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## Case Report

# Diffuse astrocytoma and the diagnostic dilemma of an unusual phenotype: A case report <sup>☆,☆☆</sup>

Sultan A. Alshoabi, MD<sup>a,\*</sup>, Amal A. Alareqi, MD<sup>b,c</sup>, Awatef M. Omer, PhD<sup>a</sup>,  
Awadia G. Suliman, PhD<sup>a</sup>, Tareef S. Daqqaq, MD<sup>d</sup>

<sup>a</sup>Department of Diagnostic Radiology Technology, College of Applied Medical Sciences, Taibah University, Almadinah Almunawwarah, 42312, Kingdom of Saudi Arabia

<sup>b</sup>Department of Radiology, University of Science and Technology Hospital (USTH), Sana'a, Republic of Yemen

<sup>c</sup>Radiology department, 21 September university of medical and applied sciences, Sana'a, Republic of Yemen

<sup>d</sup>Department of Radiology, Faculty of Medicine, Taibah University, Almadinah Almunawwarah, Kingdom of Saudi Arabia

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## ABSTRACT

Diffuse astrocytoma is an infiltrating type of glioma (World Health Organization grade II), which even with histopathology, is difficult to diagnose. Magnetic resonance imaging (MRI) is the cornerstone for diagnoses and follow-up of brain gliomas. This report describes a case of diffuse astrocytoma in a 48-year-old man who presented with sudden right-sided weakness and repeated convulsive attacks. On brain computed tomography, the case was diagnosed and treated as an acute infarction. Ten days later, the patient returned with a total loss of consciousness. Brain MRI images revealed an irregularly outlined lesion involving the splenium of the corpus callosum that extended into the left periventricular parietal lobe of the brain with cystic foci in the septum pellucidum. Contrast-enhanced and new sequences of MRI was helpful in approach to diagnosis because of its superior tissue characterization. The histopathology results ultimately confirmed the diagnosis of diffuse astrocytoma. The patient died postoperatively.

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## Introduction

Gliomas are the most common primary neoplasms of the brain, and they cause significant morbidity and mortality.

Glioblastoma (GBM) is the most common, aggressive brain tumour in adults and is associated with low survival rates and dismal prognoses [1]. Diffuse astrocytomas (which include GBM) have worse prognoses than other gliomas [2]. The World Health Organization's (WHO) classification of gliomas

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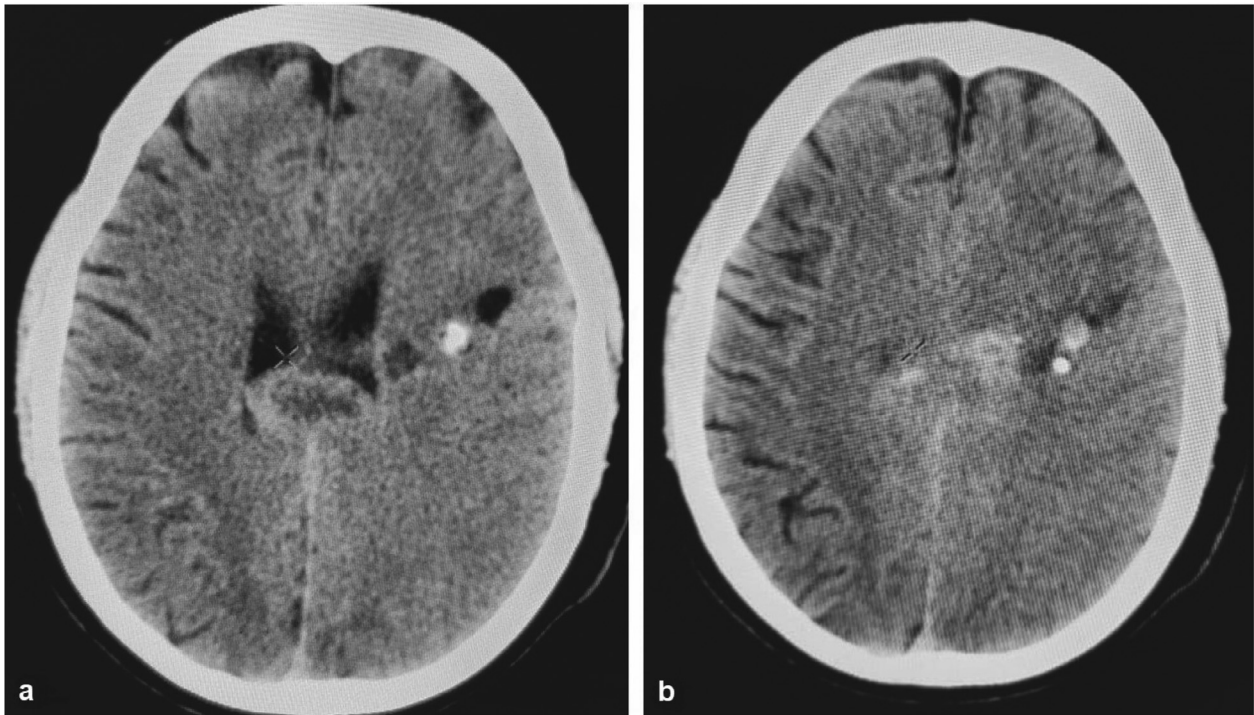
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\* Corresponding author.

