ORIGINAL RESEARCH PAPER

Radiodiagnosis

COMPARISON STUDY OF DIFFUSION WEIGHTED IMAGING VERSUS CONVENTIONAL SEQUENCES OF MRI IN DIFFERENTIATING BRAIN ABSCESS AND CYSTIC/ NECROTIC BRAIN TUMORS

KEY WORDS: brain abscess, brain tumor, MRI, diffusion.

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ABSTRACT

AIM: To compare the effectiveness of diffusion Weighted Imaging (DWI) sequence with other routine magnetic resonance imaging(MRI) sequences in the detection of cystic/necrotic brain tumors and brain abscess. **MATERIALS&METHODS:** The study was carried out at Department of Radio-diagnosis, S.A.I.M.S, Indore from October,2018 to March,2020 after clearance from the Institutional Ethical committee.The sample size consists of 54 patients[11 patients with brain abscess and 43 with cystic/necrotic brain tumors]. The MRI was performed using 1.5-T system including fast spin-echo T1-weighted image (T1WI),contrast-enhanced T1WI,T2-weighted image(T2WI), fluid-attenuated inversion recovery(FLAIR) sequence and DWI with apparent diffusion coefficient(ADC) maps.ADC values were noted in cystic portion, wall, and perilesional edema of the lesions. **RESULTS:** Most of the brain abscesses and brain tumors appeared hypointense on T1WI and hyperintense on T2WI/FLAIR. All patients with brain abscess except one on treatment, showed high core signal intensity(SI) on DWI and low SI on ADC maps with mean ADC value of 0.637±0.141x10-3mm2/s. Mean ADC value in the wall of brain abscess was higher (1.369X10-3mm2/s) than its core. All patients with cystic/necrotic brain tumors except two, showed low core SI on DWI and high SI on ADC maps with mean ADC value of 2.446±0.613x10-3mm2/s.The mean ADC value of wall of cystic brain tumor (1.012±0.264X10-3mm2/s) was comparatively lower than its core. Almost similar ADC values were noted in perilesional edema around both lesions.The sensitivity, specificity, positive predictive value(PPV) and negative predictive value(NPV) in diagnosing brain abscess and brain tumor with DWI+ADC map were higher than conventional MRI sequences alone. **CONCLUSION:** Conventional MRI has limited application and DWI-ADC map is a good tool for differentiating brain abscess from cystic or necrotic brain tumors with few exceptions. Diffusion imaging can also be used for follow-up of brain abscess after antibiotic therapy.

INTRODUCTION:

Brain abscess is a severe life-threatening emergency. It is a focally developed intracranial suppuration[1]. It proceeds from a localized zone of cerebritis to a capsulated pus collection presenting as a mass-like lesion.[2] In developing countries the incidence of brain abscess is approximately 8%.[3] A brain tumour is a mass of abnormal cells multiplying in or around the brain. Central nervous system tumors constitute 2% of all malignancies in India.[4] Gliomas being the leading cause of primary CNS tumors, accounting for 40–50% of cases.[5] Excessive tumor growth and inadequate blood supply result in tissue hypoxia which further lead to tumor necrosis. Clinical presentation of both the pathologies, brain abscess, and cystic/necrotic tumors of the brain is non-specific. Symptoms representing raised intracranial tension, seizures, and focal neurological deficits are the most common forms of presentation, with most cases having no convincing inflammatory or septic symptoms. Only 40-50% of patients of brain abscess are febrile on examination. Early differentiation between infectious and neoplastic brain lesion is very important for treatment planning. Tumors that cannot be removed by en-bloc resection alone, radiation therapy and chemotherapy are used to treat them. A brain abscess can be treated successfully by a much less invasive approach of stereotaxic aspiration and antibiotic therapy.

Magnetic resonance (MR) imaging has greater sensitivity than computed tomography (CT) in the diagnosing of brain abscess because it has more sensitivity to changes in tissue water content, resulting in more excellent contrast between the edematous brain and normal brain during the early stages of cerebritis and abscess formation. The abscess center demonstrated high SI relative to CSF and low SI relative to white matter on T1 sequence and iso- to mild hyperintensity relative to CSF and grey matter on T2 sequence. The abscess capsule is a smooth, peripheral ring which is isointense to hyperintense to white matter on the T1 sequence, isointense to hypointense on the T2- weighted sequence, and shows enhancement on postcontrast images.[6]

This intensity pattern is additionally encountered in cystic/necrotic neoplasms. Primary brain tumor and metastatic tumors, often manifest as rounded, well-circumscribed, rim-enhancing variable-sized lesions surrounded by a variable amount of perilesional vasogenic oedema. Contrast-enhanced computed tomography (CECT) and conventional magnetic resonance imaging (MRI) provide a provisional diagnosis as well as accurate localization of CNS lesions but differentiating these two- ring-enhancing lesions by CT or conventional MR imaging can be difficult due to their morphological similarities.

