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ORIGINAL ARTICLE

Evaluation of Central Nervous System Tuberculomas by Using Modern Diagnostic Techniques

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ABSTRACT

Aim: To assess central nervous system tuberculomas by using modern MRI techniques such as Diffusion MRI (dMRI), Nuclear magnetic resonance spectroscopy (NMR spectroscopy) and BOLD venographic imaging.
Study design: A retrospective study design
Study setting: From 5th Feb 2021 to 5th Feb 2022 at the department of Neurology of Ibe-e-Siena Hospital, Multan.
Methods: A retrospective study was conducted in the neurology department of Ibe-e-Siena Hospital & Research Institute Multan from 5th February 2021 to 5th February 2022. A total of 100 patients with suspected intracranial tuberculomas were included in the study. Advanced MRI techniques, including Diffusion MRI (dMRI), Nuclear magnetic resonance spectroscopy (NMR spectroscopy) and BOLD venographic imaging and conventional MRI, was performed on the patients. The study was approved by the ethical committee of the hospital, and all the patients provided their written consent for inclusion in the study
Results: NMR spectroscopy evaluation showed that N-acetylaspartate /Creatine and N-acetylaspartate /Choline ratios of tuberculomas did not differ significantly from malignant brain lesions (p>0.04). But the malignant brain lesion (2.59) were significantly higher than the Choline/Creatine ratio of tuberculomas(1.29). BOLD venographic imaging evaluation showed no hypointense peripheral ring in malignant brain lesions but showed complete and regular rings in 36 (58.1%) of tuberculomas.
Conclusion: Diffusion MRI did not help distinguish tuberculomas from metastasis and gliomas. However, NMR spectroscopy did offer this advantage by evaluating their unique metabolite pattern. BOLD venographic imaging showed the presence of a complete peripheral hypointense ring helping in diagnosing tuberculomas
Keywords: Intracranial tuberculomas, Nuclear magnetic resonance spectroscopy, diffusion MRI,

INTRODUCTION

Tuberculoma is a type of tuberculosis that is commonly identified as a caseous mass in the lungs caused by Mycobacterium tuberculosis[(1)]. Tuberculomas results in a variety of disorders. CNS tuberculomas are one the most contagious form of tuberculomas and occur as a result of haematogenous spread from a distant focus of tuberculous infection, usually the lung. CNS tuberculomas may present as meningitis or localized tuberculous lesion, abscess or myelitis[2]. Tuberculomas are lesions developed from tuberculous granuloma called Rich's focus which occur in the brain cortex[3,4].

Tuberculomas usually occur in the form of nodular lesions, but sometimes they also exist in multilocular or en plaque forms[5]. The occurrence of tuberculomas in developed countries is uncommon, but 5–30% of intracranial masses in developing countries consist of tuberculomas[6]. CNS tuberculosis has risen as a resurgent disease globally due to the HIV pandemic.

As it is a curable condition, it is important to employ techniques to differentiate intracranial tuberculoma from other various brain lesions to administer antituberculous therapy. It has been observed that conventional techniques like CT and MRI pose quite a challenge to diagnose CNS tuberculomas that present without meningitis.

MRI is not significantly effective in diagnosing tuberculomas, usually due to overlapping with other brain lesions. But if tuberculomas are diagnosed non-invasively, invasive procedures like biopsy can be avoided[7]. This highlights the need for procedures like MR spectroscopy (NMR spectroscopy), bolus-tracking MRI, Diffusion MRI (dMRI) and BOLD venographic imaging) which are not only more effective but also have reduced risks. With such modern diagnostic techniques, specific and improved diagnosis of intracranial tuberculomas can be made possible.

The chemical composition of the brain can be known by Proton NMR spectroscopy which helps in tuberculoma diagnosis. dMRI measures the water's Brownian motion within the tissue determining the apparent diffusion coefficient (ADC)[8].

BOLD venographic imaging techniques employ susceptibility differences to detect compounds like venous blood, hemorrhage and iron storage[9]. Tuberculoma lesions have an abundance of paramagnetic ions with consequent hypointense signal on CT chest (non-contrast) protocol. These lesions will present a more clear hypointense signal on BOLD venographic imaging, indicating the presence of paramagnetic ions. Thus, BOLD venographic imaging is expected in contributing to distinguishing tuberculomas from neoplastic lesions. This will add to data obtained by other diagnostic techniques. The present study is aimed to assess central nervous system tuberculomas by using modern MRI techniques such as Diffusion MRI (dMRI), NMR spectroscopy (NMR spectroscopy) and BOLD venographic imaging.

