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DIFFUSION-WEIGHTED MRI FOR DIFFERENTIATING PYOGENIC, TUBERCULOUS, AND FUNGAL BRAIN ABSCESSES: A RADIOLOGICAL-MICROBIOLOGICAL CORRELATION STUDY

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ABSTRACT

Background: Pre-culture diagnosis of a brain abscess is clinically significant as the treatment of bacterial, antitubercular, and antifungal brain abscesses varies significantly and the ring-enhancing appearance is common in both conventional contrast-enhanced MRI and in the majority of bacterial and tuberculous brain abscesses.

Objective: To assess the ability of diffusion-weighted imaging (DWI) patterns and apparent diffusion coefficient (ADC) measurement to differentiate pyogenic, tuberculous and fungal brain abscesses and to correlate with microbiological findings.

Method: This was an observational radiological-microbiological correlation study involving 86 patients with brain abscesses (46 pyogenic, 23 tuberculous, and 15 fungal). Pre-treatment or early-treatment 3-T MRI with DWI and ADC mapping were performed in all patients. The following parameters were compared between groups: central cavity ADC, normalized ADC ratio, distribution of restricted diffusion, intracavitary projections, multiplicity, and wall morphology.

Results: Mean central ADC was lowest in pyogenic abscesses ($0.58 \pm 0.14 \times 10^{-3}$ mm²/s), intermediate in tuberculous abscesses ($0.76 \pm 0.18 \times 10^{-3}$ mm²/s), and highest in fungal abscesses ($1.02 \pm 0.27 \times 10^{-3}$ mm²/s; $p < 0.001$). Pyogenic lesions were more likely to have homogeneous central restriction (82.6%) compared to fungal abscesses, which were more likely to have heterogeneous peripheral or intracavitary projection restriction (73.3%; $p < 0.001$). An ADC threshold of $\leq 0.67 \times 10^{-3}$ mm²/s was found to be 80.4% sensitive and 78.9% specific for the diagnosis of pyogenic abscess. The combined DWI model with central ADC and restriction pattern and intracavitary projections yielded a three-class diagnostic accuracy of 82.1% ($\kappa = 0.71$).

Conclusion: DWI is a valuable etiological stratification tool if used as a pattern-based technique, not just based on central diffusion restriction. The quantitative ADC assessment can be used to assist with earlier targeted microbiological investigation and antimicrobial decision making, when used in conjunction with lesion morphology.

Keywords: Brain Abscess, Diffusion-Weighted Imaging, Apparent Diffusion Coefficient, Pyogenic Abscess, Tuberculous Abscess, Fungal Abscess.

INTRODUCTION

Brain abscess is a localized infection of the brain with the presence of cerebritis, necrosis of tissue and eventual capsule formation. Although modern neuro-imaging, neurosurgery and antimicrobial therapy have improved the outlook, It continues to be associated with significant neurological morbidity due to delayed diagnosis or inadequate initial therapy, which can allow mass effect, rupture of the ventricles, vascular complications and irreversible parenchymal damage [1]. The clinical presentation is often non-specific and the classic triad of fever, headache and focal neurological deficit is only seen in a minority of patients [2].

The main imaging modality used for the characterization of suspected abscesses is contrast-enhanced MRI. The ring-enhancing pattern is common with mature lesions, but may mimic necrotic neoplasms and may be confused with abscesses from other microorganisms [3]. The use of

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diffusion-weighted imaging (DWI) helped to increase the confidence of identifying purulent cavities, as viscous inflammatory materials usually have low water mobility and high DWI signal and low apparent diffusion coefficient (ADC) [4]. Studies since then have validated DWI as a superior modality to conventional MRI for distinguishing abscesses from cystic or necrotic tumors [5] and meta-analysis has demonstrated good diagnostic accuracy for distinguishing infectious from noninfectious ring-enhancing lesions [6].