DWI is a fast echo-planar imaging technique and requires less imaging time, no contrast, and is more practical in clinical use.[7] It provides a way to evaluate the diffusion properties of water molecules in tissue and has been used for the evaluation of diseases such as ischemia, tumors, infection, and white matter disorders.[8] It depends maximally on the water located outside the cells. To quantify the degree of water motion, ADC maps are needed.[9]

The necrotic material in cerebral abscesses is composed of inflammatory cells, proteins, cellular debris, and bacteria in high-viscosity pus which lead to restricted water motion. Additionally, water molecules get attached to amino acid groups on the surface of macromolecules, further restricting their motion. So, restricted water motion in cerebral abscesses has high SI on DW imaging and low ADC values. On the contrary, necrotic material in tumors is cellular debris, serous fluid, and fewer inflammatory cells; thus, water molecules have greater freedom of motion.[7] Most necrotic tumors show mildly increased diffusion with low SI on DW images and high ADC values.

AIM:

The aim of present research was to compare effectiveness of diffusion Weighted Imaging (DWI) sequence and compare with other routine MRI sequences including T1,T2, T1+contrast for detection and evaluation cystic/necrotic brain tumours and brain abscess.

OBJECTIVES:

1. To study DWI morphology of various cystic/necrotic brain tumors and brain abscess.
2. To evaluate ADC as a quantitative parameter in differentiating cystic or necrotic brain tumor from brain abscess.

MATERIALS & METHODS:

This prospective observational study was carried out in the Department of Radio-diagnosis, Sri Aurobindo Medical College and P.G. Institute, Indore from December 2018 to June 2020 after clearance from the Institutional Ethical committee. Patients of all age group irrespective of sex were included in the study, after obtaining written informed consent from them, who were clinically referred for MRI of the brain and were detected to have brain abscess or brain tumors. The sample size consists of 54 patients, including 11 patients with brain abscess and 43 with cystic/necrotic brain tumors including metastasis.

Patients on life support systems, hemodynamically unstable and unconscious patients, all patients who didn't consent to be a part of this study, patients in whom MRI was contraindicated, brain tumors without necrosis/cystic changes and patients with extra-axial lesions were excluded from the study. The MRI was done on the advice of the referring doctor and no patient was made to undergo MRI for the sole purpose of this study.

All the MRI scans in this study were performed using Seimens 1.5 T MAGNETOM® Symphony® with TIM technology MRI scanner (Signa HDxt; GE Medical Systems). MR imaging was performed on all of the study patients including fast spin-echo T1WI(TR,500ms;TE,10ms;section thickness,5mm;FOV, 230mm; matrix,512×512), T2WI(TR,3000ms; TE,80ms; section thickness,5mm; FOV,230mm; matrix,512×512), FLAIR (TR,10,000ms; TE,125ms; section thickness,5mm; inversion time,2200ms; FOV,230mm; matrix, 512×512) and DWI with ADC maps using head coil. B values of 0 and 1000s/mm2 were used for diffusion weighting. Contrast-enhanced T1WI were taken after intravenous injection of 0.1 mmol/kg gadopentetate dimeglumine. Sequences was taken in axial, coronal and sagittal planes.

When multiple lesions were noted, the largest of the lesions was taken into consideration. The characteristics of the lesions were noted, like their number, cystic/necrotic areas, presence of surrounding edema,type of contrast enhancement, appearance on DWI and corresponding ADC maps. Region of interest (round shape, at least 10 mm in diameter) was placed on the cystic/necrotic portion, wall, and perilesional edema of the lesions on the ADC map and mean ADC value in mm^2/sec was calculated.

Detailed clinical history and relevant laboratory investigations were recorded for each patient. The findings were recorded on a pre-structured proforma for the study and descriptive statistics were carried out to identify characteristics of the collected data. Mean and Percentage was used to represent the quantitative data. Microsoft Excel was used to prepare the master charts. All MR diagnosis correlated with final diagnosis (histopathological/treatment response) and sensitivity, specificity, positive predictive value and negative predictive values were calculated of conventional MR + DWI and ADC maps.

