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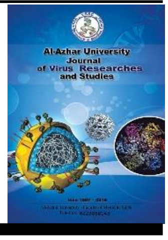

Role of Diffusion MRI in Differentiation Between Neoplastic and Non-Neoplastic Brain Lesions

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Abstract

Diffusion-weighted imaging (DWI) is an imaging manner that can detect water motion within intra, extra, and transcellular areas. Also, it can distinguish brain tumors either benign or malignant. Estimating the importance of diffusion MRI in differentiation between neoplastic and non-neoplastic brain lesions. The study was executed in the Radiology department at Al-Azhar University Hospitals of Damietta and included 40 patients of both sexes. The procedure was done using a Philips Achiva 1.5-Tesla unit system scanner. All the patients had undergone conventional MRI examination including axial, sagittal, coronal T1, axial and coronal T2 and axial flair. Post-contrast administration is axial, coronal and sagittal T1 weighted images. DWI was performed and the ADC map was generated by MRI software. We determined the signal intensity of the lesion. ADC was measured in the solid part of the lesion. Finally, the findings were correlated with the histopathological findings. Apparent diffusion coefficient (ADC) was significantly lower in high-grade malignant tumours than that of low grades, while low-grade glioma has significantly higher ADC than high-grade one, there was significantly lower ADC in patients with lymphoma than those with high-grade astrocytoma, and significant higher ADC for necrotic tumours than brain abscess. DWI is a highly sensitive and non-invasive technique that helps in the differentiation of different brain lesions. DWI must be used together with conventional MRI.

Keywords: Diffusion-weighted imaging, Apparent diffusion coefficient, FLAIR.

1. Introduction

There are multiple brain neoplastic and non-neoplastic lesions occurring at any site in brain or its linings **[1].**

Magnetic resonance imaging (MRI) is vastly utilized in evaluating tumor size in order to determine the route of treatment either surgical or radiotherapy. Also, it is important to follow up the rate of recurrence or progression after treatment. MRI illustrates primary diagnosis of brain lesions and makes a differential diagnosis between tumors and infection **[2].**

Diffusion-weighted imaging (DWI) is a subtype of MRI which shows the mechanism of water diffusion in brain tissue which changes in case of diseases. It supplies data about molecular translational motion of water and during this measuring, only apparent diffusion coefficient (ADC) can be calculated **[3].** ADC provides more data about grading and differentiation of brain lesions **[4]**.

2. Patients and Methods

A prospective study was conducted at the Radiodiagnosis department at Al-Azhar University of Damietta from June 2021 to November 2021 on 40 patients aged from 20 to 60 years, 21 cases were male while 19 cases were females. All work was done after getting the local medical ethics committee's approval. Also, A written informed consent was signed.

2.1 Inclusion Criteria

- Patient age group 20 to 60 years.
- Patient with suspected brain lesions on clinical bases.

2.2 Exclusion criteria

- Patient with contraindications to MRI as prosthetic heart valves, Pacemakers, Metallic implants, and Claustrophobia.
- Patient with contraindication to contrast media in indicated cases as renal failure, pregnancy, and history of reaction to contrast.

2.3 Imaging and Imaging Analysis

Philips Achiva 1.5-Tesla unit system was utilized for MRI images, the examination protocol included the following sequences and images: axial, sagittal, coronal T1, axial and coronal T2 and axial flair. Post contrast administration axial, coronal and sagittal T1 weighted images. Diffusion-sensitizing gradients were applied with a diffusion sensitivity of b = 0, 500 and 1000 s/mm2.

2.4 Conventional MRI

Conventional MRI was done where patients in supine position by the usage of standard head coil while head preserved in a neutral position. Sagittal and axial T1-weighted non-contrast images, and axial T2-weighted images were done. Post-contrast-enhanced axial, coronal, and sagittal T1- weighted images were done.

2.5 Matrix

256 × 256 and 256 × 192, field of view 230 mm, slice thickness 5 mm and slice gap 1 mm.

2.6 DWI

Using multi-section single-shot spin EPI sequence (b values 0.5 and 1000 mm^2/s), DWI was executed before injection of contrast agent in a dose of 0.1 m mol/kg intravenous. ADC measurements were performed using a region of interest (ROI) method. Measurements were obtained from the wall and centre of the lesion and all values were automatically calculated and expressed in 10^{-3} mm^2/s. Histopathology results confirm the final diagnosis. DWI was analyzed depending on signal intensity on diffusion images and corresponding ADC maps. Diffusion restriction is hyperintense signals on diffusion imaging with corresponding hypointense signals on ADC maps.

2.7 Data Collection and Analysis

Data was entered using the Statistical Package for Social Sciences (SPSS) program version 19.0 (SPSS Inc., Chicago, Illinois, USA). For quantitative data, mean and standard deviation were estimated while frequencies were calculated for categorical data. Simple t-test was used to compare the mean ADC values of brain abscess and cystic/necrotic neoplastic lesions. $P < 0.05$ was considered significant.