The more challenging clinical question is not the diagnosis of an abscess, but the likely cause of the abscess. Often, the antimicrobial treatment, length of treatment, surgical indications, and evaluation for systemic disease will vary significantly between pyogenic, tuberculous, and fungal abscesses. Pyogenic abscesses have been reported as having significant central restriction, tuberculous abscesses as variable but often substantial restriction, and fungal abscesses as having variable diffusion with restricted intracavitary projections or peripheral components [7]. Tuberculous lesions also exhibit a wide range of ADC responses to caseation, liquefaction, and cellular makeup [8]. Central facilitated diffusion and peripheral restriction have been reported in a few cases [9] and fungal abscesses are especially problematic as they can resemble bacterial abscesses. Further, histopathological examination of fungal cerebral infection suggests that the presence of proteinaceous necrosis and inflammatory cellularity, without the presence of typical bacterial suppuration, can also cause restricted diffusion [10].

The literature that is available is still limited in scope, due to the small number of fungal groups included, the use of various MRI techniques, the inclusion of unconfirmed lesions, and the inconsistent use of microbiological reference standards. There is thus a need for a practical radiological-microbiological analysis that takes into account both quantitative ADC values and recognizable DWI patterns in the three major categories of infection. The purpose of the present study was to compare DWI and ADC parameters of pyogenic, tuberculous and fungal brain abscesses, to correlate imaging parameters with microbiological results, and to assess the diagnostic value of selected DWI parameters for the differentiation of the etiologies.

MATERIALS AND METHODS

Study design and setting

In a tertiary referral center, the departments of radiodiagnosis, neurosurgery, and microbiology were designed to conduct a study of the correlation of radiology and microbiology in an observational setting at the hospital.

Participants

Patients aged 12 years or older were included if they had one or more intra-axial ring-enhancing lesions that were clinically suspected to be brain abscess and the lesion was microbiologically, molecularly or histopathologically diagnosed as an etiological cause. Inclusion criteria were the availability of axial DWI with ADC maps obtained prior to definitive surgery and prior to > 7 days of organism-specific therapy. Postoperative cavity infection, subdural/epidural empyema without intraparenchymal abscess, parasitic infection, isolated tuberculoma without liquefied abscess formation, proven necrotic tumor, severe motion artifact or susceptibility artifact that prevented ADC measurement, and lack of an adequate etiological reference standard were exclusion criteria. If more than one abscess was present, the largest untreated abscess that was technically acceptable on DWI was chosen for quantitative analysis, and the number of lesions was noted at the patient level.

MRI protocol

A 3-T MRI was used with a standard brain protocol. Sequences consisted of axial T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery, susceptibility-weighted imaging, DWI, ADC mapping, and post-gadolinium T1-weighted imaging in three planes. Single-shot echo-planar acquisition was performed with b values of 0 and 1000 s/mm2, slice thickness of 5 mm, and interslice gap of no more than 1 mm. ADC maps were automatically generated on the scanner console. Images were obtained following the intravenous injection of gadolinium-based contrast material at 0.1 mmol/kg, unless contraindicated.

Image analysis

The studies were independently reviewed by two neuroradiologists with 8 and 12 years of experience, blinded to the microbiological diagnosis. Disagreements were resolved by consensus. Conventional MRI parameters recorded were the number of lesions, maximum diameter, location, wall thickness, wall regularity, multiloculation, surrounding edema, intracavitary projections, hemorrhagic susceptibility, and ventricular rupture. DWI was classified as: (1) homogeneous central restriction (high signal for at least 75% of the nonenhancing cavity with low ADC); (2) heterogeneous central restriction; (3) peripheral or intracavitary projection restriction; or (4) absent/minimal restriction. Three circular regions of interest were selected within the largest solid-appearing part of the nonenhancing cavity, excluding the wall, hemorrhage, and partial-volume effects, for ADC measurement. Central ADC was the mean of the three measurements. The central ADC was normalized by ADC in contralateral normal-appearing white matter. If fungal lesions had

internal projections visible, the smallest ADC measured within the projection was also recorded.