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MATERIALS & METHODS

A retrospective study was conducted in the neurology department of Ibe-e-Siena Hospital & Research Institute Multan from 5th February 2021 to 5th February 2022 after IRB permission. The study included 100 patients (60 males and 40 females) with suspected intracranial tuberculomas. The sample size was calculated by using Epi Info 7[10]. The patients' age ranged from 18-76 years (average age 45 years). The inclusion criteria for the study were: patients diagnosed or suspected with intracranial tuberculosis patients who displayed peripheral enhancing lesions on computerized tomography (CT) scan except for metastasis. The patients who were under MRI contradiction were excluded from the study. The patients were assessed by MRI, dMRI, NMR spectroscopy and BOLD venographic imaging after passing the inclusion and exclusion criteria and written consent of the patients. The procedure was performed by a trained radiologist.

The clinical profile and MRI analysis were assessed for administration of antitubercular therapy (ATT). ATT was only administrated to patients with focal brain lesions with related signs and symptoms of meningitis and associated findings like positive cerebrospinal fluid examination. ATT was also administered to patients with focal brain lesions alone by analyzing the conventional MRI results. The patients in which brain tumour was diagnosed after MRI were treated with surgery or stereotactic biopsy. The patients in whom metastasis was diagnosed by MRI were assessed to know the location of the tumour site. Patients in whom the tumour site could not be located underwent stereotactic core biopsy with histopathology determining lesions characteristics.

The study was approved by the ethical board of the hospital. All the data was analyzed by using SPSS version 21.

RESULTS

After performing MRI techniques, 62 patients were diagnosed with tuberculomas, and 23 patients had metastasis. Eight patients were diagnosed with gliomas, 5 with neurocysticercosis (NCC), and 2 had pyogenic abscesses. The patients were also evaluated as to response to ATT, tuberculomas were confirmed in 58 patients, and 5 patients were diagnosed with neurocysticercosis by analyzing the response to albendazole 63(63%). The diagnosis was confirmed in 27(27%) patients by histopathology, tuberculomas in 3 patients, metastasis in 14 patients, gliomas in 9 patients and pyogenic abscesses in 1 patient. The characteristics of several brain lesions are shown in Table I. All the brain lesions mostly showed ring-enhancing lesions in contrast enhancement. On diffusion MRI, the mean ADC value of tuberculomas was 1.025×10^{-3} mm^2 s^{-1}. The ADC value of hypo-intense tuberculomas was significantly high than that of T2W hyper-intense tuberculomas ($p \leq 0.0001$) (Tables II and III).

In NMR spectroscopy, we tested the lesions against several metabolites (Table IV). The NAA/Cr ratio of tuberculomas was higher than metastatic lesions, but it was statistically significant ($p = 0.134$). No statistical difference was calculated between high-grade glioma, NCC and pyogenic abscess due to a lesser number of patients. Comparatively, the Choline/Creatine ratio of tuberculomas (1.29) was significantly less than metastatic lesions (2.59).

A complete peripheral hypointense ring was observed in 36(58.1%) tuberculoma patients on BOLD venographic imaging, while 26(42%) patients showed no peripheral hypointense ring ($p\leq0.0001$) (Table V). The complete peripheral hypointense ring was not observed in metastatic lesions or gliomas patients. The difference between tuberculomas and metastatic lesions regarding the complete peripheral hypointense ring was significant ($p\leq0.0001$).

Table I: Morphology of brain lesions

Pathology	T_1 morphology		T_2 morphology	
	Isointense	Hypointense	Hypointense	Hyperintense
Tuberculoma	38 (61.2%)	24 (38.7%)	36 (58.0%)	26 (41.9%)
Metastasis	12 (52.1%)	11(47.8%)	8(34.8%)	15 (65.2%)
Neurocysticercosis	-	5 (100%)	-	5 (100%)
High-grade glioma	3 (37.5%)	5 (62.5%)	-	8(100%)
Abscess	-	2 (100%)	-	2(100%)

Table II: Average ADC of brain lesions

Pathology	n	Mean ADC value (×10–3 mm2 s–1)	Standard deviation
Tuberculoma	62	1.025	0.24
Metastasis	23	0.975	0.101
Neurocysticercosis	5	1.59	0.10
High-grade glioma	8	0.889	0.139
Abscess	2	0.395	-

Table III: ADC values for tuberculomas

Pathology	T_2W morphology	n	Range of ADC value (×10–3 mm2 s–1)	Mean ADC value (×10–3 mm2 s–1)	Standard deviation	P-value
Tuberculoma	Hypointense	32	0.400-1.409	1.1765	0.1902	≤0.0001
	Hyperintense	30	0.408-1.039	0.815	0.15	