E-mail address: [alshoabisultan@yahoo.com](mailto:alshoabisultan@yahoo.com) (S.A. Alshoabi).

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**Fig. 1** – Selected images of computed tomography show a) a partially well-defined heterogeneous lesion in the posterior part of the septum pellucidum with low-density ill-defined lesion in the left parietal lobe which containing calcific focus, and b) multiple high-density calcific foci in the lesion with effacement of the cortical sulci in the left cerebral hemisphere.

uses histologic criteria to classify gliomas as low grade (grades I and II) and high grade (grades III and IV) [3]. In 2016, the WHO's updated classification of central nervous system (CNS) tumours significantly restructured the classification of diffuse gliomas and other embryonal tumours. This classification system incorporated new glioma entities, which were defined by the integration of classic histological features and molecular biomarkers, such as diffuse midline gliomas [4]. Diffuse astrocytoma is an infiltrating type of glioma (WHO grade II), which even with histopathology, is difficult to diagnose [5].

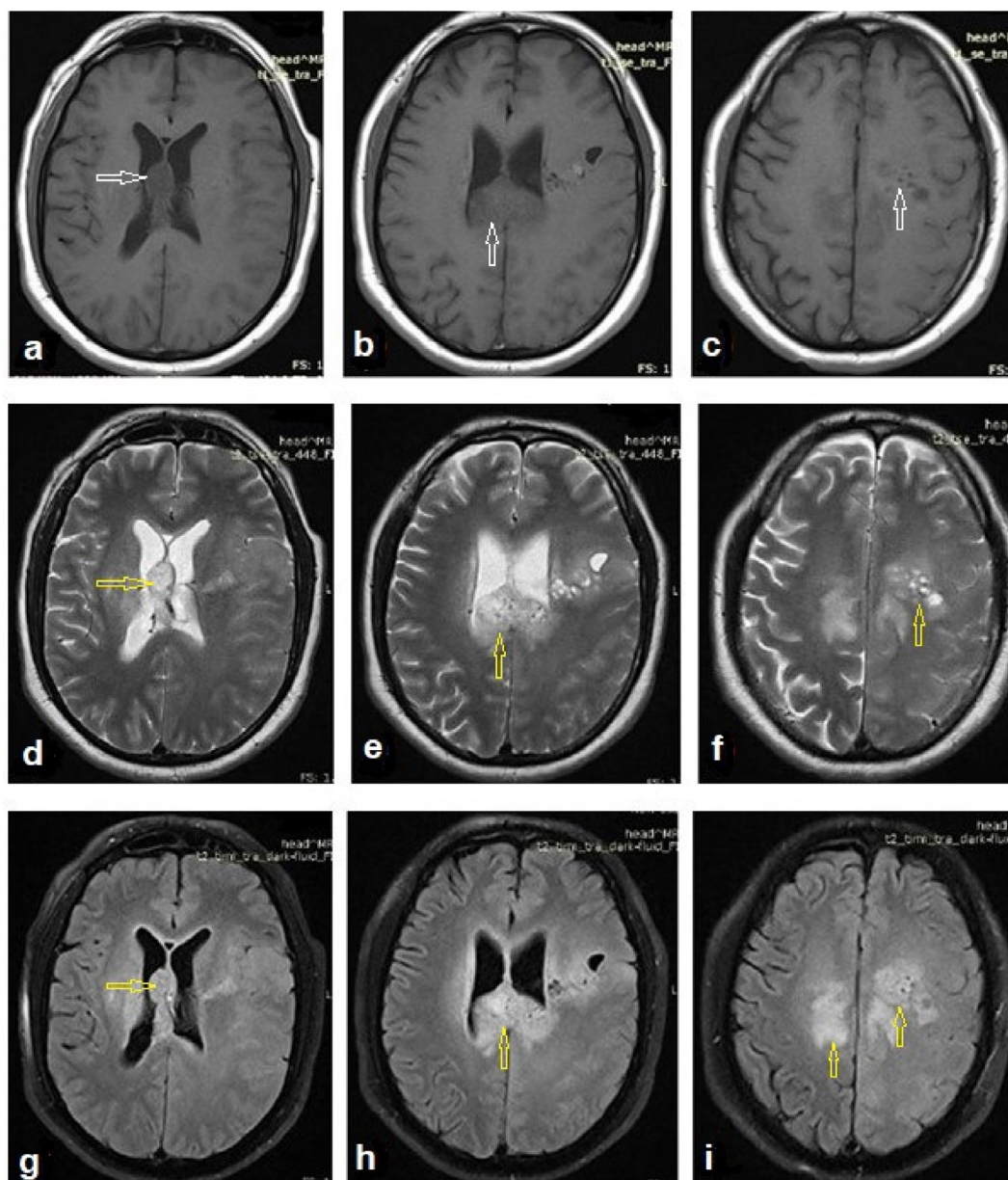
Magnetic resonance imaging (MRI) is a widely used imaging modality in the diagnoses and post-operative management of brain gliomas. Basic MRI modalities, native T1-weighted images (T1WIs), T2-WIs and T2-fluid-attenuation inversion recovery (T2-FLAIR) sequences, provide basic information about tumours. In recent decades, new and advanced MRI modalities have been used to further characterize and differentiate brain tumours. These have included multi-parametric MRI sequences, such as (1) dynamic contrast enhancement, (2) dynamic susceptibility contrast, (3) diffusion tensor imaging and (4) magnetic resonance spectroscopy (MRS). In addition, to decrease post-surgical neuro deficits, tractography and functional MRI have seen increased use in neuro-oncology [6].