Microbiological and histopathological reference standard

The abscess material collected from the stereotactic aspiration or surgical excision was subjected to Gram stain, aerobic and anaerobic bacterial culture, potassium hydroxide mount, fungal culture, acid fast staining, mycobacterial culture, and molecular testing based on clinical suspicion. Diagnosis of tuberculosis was made by the detection of Mycobacterium tuberculosis complex by nucleic-acid amplification testing or culture, or by compatible histopathology with corroborating clinical response in cases where microbiological testing was negative. Fungal infection was dependent on fungal growth, the presence of hyphae or yeast in tissue, or species-specific molecular confirmation. Pyogenic abscess was included if a bacterial culture or broad-range bacterial molecular testing was performed and a likely pathogen was identified, and culture-negative cases were included only if the histopathology confirmed suppurative abscess and other investigations for tuberculosis and fungi were negative. All of these results were masked from the radiologists in the initial reading.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation or median (interquartile range) depending on the distribution. Categorical variables were presented as frequency and percentage. Normally distributed continuous variables were analyzed by one-way analysis of variance with Tukey post-hoc testing and non-normal continuous variables were analyzed by Kruskal-Wallis test. The chi-square test or the Fisher exact test was used to compare categorical variables. ADC thresholds with the highest Youden index were determined using receiver operating characteristic (ROC) analysis. The sensitivity, specificity, positive predictive value, negative predictive value, accuracy, and area under the ROC curve (AUC) were computed. A three-class imaging rule was tested against the microbiological reference standard, which included central ADC, restriction pattern, and intracavitary projections. Weighted kappa was used to measure interobserver agreement for categorical features, and the intraclass correlation coefficient was used for ADC measurements. The p value was calculated for both sides and was considered statistically significant if <0.05. SPSS Statistics version 29.0 was used for analyses.

RESULTS

Of 112 screened patients, 28 were excluded because of absent etiological confirmation (n = 12), prior prolonged organism-specific treatment (n = 7), postoperative infection (n = 4), inadequate DWI quality (n = 3), or final diagnosis of necrotic neoplasm (n = 2). The final cohort comprised 84 patients: 46 with pyogenic abscesses, 23 with tuberculous abscesses, and 15 with fungal abscesses. Mean age was 41.7 ± 16.3 years, and 55 patients (65.5%) were male. Immunocompromised status was substantially more frequent in the fungal group (73.3%) than in the pyogenic (19.6%) or tuberculous (26.1%) groups ($p < 0.001$). The fungal group also showed a higher frequency of multiple lesions (66.7%, $p = 0.006$). Baseline characteristics and microbiological findings are presented in Table 1.

Central cavity diffusion differed significantly among etiological groups. Mean central ADC was $0.58 \pm 0.14 \times 10^{-3}$ mm²/s in pyogenic abscesses, $0.76 \pm 0.18 \times 10^{-3}$ mm²/s in tuberculous abscesses, and $1.02 \pm 0.27 \times 10^{-3}$ mm²/s in fungal abscesses ($p < 0.001$). The corresponding normalized ADC ratios were 0.74 ± 0.18, 0.94 ± 0.22, and 1.24 ± 0.31, respectively ($p < 0.001$). Homogeneous central restriction was present in 82.6% of pyogenic abscesses but only 60.9% of tuberculous and 20.0% of fungal abscesses ($p < 0.001$). In contrast, peripheral or intracavitary projection restriction was identified in 73.3% of fungal abscesses compared with 13.0% of tuberculous and 6.5% of pyogenic lesions ($p < 0.001$). Detailed MRI findings are shown in Table 2.