3. Results

Our results are illustrated in the following tables and figures. As regarding **age**, patients were between 20 to 60 years with a mean ± SD of 41.7 ± 4.6 years. Regarding **sex**, 21 cases were male while 19 cases were females. Male to female ratio was 52: 48 % of all cases. (Table 1 and figure 1). Patients were arranged into 2 groups regarding MRI findings: **Group I:** neoplastic group included 24 patients (60 %). **Group II:** non-neoplastic group included 16 patients (40 %). **Among the neoplastic lesions**, 14 of 24 (35 % of all cases) were found to be restricted, and 10 of 24 (25 % of all cases) were nonrestricted. Neoplastic lesions included: glioblastoma multiforme was found in 6 patients (15 % of all cases), meningioma in 4 patients (10 % of all cases), and intracranial metastases in 2 patients (5 % of all cases) **(Table .2)** There was significance lowering in ADC value of high-grade malignant tumors than those of low grades. No significant difference was noticed in ADC values of high-grade primary tumors (0.6–1.1 × 10^{-3} mm^2/s) and metastases (0.6–1 × 10^{-3} mm^2/s) **(Figure .2A).**

GIII glioma was detected in 1 patient (2.5 % of all cases), while GII glioma in 2 patients (5%of all cases). Low-grade glioma has significantly higher ADC than high-grade one. P value was 0.015 as shown in **Table (3).** Oligodendroglioma was found in 2 patients (5 % of all cases). Lymphoma was diagnosed in 2 cases (5 % of all cases). Medulloblastoma was found in 2 patients (5 %of all cases), and pilocytic astrocytoma in 1 patient (2.5 % of all cases). There was significantly lower ADC in patients with lymphoma than those with high-grade astrocytoma. P value was 0.049 **(Figure .2B).** Ependymoma was found in 1 case (2.5 % of all cases) and hemangioblastoma in one patient (2.5 % of all cases).

Table (1): Distribution of age of patients.

Age	Number	Percentage %	P value
20 to < 30	9	22.5	0.213
30 to < 40	10	25	
40 to < 50	11	27.5	
50 to 60	10	25	

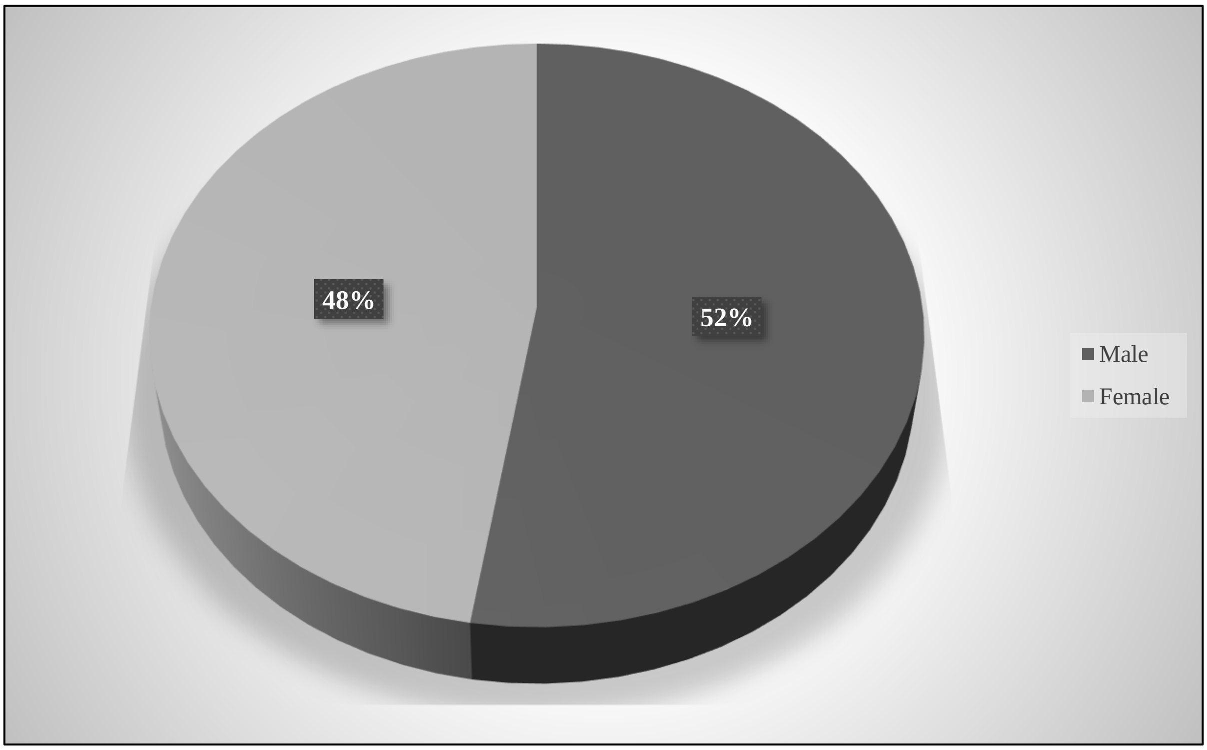

Figure (1): Sex distribution in the studied patients.

Table (2): Neoplastic group in our study of all cases.

Neoplastic tumor	No	Percentage % of all cases
Glioblastoma multiforme	6	15
Meningioma	4	10
Intracranial metastases	2	5
GII glioma	2	5
Oligodendroglioma	2	5
Lymphoma	2	5
Medulloblastoma	2	5
GIII glioma	1	2.5
pilocytic astrocytoma	1	2.5
Ependymoma	1	2.5
Hemangioblastoma	1	2.5