In the present case, we reported an unusual phenotype of diffuse astrocytoma that caused a diagnostic dilemma on medical imaging modalities. This report aims to elucidate the importance of conducting full investigations and medical imaging methods for any brain lesions during the beginning of presentation to avoid misdiagnoses, mismanagement, and subsequently fatal complications.

## Case presentation

A 48-year-old man presented to the emergency room with right-sided weakness, facial palsy, and repeated tonic/clonic convulsive attacks that persisted for two minutes at a time since one day. The patient had a one-year history of hypertension and took regular antihypertensive drugs. Upon clinical examination, the patient was conscious, oriented with right-sided weakness (right side power 4/5 in upper and lower right limbs) and the plantar reflex was equivocal. The provisional diagnosis was a cerebrovascular accident. A brain computed tomography (CT) scan was completed and revealed a partially well-defined heterogeneous lesion in the posterior parts of the corpus callosum and septum pellucidum, in addition to low-density ill-defined lesion in the left parietal lobe with multiple high-density calcific foci in the lesion and effacement of the cortical sulci in the left cerebral hemisphere (Fig. 1). Ischemic stroke was the primary suggested diagnosis, but the calcified foci suggested tuberculous infection as a differential diagnosis. The patient was admitted and treated with anticonvulsants, antibiotics, Neurozan and other supportive drugs. The patient improved and was discharged after five days on 1 × 2 80 mg ginkgobiloba tablets, 1 × 1 20 mg Suvican tablets, 1 × 1 100 mg aspirin tablets, 1 × 1 Neurozan capsules, 1 × 1 30 mg Doxirazol tablets and his regular antihypertensive drugs.