ROC analysis demonstrated that a central ADC threshold of $\leq 0.67 \times 10^{-3}$ mm²/s differentiated pyogenic from non-pyogenic abscesses with 80.4% sensitivity, 78.9% specificity, and an AUC of 0.85. A central ADC $>0.90 \times 10^{-3}$ mm²/s combined with peripheral or intracavitary projection restriction identified fungal abscesses with 73.3% sensitivity and 91.3% specificity. Tuberculous abscesses were most accurately classified when intermediate ADC values ($0.68\text{-}0.90 \times 10^{-3}$ mm²/s) were considered together with smooth thin walls and absence of fungal-type intracavitary projection restriction. The combined three-class DWI rule correctly categorized 69 of 84 patients (82.1%) with a weighted kappa of 0.71 against the etiological reference standard (Table 3). Interobserver agreement was excellent for central ADC measurement (intraclass correlation coefficient = 0.93) and substantial for DWI pattern classification ($\kappa = 0.79$).

Table 1. Clinical Characteristics and Microbiological Distribution of the Study Groups

Characteristic	Pyogenic (N = 46)	Tuberculous (N = 23)	Fungal (N = 15)	P Value
Age, Years	40.1 ± 15.8	38.9 ± 14.2	48.8 ± 18.0	0.080

Male Sex	29 (63.0%)	14 (60.9%)	12 (80.0%)	0.386
Immunocompromised Status	9 (19.6%)	6 (26.1%)	11 (73.3%)	<0.001
Fever At Presentation	31 (67.4%)	12 (52.2%)	7 (46.7%)	0.214
Focal Neurological Deficit	25 (54.3%)	14 (60.9%)	9 (60.0%)	0.840
Multiple Abscesses	10 (21.7%)	8 (34.8%)	10 (66.7%)	0.006
Median CRP, Mg/L (IQR)	54 (28-92)	26 (13-51)	39 (19-78)	0.018
Dominant Microbiological Findings	Streptococcus Anginosus Group 12; S. Aureus 8; Gram-Negative Bacilli 7; Anaerobes/Polymicrobial 19	M. Tuberculosis Complex By NAAT/Culture 19; Histopathology-Supported 4	Aspergillus 7; Mucorales 4; Candida 2; Dematiaceous Fungus 1; Cryptococcus 1	—

Table 2. Diffusion-Weighted and Conventional MRI Characteristics According To Abscess Etiology

MRI Feature	Pyogenic (N = 46)	Tuberculous (N = 23)	Fungal (N = 15)	P Value
Maximum Diameter, Cm	3.4 ± 1.2	3.1 ± 1.0	3.7 ± 1.4	0.290
Central ADC, $\times 10^{-3}$ Mm^2/S	0.58 ± 0.14	0.76 ± 0.18	1.02 ± 0.27	<0.001
Normalized ADC Ratio	0.74 ± 0.18	0.94 ± 0.22	1.24 ± 0.31	<0.001
Homogeneous Central Restriction	38 (82.6%)	14 (60.9%)	3 (20.0%)	<0.001
Heterogeneous Central Restriction	6 (13.0%)	7 (30.4%)	8 (53.3%)	0.003
Peripheral/Intracavitary Projection Restriction	3 (6.5%)	3 (13.0%)	11 (73.3%)	<0.001
Intracavitary Projections On Post-Contrast MRI	4 (8.7%)	3 (13.0%)	10 (66.7%)	<0.001
Thin Smooth Wall	30 (65.2%)	18 (78.3%)	4 (26.7%)	0.004
Irregular Or Crenulated Wall	10 (21.7%)	3 (13.0%)	10 (66.7%)	0.001
Hemorrhagic Susceptibility	5 (10.9%)	2 (8.7%)	6 (40.0%)	0.012

Table 3. Diagnostic Performance of Selected DWI Criteria

Diagnostic Criterion	Sensitivity	Specificity	PPV	NPV	Accuracy / AUC
Central ADC ≤0.67 $\times 10^{-3}$ Mm^2/S For Pyogenic Abscess	80.4%	78.9%	82.2%	76.9%	AUC 0.85
Central ADC >0.90 $\times 10^{-3}$ Mm^2/S Plus Projection/Peripheral Restriction For Fungal Abscess	73.3%	91.3%	64.7%	94.0%	AUC 0.88
Intermediate ADC 0.68-0.90 $\times 10^{-3}$ Mm^2/S Plus Smooth Wall For Tuberculous Abscess	69.6%	83.6%	61.5%	88.0%	AUC 0.79
Combined Three-Class DWI Rule	—	—	—	—	82.1% Accuracy; K = 0.71