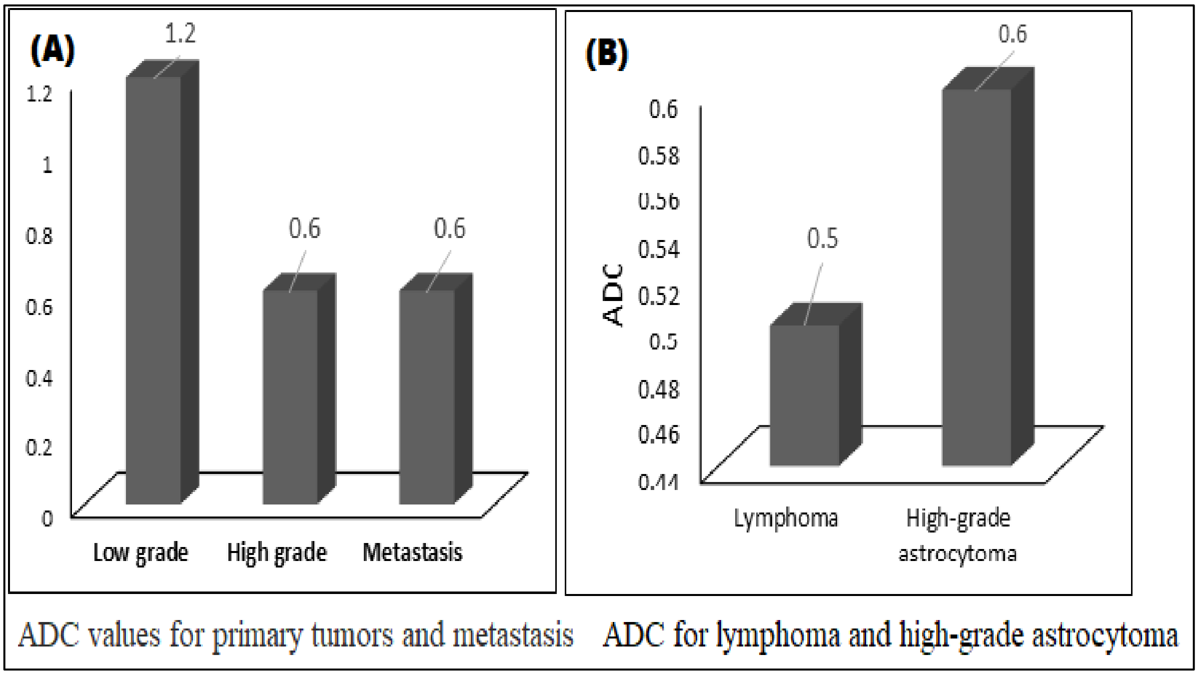

Figure (2): Sex distribution in the studied patients.

Table (3): ADC and glioma grading.

	Glioma grade	Range	Mean	SD	Cutoff value	t-Test	P value
ADC value ($\times10^{-3}$/mm^2)	Low-grade glioma	0.8- 1.2	1.1	0.12	0.98×10^{-3} mm^2 /s	2.11	0.015
	High-grade glioma	0.6- 1.5	0.7	0.21			

3.1 Regarding the Non-Neoplastic Group

This group included 16 patients (40 % of all cases): Among all these lesions, the restricted lesions were 9 of 16 (22.5 % of all cases) and the nonrestricted lesions were 7 of 16 (17.5 % of all cases). No statistical significance was found between the diffusion pattern and the nature of the lesion ($\chi 2 = 0.16$, $P = 0.68$) **(Table 4).**
Among these group, 2 cases were found to have demyelinating diseases (multiple sclerosis/acute disseminated encephalomyelitis) (5 %of all cases), 1 case (2.5 %of all cases) of encephalitis, 4 cases (10 %of all cases) with intracranial suppuration, and 3 cases (7.5 % of all cases) with intracerebral hemorrhage **(Table 5).**

Also, 4 cases were of epidermoid cysts (10 % of all cases), and 2 cases of arachnoid cysts (5 % of all cases). Epidermoid cysts have ADC of 0.5 to 0.6 × 10^{-3} mm2 /s. ADC of arachnoid cysts ranged from 3 to 4 × 10^{-3} mm^2 /s. Analysis of the values of ADC indicates a significant difference between epidermoid and arachnoid cysts (t-test = 3.22, P = 0.001*) **(Figure 3A).**
The ADC of pyogenic brain abscesses was ranged from 0.5-0.7 × $10^{–3}$/mm2. Necrotic tumors included glioblastoma multiform (GBM) and cases of metastases. Overall, necrotic tumors have ADC of 0.4 to 2.0. On comparing both groups, we found significantly higher ADC for necrotic tumors than brain abscess **(Figure 3B)**.

Table (4): Diffusion image evaluation for neoplastic and non-neoplastic groups.

	Neoplastic group	Non neoplastic group	χ2	P value
Restricted	14 (35 %)	9 (22.5 %)	0.16	0.8
Non restricted	10 (25 %)	7 (17.5 %)		

Table (5): Non-neoplastic group in our study.

Non-neoplastic tumor	No	Percentage % of all cases
Epidermoid cysts	4	10
Pyogenic brain abscesses	3	7.5
Intracerebral hemorrhage	3	7.5
Arachnoid cysts	2	5
Demyelinating diseases	2	5
Subdural empyema	1	2.5
Encephalitis	1	2.5