Two weeks later, the patient returned with a total loss of consciousness, and a brain MRI was performed. The MRI images revealed an irregularly outlined lesion involving the splenium of the corpus callosum that extended into the left periventricular parietal lobe of the brain with cystic lesions in

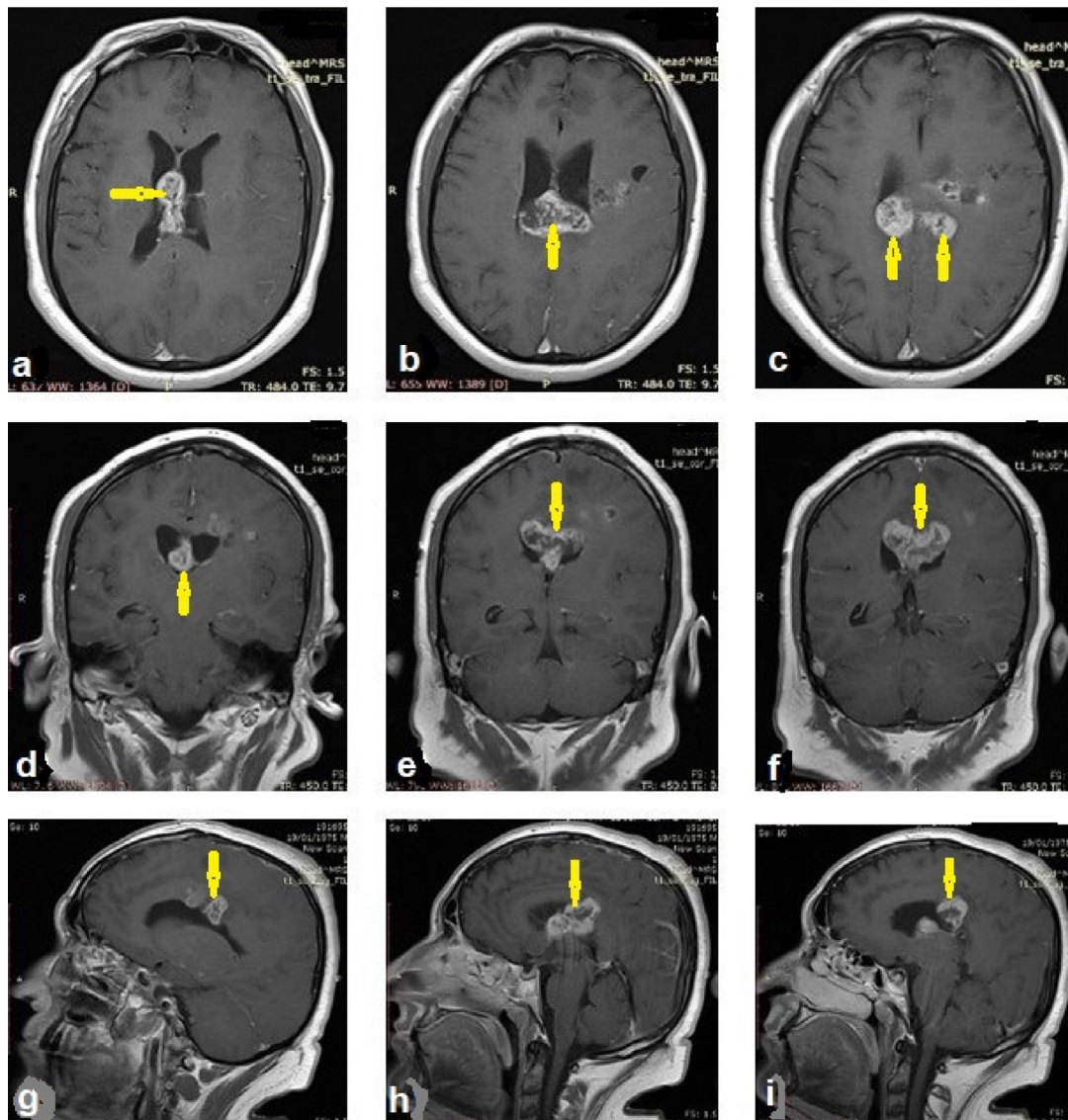


**Fig. 2** – Selected images of: (a, b, and c) T1-weighted images (T1WIs) of brain MRI show irregularly outlined lesion involving the splenium of the corpus callosum, extended into the left periventricular parietal lobe of the brain with cystic foci in the septum pellucidum with multiple low signal intensity foci in the left parietal lobe, (d, e, and f) T2-weighted images (T2WIs) of brain MRI show high signal intensity (SI) irregularly outlined involving the splenium of the corpus callosum, extended into the left periventricular parietal lobe of the brain with cystic foci in the septum pellucidum and multiple high signal intensity foci in the left parietal lobe, and (g, h, and i), fluid-attenuation inversion recovery (FLAIR) of brain MRI show high signal intensity (SI) irregularly outlined lesion involving the splenium of the corpus callosum, extended into the left periventricular parietal lobe of the brain with cystic foci in the septum pellucidum and multiple high signal intensity foci in the left parietal lobe.