DISCUSSION

This study shows that DWI can be used to aid etiological stratification of brain abscesses, especially when combined with ADC values. The central ADC values were lowest in pyogenic abscesses and the prevalence of homogeneous cavity restriction was highest in pyogenic abscesses. Tuberculous abscesses had intermediate diffusion range, while fungal lesions were more likely to show higher central ADC values, heterogeneous diffusion and restriction along intracavitary projections or peripheral components. These features were used in combination to get a significant improvement over three-class discrimination using central restriction alone.

The low ADC values found in pyogenic abscesses are biologically plausible because the presence of inflammatory cells, microorganisms, proteins and necrotic debris in bacterial pus can increase the viscosity and decrease the mobility of extracellular water. The mean ADC of 0.58×10^{-3} mm^2/s obtained in the present analysis is similar to that of the classic

DWI concept proposed by early studies on brain abscess and also comparable with the comparative results reported by Luthra et al. [7]. The present results also corroborate the general findings that a markedly hyperintense DWI cavity and the associated low ADC is strongly indicative of a pyogenic process, but not diagnostic of any specific microorganism.

The diffusion restriction of the tuberculous abscesses was found to be less than that of the pyogenic abscesses, but significantly greater than the central cavities of the majority of fungal lesions. This intermediate behavior is probably due to fluctuations in liquefaction, inflammatory content of cells, necrotic material, and protein concentration. Gupta et al. found that tuberculous abscesses and T2-hyperintense tuberculous lesions had low ADC values, highlighting the possibility of tuberculosis mimicking pyogenic infection on DWI [8]. The present data confirm that observation and suggest that a combined profile of intermediate ADC, thin smooth enhancement and absence of fungal-type peripheral restriction may be of benefit in discrimination. However, there was still significant overlap and DWI should not be used as a replacement for mycobacterial molecular testing.

The most unique pattern-based results were from the fungal group. Restricted peripheral tissue diffusion or intracavitary projections were seen in almost three-quarters of fungal abscesses, and homogeneous central restriction was rare. In previous studies, similar fungal abscesses have also been seen to have facilitated or mixed central diffusion with restricted projections containing fungal elements and inflammatory material [9]. Gaviani et al. also reported that fungal cerebral abscesses may have restricted diffusion even when the histology is non-suppurative, suggesting that the degree of diffusion restriction is related to the microstructural composition of the lesion rather than to the presence of pus [10]. The relative high prevalence of hemorrhagic susceptibility in the fungal group in our cohort is also clinically consistent with the angioinvasive nature of Aspergillus and Mucorales, but was not sufficiently discriminatory to be used as a standalone classifier.

Our results should also be viewed in the light of multiparametric MRI. Pyogenic abscesses can be distinguished from tuberculous infection by proton MR spectroscopy which can detect amino acid resonances in the abscesses [11]. The use of susceptibility-weighted imaging has been reported to show differences in rim architecture and intralesional susceptibility between pyogenic and fungal abscesses [12]. The use of combined DWI and spectroscopy has enhanced the ability to differentiate abscess from necrotic tumor [13] and serial metabolic changes may be useful during treatment [14]. Advanced spectroscopy, however, is technically challenging, can be affected by the size of the lesion and the presence of bone, and is not always available in emergency practice. DWI is faster, more widely available, and easily integrated into routine brain MRI and thus a pattern-based DWI approach is appealing as an initial triage tool.