Figure 1: A male patient of age 60-years with tubercular abscess. (A) Axial contrast-enhanced T1-weighted MR image shows a regular thin-walled ring-enhanced abscess in left occipital lobe. (B) Axial DWI(b = 1000 s/mm^2) shows marked hyperintensity in the abscess cavity and hypointensity in the wall of abscess with surrounding isointense perilesional edema. (C) ADC values calculated in the round ROI in the centre, wall and perilesional edema of abscess. The values were lowest in the centre ($0.75x10^{-3}mm^2/s$), followed by wall ($1.22x10^{-3}mm^2/s$) and perilesional edema ($1.31x10^{-3}mm^2/s$).

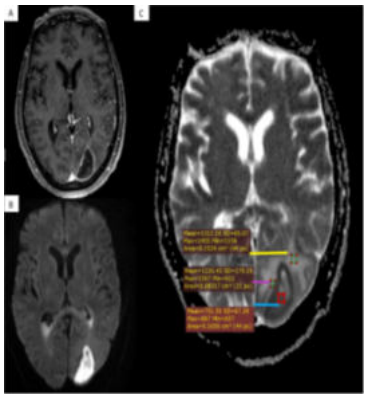


Figure 2: Cystic tumor in a 13-year-old girl with histopathology report consistent with pleomorphic xanthoastrocytoma. (A-C) Well-defined lesion with thick rim-enhancement, homogenously hyperintense on T2WI,no blooming on SWI noted in right parieto-temporal lobe. (D) DWI shows hypointense cystic lesion with hyperintense ADC map (E). ADC value of core of brain tumor is high($2.7x10^{-3}mm^2/s$) and that of enhancing wall is low($0.6x10^{-3}mm^2/s$).

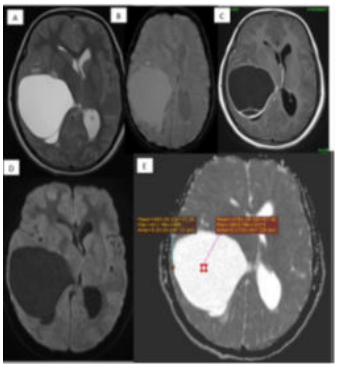


Figure 3: In a known case of Ca lung in a 39-years-old female with necrotic brain metastasis. (A-D) Irregular and thick rim-enhancing lesion, hypointense on T1, hyperintense on T2/FLAIR with mild perilesional edema noted in right cerebellar hemisphere. (E) DWI shows hyperintense lesion with corresponding hypointensity on ADC maps (F) and low ADC value($0.73x10^{-3}mm^2/s$).

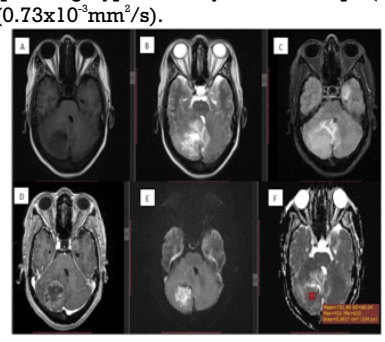
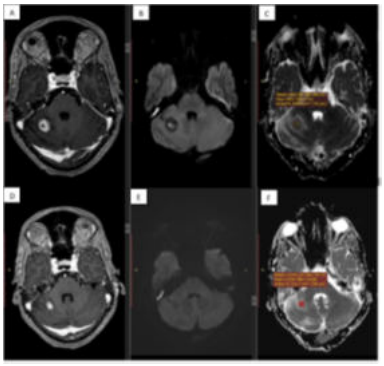


Figure 4: A 15-years-old boy with tubercular brain abscess on anti-tubercular treatment (ATT). A–C: Axial contrast-enhanced T1WI at the beginning of ATT(A) shows a thick peripheral rim-enhancing lesion with a hypointense center in the right cerebellar hemisphere. Hyperintense center at DWI(B) and a low ADC ($0.842x10^{-3}mm^2/s$)(C). D–F: Three months after ATT, the follow-up images show decrease in size

of the abscess(D), hypointense on DWI(E), and a high ADC value(1.14x10^{-3}mm^2/s)(F).