the septum pellucidum. The lesion showed low signal intensity (SI) on T1WIs (Figs. 2a, b, and c) and high SI on both T2WIs (Figs. 2d, e, and f) and FLAIR (Fig. 2g, h, and i). After gadolinium was administered intravenously, contrast enhanced T1 images showed an irregularly outlined, heterogeneous and enhancing lesion in the body and splenium of the corpus callosum that extended into the left and right periventricular parietal lobe of the brain and in the septum pellucidum (Fig. 3).

GBM multiform, oligodendroglioma and lymphoma were suggested as differential diagnoses. Carcinoembryonic antigen (CEA) from the cerebrospinal fluid was 1.05 ng/mlmL. The toxoplasmosis test was negative in both immunoglobulin G (IgG) and immunoglobulin M (IgM). Cytomegalovirus (CMV) IgG was positive, and CMV IgM was negative.

Diffusion weighted images (DWIs) images showed no restricted diffusion in most parts of the lesion (Fig. 4a, b, and c).



**Fig. 3 – Selected images of contrast-enhanced T1-weighted images (T1WIs) of brain MRI showing irregularly outlined lesion with heterogeneous enhancement. The lesion forming butterfly shape on both axial (a, b, and c) and coronal (d, e, and f) images, and involved the splenium and body of the corpus callosum on sagittal images (g, h, and i).**

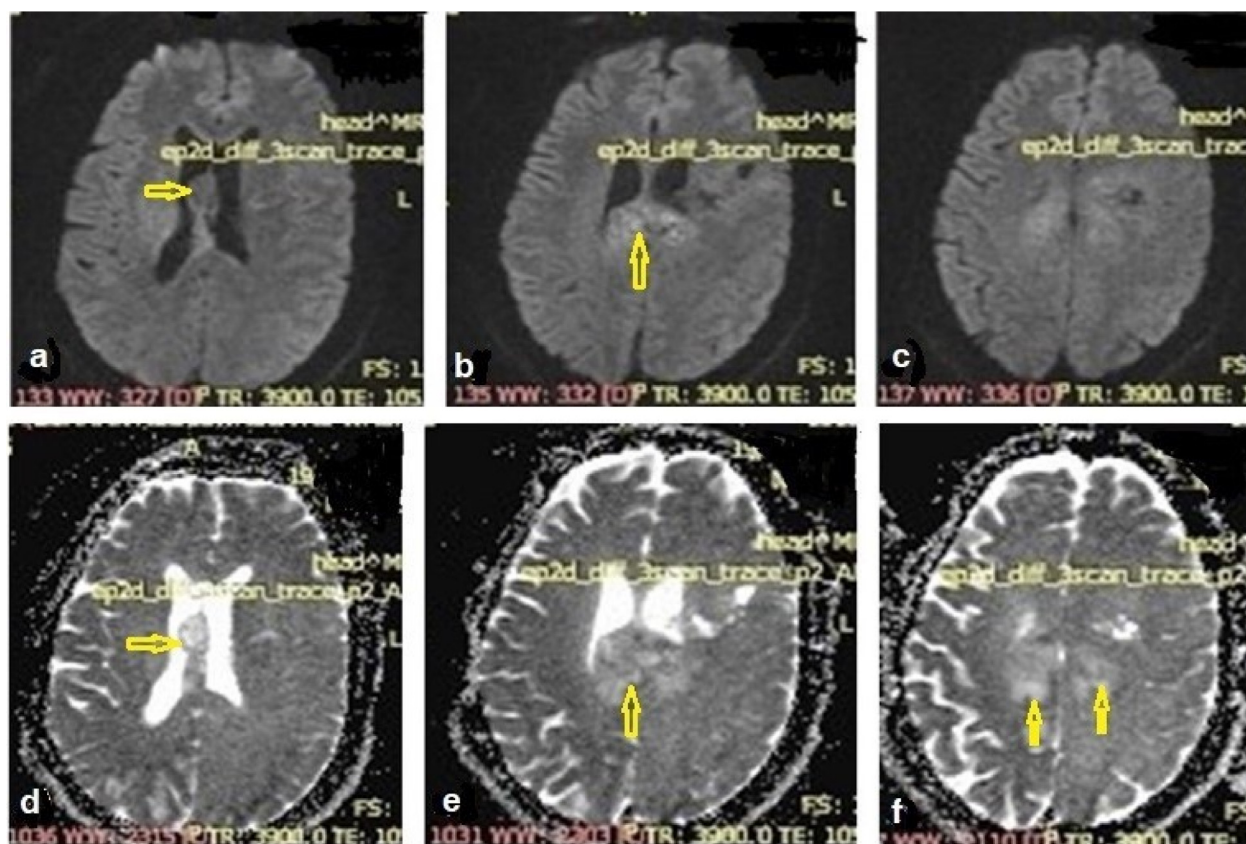
Apparent diffusion coefficient (ADC) showed slightly high SI in some parts of the lesion (Fig. 4d, e, and f). MRS showed depletion of both choline and NAA with choline/NAA ratio less than 1 ( $< 1$ ). This was not very helpful in suggesting primary neoplasms which typically exhibit decreased N-acetyl aspartate (NAA) and elevated Choline and choline/NAA ratio expected to be more than 1 ( $> 1$ ), (Fig. 5).