The diagnostic performance analysis demonstrates the usefulness and the weaknesses of ADC thresholds. A cut-off value of 0.67×10^{-3} mm²/s was found to be moderately sensitive and specific for pyogenic abscesses, but there was still a significant overlap. ADC values can be influenced by scanner platform, field strength, b values, maturation of lesions, treatment exposure, positioning of the region of interest, hemorrhage, and partial volume effects. Without protocol harmonization, therefore, universal thresholds are unlikely to be reliable. Therapy may also change the serial DWI, and if the cavity restriction persists or recurs, it may indicate the presence of purulent material and help monitor therapy [15]. Thus, the key advantage of DWI is that it uses quantitative values and the anatomical distribution of restriction, not a single value.

The relatively high diagnostic accuracy of the combined rule is also a reflection of the complementary information provided by morphology. Smooth, thin walls are more suggestive of an organized abscess, but do not indicate the cause of the abscess; irregular walls, projections, and hemorrhagic foci may indicate fungal infection. The dual-rim sign on susceptibility-weighted imaging is closely related to pyogenic abscess and may also enhance the differentiation from necrotic tumors [16]. The presence or absence of restricted diffusion is a binary statement that may be less useful in clinical reporting than a structured description of restricted diffusion, ADC, homogeneity of restriction, peripheral restriction, intracavitary projections, hemorrhage, and multiplicity.

One of the most practical parts of the present work is the radiological-microbiological correlation. Conventional culture is still necessary to conduct antimicrobial susceptibility testing, but may be affected by prior therapy and fastidious or anaerobic organisms. In polymicrobial and culture-negative brain abscesses, broad-range 16S rDNA sequencing has been shown to have further diagnostic utility [17]. Combining culture, molecular techniques and imaging/spectroscopy can enhance the etiological classification, a multimodal approach [18]. Polymicrobial infections and anaerobes have also been detected more often than by routine culture using more recent sequencing methods [19]. These advances highlight the value of MRI in guiding immediate differential diagnosis and specimen

processing, not as a substitute for microbiological confirmation.

There are several limitations of the study. The sample size was moderate, especially in the case of fungal infection, and the fungal species were heterogeneous. In those with multiple abscesses, a single index lesion was used for quantitative analysis, which may not accurately reflect intra-patient variation. Short courses of empirical antimicrobial therapy were received by some patients prior to MRI or aspiration. A degree of reference-standard heterogeneity was added with the inclusion of histopathology-supported diagnoses when direct microbiological confirmation was unavailable. ADC thresholds were internally calculated and need to be validated in other scanners and patient cohorts. Lastly, the study did not create a comprehensive model that incorporates spectroscopy, perfusion, susceptibility metrics, clinical biomarkers, and machine-learning features.

These limitations notwithstanding, the results are clinically relevant. Very low ADC with homogeneous restriction should suggest pyogenic infection in a patient with a ring-enhancing lesion, whereas intermediate ADC with smooth wall should keep the diagnosis of tuberculous abscess high in the differential diagnosis, and higher ADC with peripheral or projection-based restriction should strongly suggest fungal infection, especially in an immunocompromised host. This method is similar to the practical contemporary imaging frameworks that focus on the integration of diffusion behaviour with morphology and clinical context [20]. Future multi-center studies should establish a standard protocol for DWI acquisition, validate absolute and normalized ADC thresholds, and explore the feasibility of multiparametric imaging models for predicting the class of pathogen prior to invasive sampling.

CONCLUSION

The pyogenic, tuberculous and fungal brain abscesses were found to be significantly different on diffusion weighted MRI. The lowest central ADC values were observed in pyogenic abscesses, which also had the most homogeneous cavity restriction; the highest central ADC values were observed in fungal abscesses, which had a more frequent peripheral or intracavitary pattern of restriction; and tuberculous abscesses had intermediate central ADC values. However, a composite interpretation of quantitative ADC and spatial diffusion morphology can provide enhanced early etiological stratification, direct microbiological testing, and aid in prompt antimicrobial decision-making, but definitive diagnosis should be microbiologically or histopathologically established.

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