RESULTS:

Out of 54, 80 % (n=43) of patients had cystic/necrotic brain tumors and 20% (n=11) of them had brain abscess.Majority of patients of both the diseases were in age group 41-60 years. Mean age of the patients with brain abscess was 41 years and that of the patients with cystic/necrotic brain tumor was 42.80 years.Male preponderance was observed in patients with brain abscess in our study with 64% patients being male and 36% patients being female. No sex predominance was observed in patients with brain tumor with 51% being female and 49% being male.

Since 6 patients with brain abscess had multiple lesions, the total number of these lesionswere 22.Since 11 patients with cystic necrotic brain tumor had multiple lesions, the total number of these lesions were 53.Most (73%) of the patients with brain abscess appeared hypointense on T1WI and 91% of them appeared hyperintense on T2WI/FLAIR. Most (86%) of the patients with brain tumor appeared hypointense on T1WI and 100% of them appeared hyperintense on T2WI/FLAIR.

Table 1: Distribution of patients according to presence or absence of diffusion restriction on DWI.

DIFFUSION RESTRICTION	PTS.WITH BRAIN ABSCESS		PTS.WITH BRAIN TUMOR	
	Number	Percentage	Number	Percentage
Present	10	91	2	5
Absent	1	9	41	95
Total	11	100	43	100

- 91% (n=10) of the patients with brain abscess showed diffusion restriction [i.e.,they had high SI on DWI and low SI on ADC maps]. Rest 9% (n=1) of them did not show diffusion restriction.
- 95% (n=41) of the patients with cystic/necrotic brain tumor did not show diffusion restriction [i.e., they had low SI on DWI and high SI on ADC maps]. Rest 5% (n=2) of these patients showed diffusion restriction.(Table1)

Table 2: Mean ADC value and ADC range were calculated for CSF, brain abscess (core, wall, perilesional edema), cystic/necrotic brain tumor (core, wall, perilesional edema) and cystic metastasis (core, wall, perilesional edema).

LOCATION	ADC VALUE (x10^{-3}mm^2/s)	
	MEAN±S.D.	RANGE
CSF	2.906±0.133	2.568-3.186
BRAIN ABSCESS:		
CORE	0.637±0.141	0.421–1.143
LESION WALL	1.369±0.301	1.095-2.13
PERILESIONAL EDEMA	1.577±0.165	1.345-1.877
BRAIN TUMOR:		
CORE	2.446±0.613	0.986-3.074
LESION WALL	1.012±0.264	0.607-1.538
PERILESIONAL EDEMA	1.422±0.208	1.123-2.083
METASTASIS:		
CORE	2.017±0.742	0.754-2.937
LESION WALL	0.964±0.229	0.609-1.4
PERILESIONAL EDEMA	1.654±0.187	1.241-1.892

- The mean ADC value of the CSFwas 2.906±0.133x10^{-3} mm^2/s.
- The mean ADC value in brain abscess core was low [0.637±0.141x10^{-3}mm2/s] as compared to that in core of brain tumor [2.446±0.613x10^{-3}mm^2/s].
- The mean ADC value in the wall of brain abscess was slightly higher [1.369±0.301x10^{-3}mm^2/s] than those compared to the wall of brain tumor [1.012±0.264x10^{-3}mm^2/s].
- No significant difference was noted between the ADC values of core, wall and perilesional edema of primary cystic brain tumor and brain metastasis.
- Almost similar ADC values were noted in perilesional edema around brain abscess, brain tumor and metastasis.(Table2)

Table 3: Comparison between the provisional MR diagnosis (based on T1,T2,T1+contrast), final MR diagnosis (conventional MR sequences + DWI and ADCalues) and final discharge diagnosis (based on histopathological report/treatment response).

S.No	Lesion	Provisional MR Diagnosis(T1, T2,T1+Contrast)	Final MR Diagnosis With DWI And ADC Values	Final Diagnosis (Histo-Pathology, Treatment response)
1.	Brain abscess	10 (TP=3,FP=7, FN=8)	12 (TP=10,FP=2 ,FN=1)	11
2.	Brain tumor	44 (TP=36,FP=8,FN=7)	42 (TP=41,FP=1 ,FN=2)	43
	Total	54	54	54

There were 3 true positive and 7 false positive cases of brain abscess in diagnosis based on conventional MRI. On MR diagnosis with DWI and ADC, there were 10 true positive cases and 2 false positive cases of brain abscess.There were 36 true positive and 8 false positive cases of brain tumorin diagnosis based on conventional MRI. On MR diagnosis with DWI and ADC values, there 41 true positive and 1 false positive case.(Table3)

Table 4: Comparison of sensitivity, specificity, positive predictive value and negative predictive values between conventional MR+T1 contrast and conventional MR+DWI+ADC values in diagnosing brain abscess.