On MRI, there was another small, well-defined lesion in the left temporal lobe with high SI on the DWIs and low SI on the ADC map. This explained the patient's presentation of right-sided weakness as an acute lacunar infarction superimposed on the tumour lesion (Fig. 6).

Ultimately, stereotactic biopsy by burr hole was taken, and two independent histopathologists confirmed the diagnosis of diffuse astrocytoma through histopathological examination (Fig. 7). Unfortunately, the patient died postoperatively.

## Discussion

This case study reported an unusual phenotype of diffuse glioma that was initially misdiagnosed as brain infarction and then as focal encephalitis. These diagnoses led to mismanagement in the treatment of the disorder. The lesion appeared like a tumour with mass effect and involved the splenium of the corpus callosum, suggesting GBM or primary CNS lymphoma as a differential diagnosis. According to Park et al. [7], who reported that primary CNS lymphomas are rare tumours of the corpus callosum which commonly present as multifocal nodular lesions and typically appears as intermediate or low SI on T1WIs, high or intermediate SI on T2WIs with restricted diffusion on DWIs due to dense cellularity and usually shows homogenous enhancement after contrast admin-



**Fig. 4 – Selected images of (a, b, and c) Diffusion weighted images of brain MRI show no restricted diffusion in most parts of the lesion, (d, e, and f) apparent diffusion coefficient (ADC) map show no significant low signal intensity in the lesion.**

istration. GBMs are the most common diffuse and commonly spread along the white matter of the splenium of the CC which shows heterogeneous low SI on T1WIs, high SI on T2WIs with prominent internal necrosis, peritumoral vasogenic edema, and mass effect and it reveals irregular heterogeneous enhancement after contrast administration [7]. They also recommended that GBMs should be considered for differential diagnoses in any lesions that cross the CC. In addition, the authors reported that a focal infarction of the CC is rare due to the significant blood supply that surrounds it, which forms the anastomotic plexus from the three main arterial systems of the brain [7,8].

In the contrast enhanced T1WIs, the lesion predominantly showed heterogeneous enhancement more in its margins. The lesion appeared to be diffuse and infiltrative and involved the splenium of the corpus callosum and septum pellucidum. It also extended into the bilateral cerebral hemispheres, forming a butterfly shape on the coronal sections of the MRI. This is consistent with the diagnosis of a tumour rather than an infarction or inflammatory process as reported by Claes et al [9].

The lesion was not restricted in DWIs and showed slightly high SI on the ADC map, further decreasing the likelihood of infarction [7, 10]. The lesion showed predominantly low SI and slightly high SI on ADC. According to Sui et al., and Drake-Pérez et al. [11,12], these types of findings are inconsistent with acute or subacute infarctions. White et al. [13] reported

that DWIs and ADC can be used as imaging biomarkers for detection, characterization and treatment and monitoring responses in brain tumours.