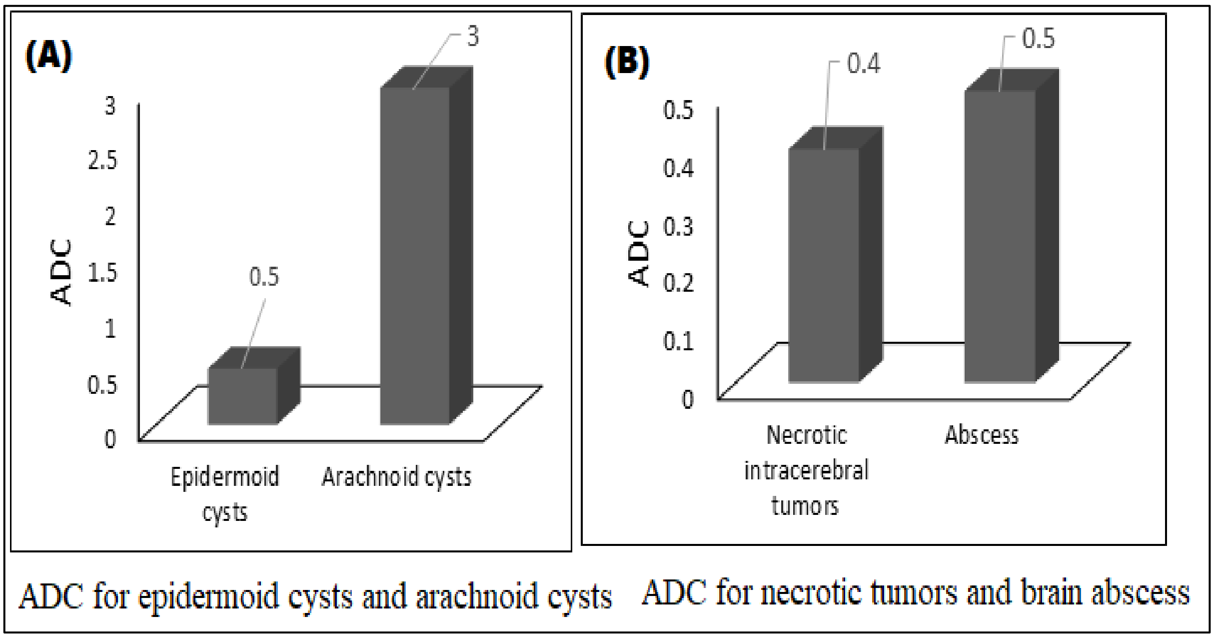

Figure (3): Sex distribution in the studied patients.

4. Cases

Case 1

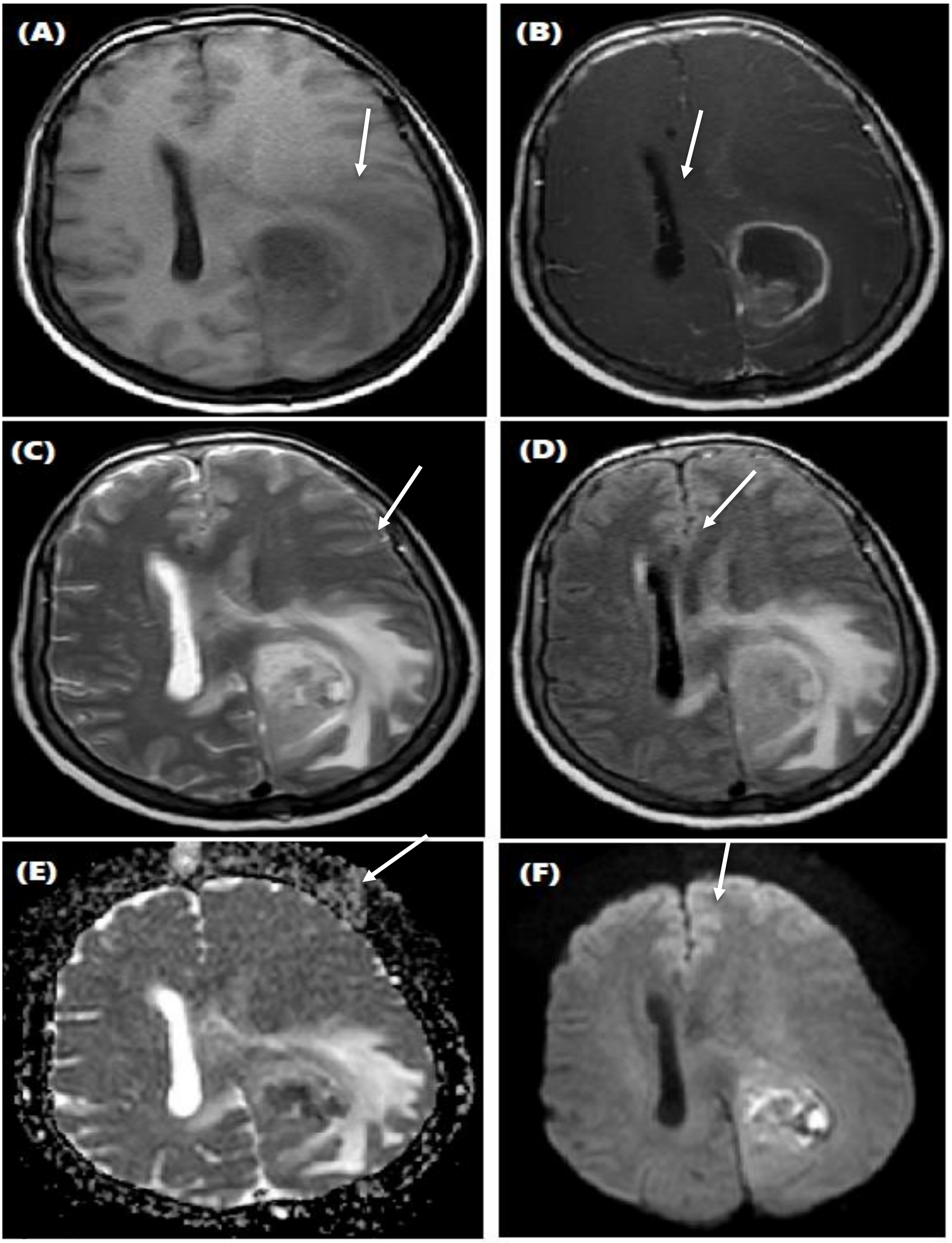

Figure (4): Male patient aged 51 years presented with headache and disturbed conscious level from few months ago. Radiological findings: Axial T1 pre-contrast (A), post-contrast (B), Axial T2 (C), axial FLAIR (D), ADC (E) and DWI (F) revealed large paramedian intra-axial lesion measuring about 4.5x4x4.2 cm in the left temporoparietal region that is resting medially on the falx cerebri and involves corpus callosum splenium. The lesion is low signal in T1, bright in T2 and FLAIR with central necrosis and marginal enhancement. The lesion was surrounded by moderate amount of edema and causing midline shift to right side. DWI shows central area of restricted diffusion. Radiological diagnosis: Glioblastoma multiformes.