S.NO.	PARAMETER	CONVENTIONAL MR+T1 CONTRAST	CONVENTIONAL MR+DWI+ADC VALUES
1.	Sensitivity	27 %	91%
2.	Specificity	84%	95%
3.	Positive predictive value	30%	83%
4.	Negative predictive value	82%	98%

The sensitivity, specificity, PPV and NPV in diagnosing brain abscess were much higher for MRI diagnosis with DWI+ADC value than conventional MRI+T1 contrast. (Table4)

DISCUSSION:

A ring-enhancing lesion is a nonspecific imaging finding. It is seen in various benign and neoplastic processes like abscess, necrotic glioblastoma, metastases, resolving hematoma, infarction, and even demyelinating disease.[10]It can be challenging to reach a differential diagnosis of ring-enhancing intracranial mass lesions based on clinical symptoms and conventional MRI. One such example is the differentiation between brain abscess and cystic or necrotic brain tumors using conventional MR images. Several practical methods using conventional MRI have been reported to differentiate between these two, like markedly low signal of the abscess capsule on T2WI andthe capsule on the ventricular side is less well developed than on the cortical side of an abscess.[10,11]However, a hypointense rim may also occur in some cases of brain tumors such as metastases. If an early and accurate diagnosis is made, antibiotics or surgical therapy can be used successfully to treat brain abscesses.

Diffusion-weighted MRI provides images in which the contrast is dependent on the molecular motion of water and it may be altered because of disease.More recently, DWI has also been applied in differentiating cystic/necrotic brain tumor from brain abscess. In our study the total sample size was 54 patients with 11 patients of brain abscess and 43 patients of cystic/necrotic brain tumor.The age group of the subjects with brain abscess ranged from 10-73 years with mean age of 41 years and male: female ratio of 1.8:1. Kim et al.[12] in their study also observed similar trends with mean age of 41 years, age range of 17 to 67 years and male: female ratio of 4:1.In our study, the age range of subjects with cystic/necrotic brain tumor was 8-86 years with mean age of 42.8 yearsand no gender predilection. Similarly, Chang et al.[13]study had mean age of 59 years in tumor group and no gender predilection.

The non- enhancing necrotic brain abscess cavity in our study on T1-WI showed hypo-intensity in 73%, iso-intensity in 18% and hyper-intensity in 9%. On T2/FLAIR, 91% showed hyperintensity and 9% cases were isointense.In Ebisu et al.[14], Haimeset al.[6] and Luthra et al.[15]studies the pyogenic cavity showed low SI relative to the brain on T1-WI and high SI on T2-WI.In our study, the non-enhancing necrotic/cystic portion of brain tumors appeared hypointense in 86% patients, isointense in 11% patients and hyperintense in 2% patients on T1-WI. On T2-WI/FLAIR, the lesion appeared hyperintense in all the patients.Tein et al.[16] reported that well-defined non-enhancing areas of tumor that were hypointense on T1-WI and markedly hyperintense on T2-WI, most likely representing cystic/necrotic regions.

Pus is a highly viscous, thick, mucoid fluid consisting of inflammatory cells, bacteria, proteineous exudate and fibrinogen. Because of this high viscosity, diffusion water motion is severely curtailed. The high ADC values we find in cystic or necrotic lesions are attributable to an intra-cavity fluid that is less viscous than that found in abscesses. It consists of necrotic tissue debris and contains fewer inflammatory cells than abscess fluid.[17]High DWI SI for brain abscesses is usually associated with a reduced ADC value and, conversely, low DWI SI is associated with a high ADC for cystic or necrotic tumors, including metastases.