Table IV: NMR spectroscopy evaluation

Pathology	n	NAA/Cr	NAA/Cho	Cho/Cr	LAC(no of patients)	LIPID (no of patients)
Tuberculoma	62	0.79	0.59	1.29	25	47
Metastasis	23	0.689	0.559	2.59	15	15
Neurocysticercosis	5	0.98	0.99	0.93	1	
High-grade glioma	8	0.58	0.39	3.28	6	4
Abscess	2	0.59	0.59	0.48	-	-

Table V: BOLD venographic imaging evaluation of brain lesions

Pathology	BOLD venographic imaging		
	Complete hypointense ring	No hypointense ring	Incomplete hypointense ring
Tuberculoma	36 (58.1%)	26 (42.0%)	-
Metastasis	-	23(100%)	-
Neurocysticercosis	2 (40%)	3 (60%)	-
High-grade glioma	-	5(83.3%)	1 (16.7%)
Abscess	2 (100%)	-	-

DISCUSSION

Our study evaluated the focal brain lesions by MRI techniques like dMRI, NMR spectroscopy and BOLD venographic imaging and conventional MRI. Our study determined the role of BOLD venographic imaging in differentiating brain lesions, especially tuberculomas, from other lesions due to the complete peripheral hypointense ring helping in diagnosing tuberculomas.

We categorized tuberculomas based on their T_2W morphology. The mean ADC value of hypointense tuberculomas was $(1.1765 \pm 0.19) \times 10^{-3}$ mm^2 s^{-1} with ADC range $(0.400\text{-}1.4090)\times10^{-3}$ mm^2 s^{-1}. While hyperintense tuberculomas had a mean ADC value $(0.815 \pm 0.15) \times10^{-3}$ mm^2 s^{-1} with ADC range $(0.408\text{-}1.039)\times10^{-3}$mm^2 s^{-1}. The results of our study are consistent with the study by Gupta et al[11] in which the Apparent Diffusion Coefficient value of hypointense tuberculomas was $(1.24\pm0.32)\times10^{-3}$mm^2 s^{-1} in and that of hyperintense tuberculomas was $(0.80 \pm 0.08) \times 10^{-3}$ mm^2 s^{-1}. Various other studies also showed concurrent results as our study[12-14].

In the present study, metastatic lesions showed an Apparent Diffusion Coefficient value of $0.975\pm 0.10 \times 10^{-3}$mm^2 s^{-1}. Comparable Apparent Diffusion Coefficient value of metastatic lesions was observed in Chatterjee et al[13], Berg Hoff[15] et al. and Kinu Ko et al[16]. The Apparent Diffusion Coefficient values of tuberculomas and metastatic lesions did not differ significantly in

our study (p=0.519). This finding is also concurrent with the results of Chatterjee et al[13].

The Apparent Diffusion Coefficient value of gliomas (0.889 ±0.13) × 10^{-3} mm^2 s^{-1} was consistent with ADC value in Kinu Ko et al[16].

All the NCC patients showed free diffusion in diffusion MRI and showed an Apparent Diffusion Coefficient value of (1.59 ±0.10)×10^{-3} mm^2 s^{-1}. Comparable values were observed in Gupta et al[11] (1.66 ± 0.29 × $10^{-3}$$mm^2$ s^{-1}).

NMR spectroscopy evaluation of tuberculomas showed an increased Cho/Cr ratio (1.29) and reduced NAA/Cr and NAA/Cho ratios (0.79 & 0.59, respectively). Peng Juan et al[17-19] conducted three consecutive studies in which the NAA/Cho ratio was found to be 0.55, 0.58 and 0.74. An elevated Cho/Cr ratio was also observed in Kumar et Al[19], Pretell et al[20] and Batra and Tripathi[14]. A lipid peak was observed in 47 tuberculomas patients (75.9%), several other studies also reported elevated lipid peak in tuberculomas[13.20,22].

In metastatic lesions and gliomas elevated chlorine levels were observed leading to reduced N-acetylaspartate /Creatine and N-acetylaspartate /Choline ratios (0.689 and 0.58, 0.559 & 0.38 respectively). Consistent results were reported by other studies[18,19].

According to the results of our study, lipid-lactate peaks did not contribute to distinguishing brain lesions. The same conclusions were reported by Peng Juan et al[17], Kumar et a[l9], Alamet al[22] and Kim et al[16].

CONCLUSION

Diffusion MRI did not help distinguish tuberculomas from metastasis and gliomas. However, NMR spectroscopy did offer this advantage by evaluating their unique metabolite pattern. BOLD venographic imaging showed the presence of a complete peripheral hypointense ring helping in diagnosing tuberculomas.

Limitations of the study: Our study had a small size and use of BOLD venographic imaging in differentiating tuberculomas from other brain lesions was observed in a limited study setting.

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Conflict of interest: Nil

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