Case 2:

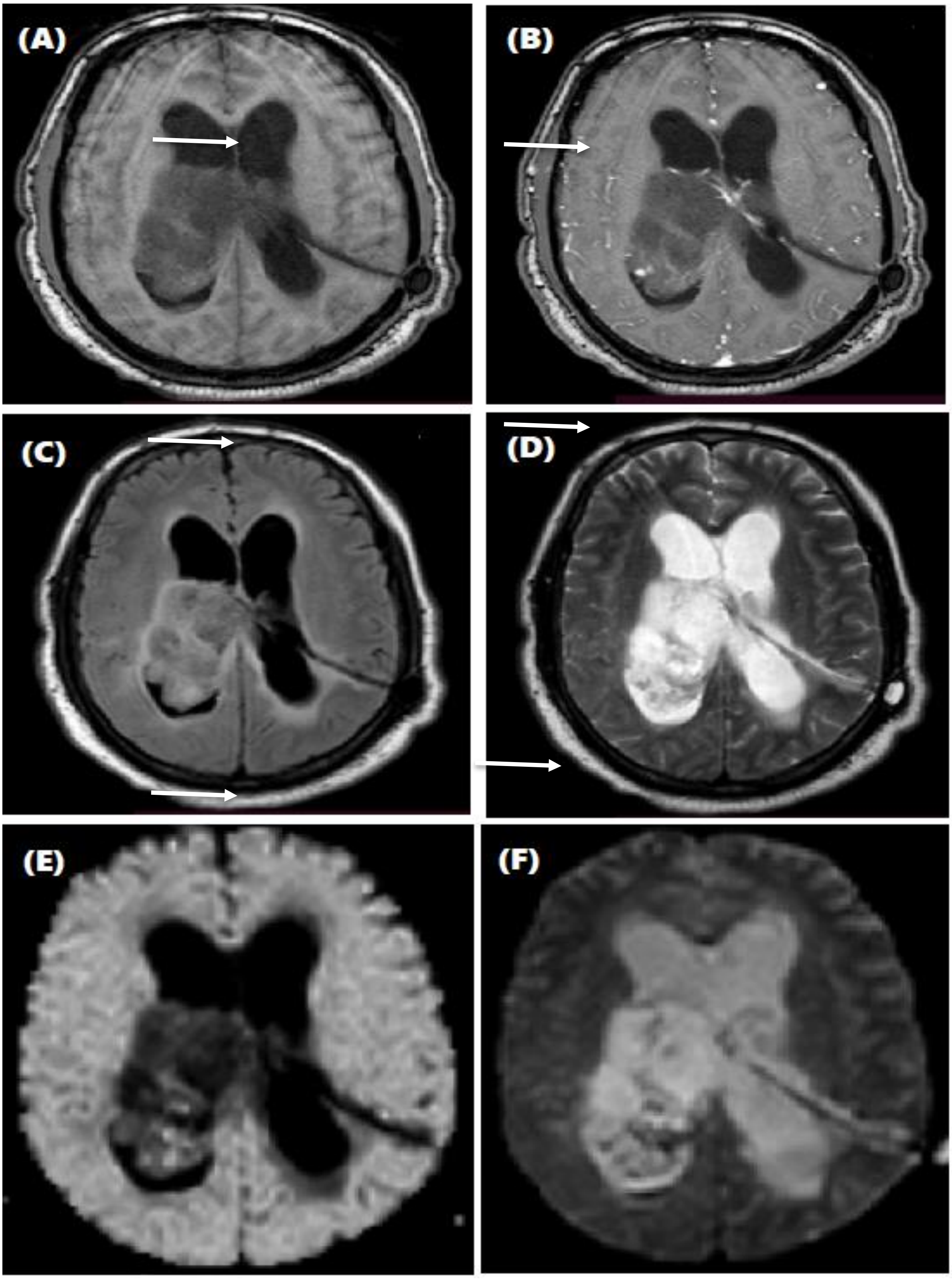

Figure (5): Male patient aged 41 years suffering from headache and blurring of vision having a history of V. P shunt few months ago. **Radiological findings:** Axial T1 pre-contrast (A) and post-contrast (B), Axial FLAIR (C) and axial T2 (D) revealed large intraventricular lobulated heterogeneous space occupying lesion measuring about 6x6.5x5.5 cm that is seen at body of right lateral ventricle involving septum pellucidum with minimal extension into left lateral ventricle, there is associated with supra-tentorial hydrocephalic changes with shunt noticed in the Rt lateral ventricle. The lesion is heterogenous low T1, bright T2/FLAIR signal and heterogenous post-contrast enhancement. Axial DWI (E) and ADC (F) revealed slightly diffusion restriction. **Radiological diagnosis: Ependymoma.**

Case 3:

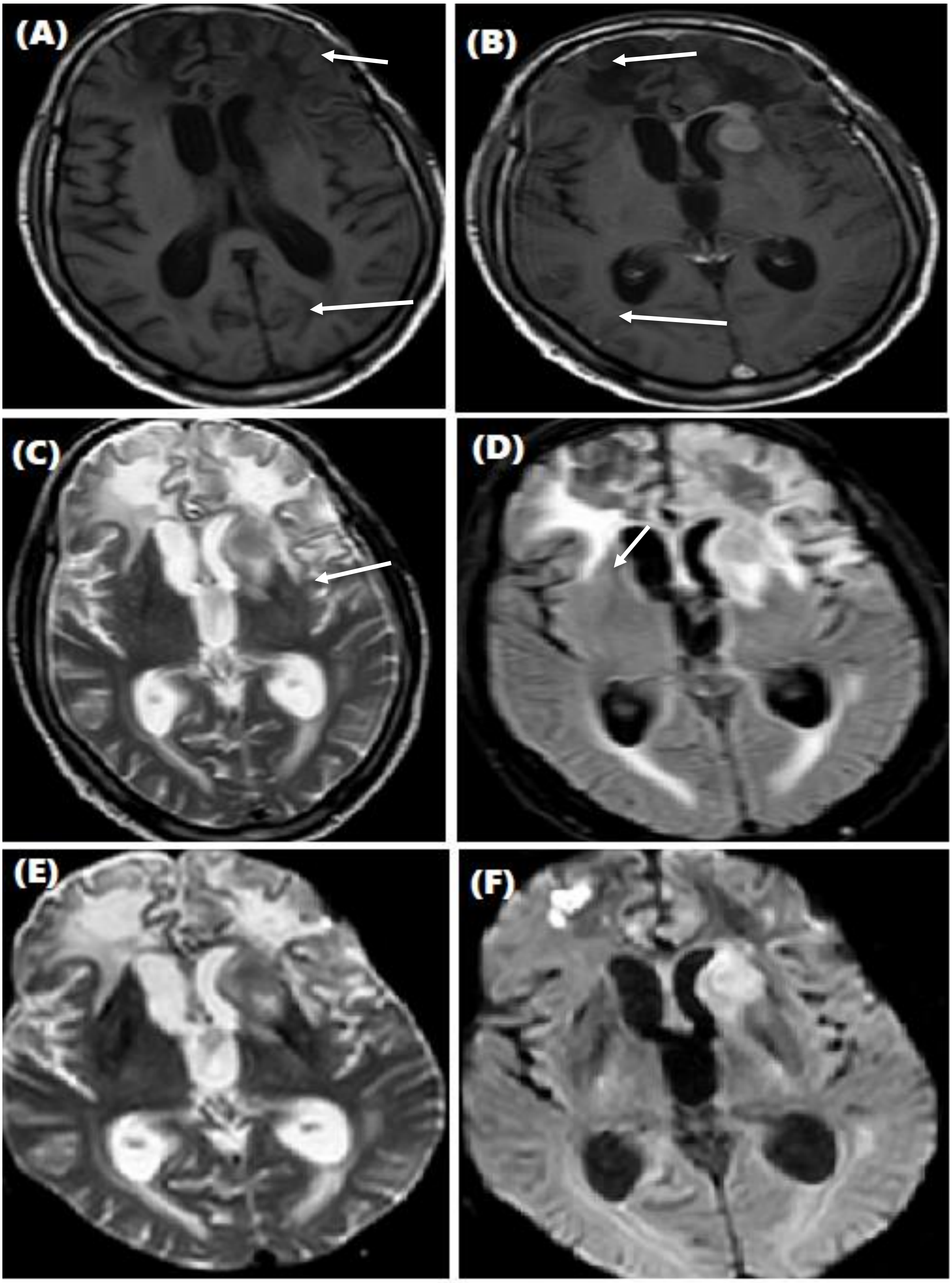

Figure (6): Male patient aged 44 years presented by headache and disturbed conscious level few months ago. **Radiological findings:** Axial T1 pre-contrast (A), post-contrast (B), Axial T2 (C) and axial FLAIR (D) revealed a well-defined rather rounded lesion at Lt frontal region causing partial effacement of frontal horn of ipsilateral lateral ventricle with moderate surrounding vasogenic oedema. The lesion is intermediate signal T1, high in T2/FLAIR and homogenous post contrast enhancement. Axial ADC (E) and DWI (F) shows restricted diffusion. **Radiological diagnosis: Primary CNS lymphoma.**

Case 4:

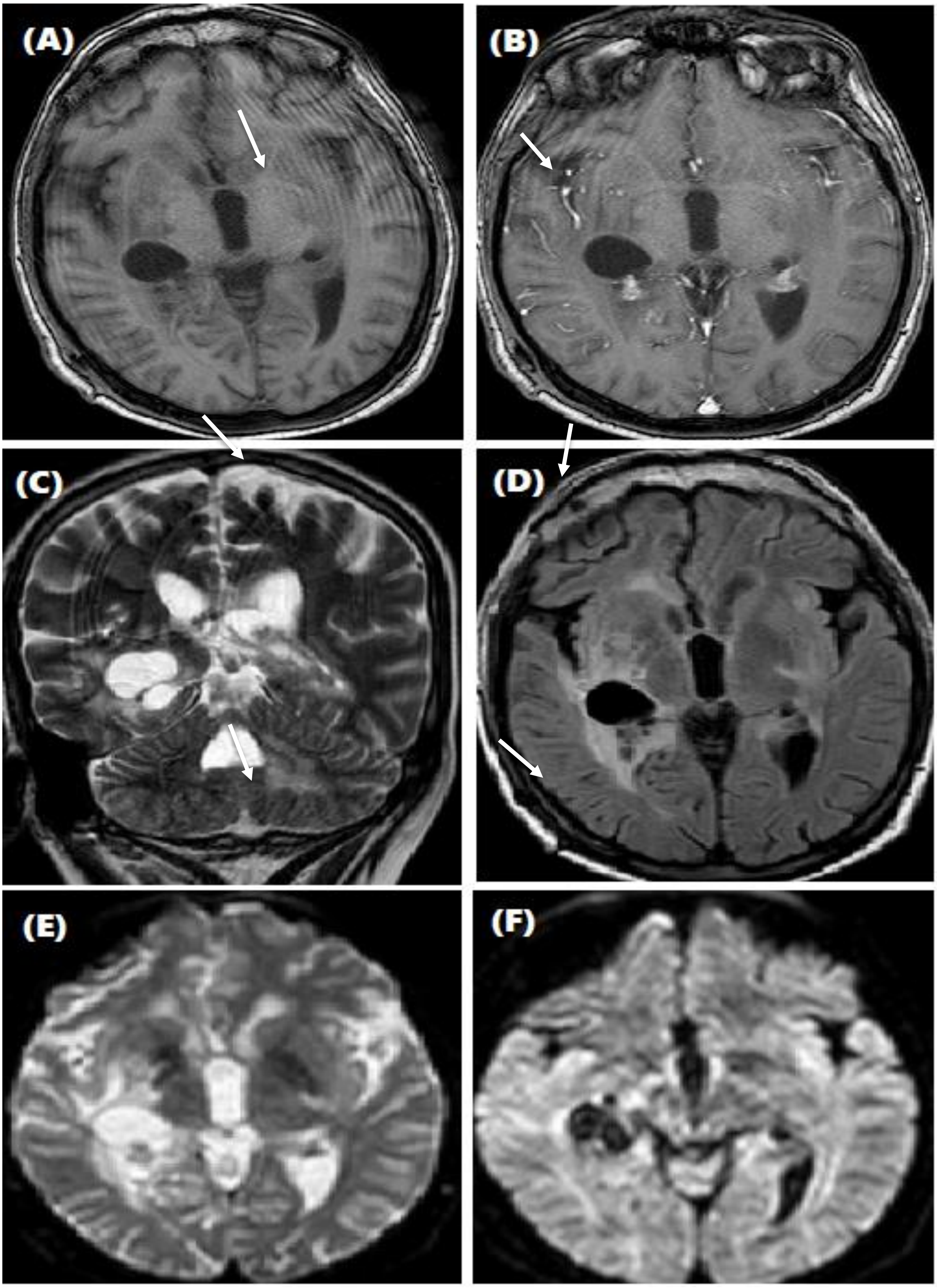

Figure (7): Male patient aged 40 years presented by signs of increase intracranial tension, seizures and focal neurological deficit few months ago. **Radiological findings:** Axial T1 pre-contrast (A) and post-contrast (B), coronal T2 (C) and axial FLAIR (D) revealed multiple cystic lesions seen scattered in both cerebral hemispheres. The largest seen at right temporal lobe displaying hypointense T1, bright in T2 and hypointense in FLAIR with pre focal edema and no post-contrast enhancement. Axial ADC (E) and DWI (F) revealed free diffusion. **Radiological diagnosis: Multiple hydatid cyst.**

Case 5:

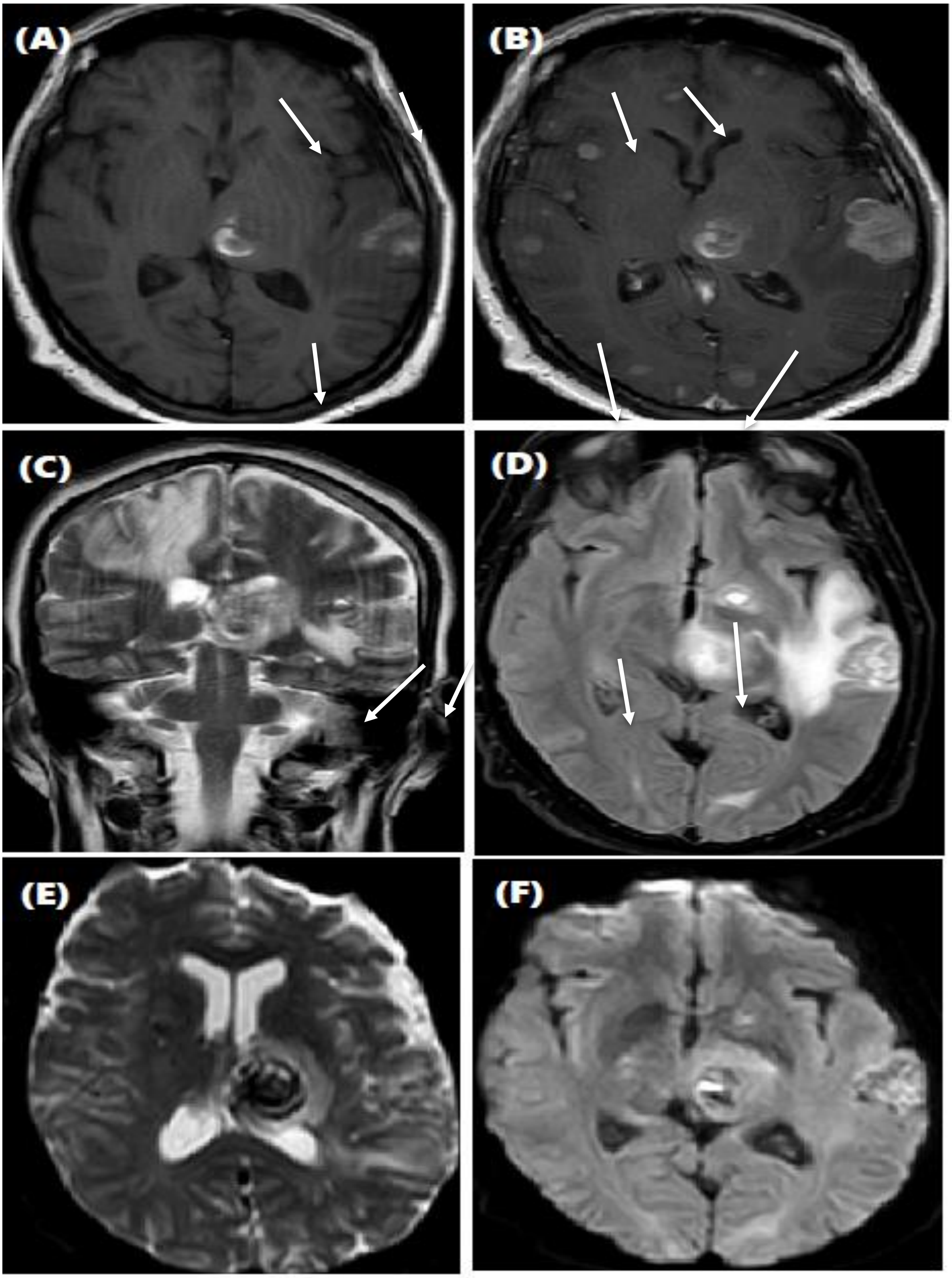

Figure (8): Male patient aged 60 years with history of bronchogenic carcinoma presented by headache, confusions and disturbed conscious level few months ago. **Radiological findings:** Axial T1 pre-contrast (A) and post-contrast (B), coronal T2 (C) and FLAIR (D) revealed multiple solid lesions at both cerebral hemispheres, the largest is seen at the left temporal region measuring about 2.9x2.4x2.3 cm with mild vasogenic edema, The lesion is hyperintense in T1, T2, and FLAIR with post contrast homogenous enhancement. Axial ADC (E) and DWI (F) revealed restricted diffusion. Another lesion noted at Lt thalamic region. **Radiological diagnosis: Bronchogenic carcinoma hemorrhagic metastases (brain Mets).**

4. Discussion

Brain lesions are defined as damage to any area of brain. Lesions may appear in a specific region of brain. Sometimes, lesions are lied in a large area of brain. Patients with brain lesion may not suffered from any symptoms but as the condition get worsen, symptoms appear gradually **[5].**

Conventional MRI has the ability to evaluate location, morphology, and extent of tumors, but it has a little role in diagnostic evaluation. So, another technique must be used together with conventional MRI. DWI can help in reaching a diagnosis and making a differential diagnosis between tumors **[6].** Diffusion-MRI has demonstrated its usefulness in acquiring information to better define neurodegenerative microstructural alterations and mechanisms of neurophysiological activity **[6].**

In this study, glioma with low grading has significantly higher ADC than that of high grading. P value was 0.015. This result aligned with **Balos et al., (2013) [7],** whose study reported that ADC of different glioma grading was significantly different. They explained these results by augmented cellularity of glioma with high grading. Also, proliferation of small blood vessels and necrosis may be a cause. They found there was indirect relationship between diffusivity and cellularity of glial tumors **[7].**

Regarding high-grade gliomas, all patients showed restriction of diffusion, except one patient with pilocytic astrocytoma who showed increased diffusion pattern and hyperintense ADC signal. ADCs could not be utilized in individual cases in order to distinguish types of tumors of the same grade. This was emphasized in our study; a false-positive result was encountered in one case; whereas cMRI and DWI revealed a diagnosis of high-grade glioma (astrocytoma), histopathological examination revealed high-grade (anaplastic) oligodendroglioma. In our study, there was significant lower ADC in patients with lymphoma than those with high grade astrocytoma using DWI and ADC. P value was 0.049 as ADC for lymphoma was 0.5- 0.7 and that of astrocytoma was 0.6 – 1.5. This matched with the results of **Kitis et al., (2015)** [8] whose study was conducted on 65 cases having brain tumors as reported by histopathological or clinical examination. By using DWI, ADC of all tumors were measured and the differences between groups were recorded and statistically analyzed. Their results showed that gliomas with low grading have higher ADC when compared to those of high grading. Also, glioblastomas, astrocytomas, lymphomas, and metastases showed no statistically significant changes in their ADC. However, on comparing lymphomas and high-grade gliomas, lymphomas had lower ADC **[8].** Also, **Kuker et al., (2015),** showed the same previous results about lymphomas and other tumors that their ADC were significantly lower than other tumors **[9].**

The ADC of pyogenic brain abscesses was ranged from 0.5-0.7 × 10–3/mm2. Necrotic tumors included GBM and cases of metastases. Overall, the ADC values of necrotic tumors ranged from 0.4 to 2.0. On comparing between both groups, we found significant higher ADC for necrotic tumors than brain abscess. P value was 0.043. These findings were in line with **Baghdady et al., (2016)** [1] whose research showed that ADC values at the cerebral abscesses was 0.56 ± 0.005 × 10–3 mm2 and intracerebral tumors was 0.925 ± 0.497 × 10–3 mm2 /s (mean ± SD) **[1].**

In the current study, estimated ADC of epidermoid cysts was between 0.5 to 0.6 × 10^{-3} mm2 /s. ADC results of arachnoid cysts ranged from 3 to 4 × 10^{-3} mm^2 /s. Analysis of the values of ADC indicate a significant difference between epidermoid and arachnoid cysts (t-test = 3.22, P = 0.001*). This result goes in line with

Tsuruda et al., (2014) [10], whose study illustrated arachnoid cysts ADC was the same value of stationary water. On the other hand, ADC of epidermoid tumors showed the same results of parenchyma of brain, concluding slower diffusion rate and solid nature of epidermoid tumors **[10].**

5. Recommendations

- DWI is an effective imaging procedure for differentiation of a wide variety of space occupying brain lesions.
- DWI is an important technique helping to differentiate brain abscesses from necrotic neoplasms, and epidermoid from arachnoid cysts.
- DWI helps in differentiating brain lymphoma from high-grade glioma. DWI can help in determination of glioma grade.
- DWI entailed less imaging time; and is available in many imaging centers.

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Conflicts of interest: No competing interest

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