In our study 91% the brain abscess cavities showed high SI on DWI and low SI on ADC maps with ADC range of $0.421–1.143x10^{-3}mm^2/s$ and$meanADC0.637±0.141x10^{-3}mm^2/s$. Thus, 91% brain abscess cavities showed restricted diffusion expect in 9%. The enhancing abscess wall had ADC range of $1.095-2.13x10^{-3}mm^2/s$ with $meanADC1.369±0.301x10^{-3}mm^2/s$. Thus, the core of abscess had lower ADC values as compared to the wall of abscess. 95% of cystic /necrotic brain tumors showed low SI on DWI and high SI on ADC images. Thus, 95% of the cystic /necrotic brain tumors in our study did not show diffusion restriction. Rest 5% of them showed diffusion restriction. The mean ADC values of core of brain tumor and metastasis were $2.446±0.613x10^{-3}mm^2/s$ [range=$0.986-3.074x10^{-3}mm^2/s$] and $2.017±0.742x10^{-3}mm^2/s$ [range=$0.754-2.937x10^{-3}mm^2/s$], respectively. The mean ADC values of the enhancing wall of the brain tumor and metastasis were $1.012±0.264x10^{-3}mm^2/s$ and $0.964±0.229x10^{-3}mm^2/s$, respectively. In our study, the metastases were probably in the liquefaction stage and behaved like high-grade gliomas. They both had a high ADC, and so we included both these lesions in a single group. However, the core of cystic/necrotic brain tumor including metastases had higher ADC values as compared to their wall.

In Chiang et al.[18] study they found that on DWI, the central cavities of the cerebral abscesses had very low ADCs ($0.94±0.42x10^{-3}mm^2/s$) as compared to that of necrotic tumours ($1.45±0.67x10^{-3}mm^2/s$).The ADCs in the wall of cerebral abscesses ($0.69±0.08x10^{-3}mm^2/s$) did not differ statistically from those seen in the peripheral portions of necrotic tumours ($0.75±0.16x10^{-3}$ mm^2/s).Similar DWI findings and ADC values were also noted in Leuthardt et al.[19], Mishra et al.[20], Chang et al.[13] and Reddy et al.[21] studies.

The patient in whom the abscess cavity did not show diffusion restriction in our study was latter found to be on anti-tubercular drugs treatment.The cavity reduced in size as compared to the images of previous scan and did not show diffusion restricton after the treatment.The only example of an abscess with an elevated ADC ($1.88 x 10^{-3}$ mm^2/s) was a single lesion reported by Krabbe et al.[22]. In Mishra et al.[20] study, 30% of brain abscess patients presented with low SI on DWI and high ADC values ($0.96–2.99 x 10^{-3}$ mm^2/s). However, pus culture from 5 out of 8 patients with high ADC values was sterile. Likely to represent that a high ADC may suggest a response to specific therapy in these patients who did not show growth of any microorganism on culture and were taking antibiotics for a variable period.

In our study two cases of brain metastasis appeared hyperintense on DWI and had low ADC values. Surgery revealed that the necrotic portion had a viscous, thick, and creamy content similar to pus. Similar contrasting DWI studies of cystic or necrotic tumors still exist in the literature. Park et al.[23]published two cases of cystic/necrotic brain metastasis with markedly high SI on DWI. Holtas et al.[24]reported a ring-enhanced brain metastasis hyperintense on DWI and a low ADC value ($0.55X10^{-3}mm^2/s$) in its necrotic part. On follow-up scans 4 weeks later, increased lesion size and numbers were noted, and pathology revealed metastatic adenocarcinoma. The reason for restricted diffusion was possibly early necrosis with intracellular edema of the lesions.

In our study the sensitivity, specificity, PPV and NPV of DWI in diagnosing brain abscess are 91%, 95%, 83% and 98% respectively. In Taj aldem et al.[25] and Leuthardt et al.[19]studies the sensitivity of DWI for diagnosis brain abscess was 100% . In our study the sensitivity, specificity, PPV and NPV of DWI in diagnosing brain tumor are 95%, 91%, 98% and 83% respectively. In Taj aldem et al.[25] study sensivity of diffusion-weighted MRI for diagnosis cystic malignant brain tumor 60% . In Alam et al.[26] study DWI had 94.73% sensitivity, 94.44% specificity and diagnostic accuracy of 94.5% in differentiating brain abscess from neoplastic brain lesions.

CONCLUSION:

This prospective observational study comprised of 54 patients who were clinically referred for MRI brain and were given a MR diagnosis of brain abscess or cystic/necrotic brain tumor using conventional MRI sequences including post-contrast images and DWI+ADC values. A final discharge diagnosis was made based on histopathological report or treatment response of the patients. In conclusion, conventional MRI sequences has limited application and DWI is a good method for differentiating brain abscess from cystic or necrotic brain tumors in most cases. However, exceptions exist, and care should be taken when unusual presentation is encountered. Diffusion imaging can also be used for follow-up of brain abscess after antibiotic therapy. This sequence should be used in addition to routine imaging and not avoid histopathology.

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