrated central mixed isointensity and slight hyperintensity with hyperintense rim. On T2-weighted and FLAIR images, 35 lesions showed mildly hyperintense signals, 80 lesions demonstrated hypointense core with hyperintense rim, and central mixed isointensity and hypointensity with hyperintense rim was seen in seven lesions. On contrast-enhanced T1-weighted images, 35 lesions exhibited homogeneously nodular enhancement, and the rest manifested ring-like enhancement, either single ring or multiple conglomerate rings. Thirty-one tuberculomas exhibited peripheral edema and blurred the margin of lesions on T2- weighted and FLAIR images. There was accompanying meningitis in four patients, hydrocephalus in five, and unilateral or bilateral basal ganglia infarction in six. Meningitis manifested as meningeal enhancement, usually most pronounced in the basal cisterns on contrast-enhanced T1- weighted images.

Although cerebral tuberculoma is usually solitary and neurocysticercosis often presents as multiple lesions, the differential diagnosis of cerebral tuberculoma with multiple nodular lesions from neurocysticercosis is difficult, owing to similarities in clinical symptoms and CT/MRI imaging findings. Recently, Yuzawa et al described a case cerebral tuberculoma mimicking neurocysticercosis.[9] Magnetic resonance imaging (MRI) showed several lesions. Some were isointense on T1-weighted imaging and hyperintense on T2-weighted imaging. Others were hypointense on T1- weighted imaging and showed a hypointense area with a hyperintense fringe on T2- weighted imaging. Gadolinium-enhanced MRI showed ring-enhancing lesions. There were no findings suggesting bleeding on T2* imaging. The key to the diagnosis in the present case were the CSF ADA levels and peripheral blood T-SPOT assay.

In addition, 73.9% of our patients showed low glucose and 78.3% had high protein level in CSF examination. These results may be due to the presence of meningeal involvement. The presence of myco-bacterium tuberculosis may have stimulated a T-cell-mediated delayed allergic response accompanied by antibody release, resulting in elevated protein levels.[10] Low CSF glucose is attributed to consumption of glucose by mycobacterium tuberculosis. These results may be associated with mycobacterium infection but not specific for the diagnosis. As with other forms of TB, the gold standard of diagnosis is isolation of the organism through culture or detection of its presence by acid-fast staining.[11]

CONCLUSION

MRI and CSF analysis are used for diagnosis of CNS infection. MRI has a huge potential superiority in the diagnosis of CNS infections. 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. CSF may provide with etiological basis of the disease, but may miss some diagnosis, as was in our study.

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