Horská et al. reported that nearly all brain neoplasms typically exhibit decreased N-acetyl aspartate (NAA) signals with elevated Choline (Cho) and Cho/NAA ratio expected to be more than 1 ( $>1$ ) [14]. In the current case, MRS was not very helpful in suggesting primary brain neoplasm which reveals the Cho/NAA ratio less than 1 ( $<1$ ). This can be explained by the critical location of the lesion with extensive necrosis that limiting a good sampling of the lesion where the sampled voxel probably located in the necrotic part of the lesion.

Roldan-Valadez et al. [15] indicated that high pre-operative Cho/NAA and low lipid-lactate/creatinine ratios are significant predictors of survival in brain tumours. In the present case study, the Cho/NAA ratio was  $<1$ . Sarrazin et al. reported that, the presence of brain tissue markers (peaks in NAA, choline, and creatine) indicate a low likelihood of infection [16] reported that, the presence of brain tissue markers (peaks in NAA, choline, and creatine) indicate a low likelihood of infection. Therefore, tuberculosis, toxoplasmosis and fungal infection were not possible in the current case. The patient was taking ant tuberculous drugs one month before he died, and he died postoperatively. This is consistent with findings by Mohan et al. [17] who reported that corpus callosum involvement is a poor prognostic factor in gliomas. Tunthanathip et al. [18] reported that butterfly tumor of the corpus callosum is

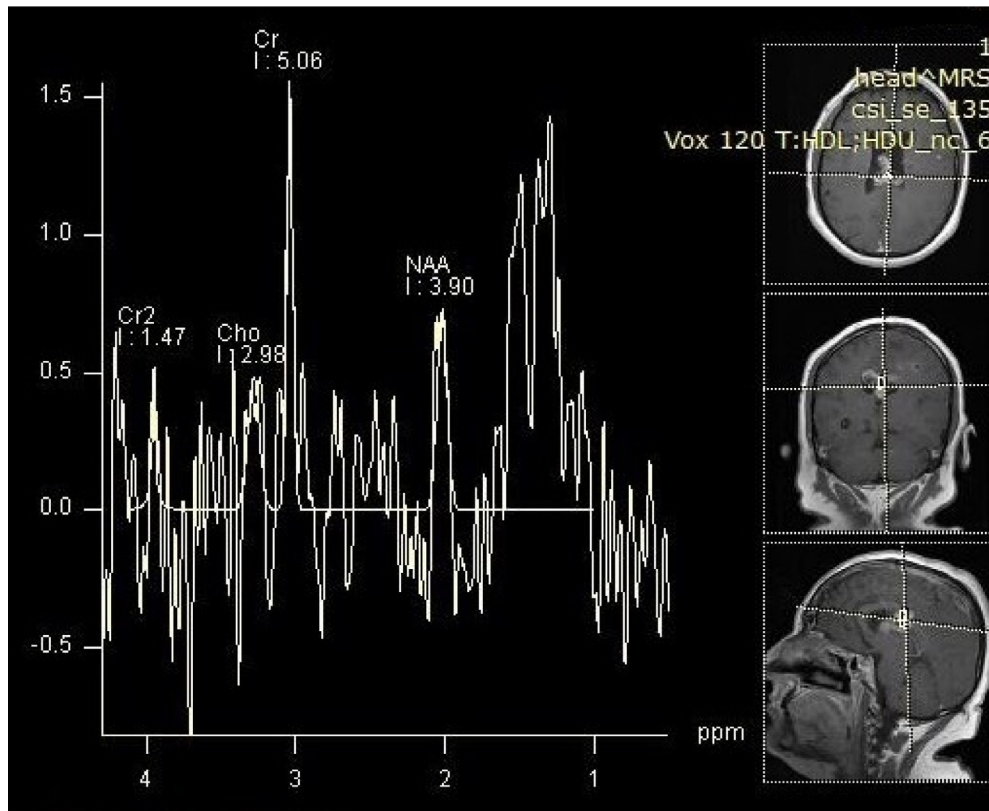


Fig. 5 – Intermediate echo MR spectrum demonstrates a significant decrease of all the metabolites as concluded by high creatine (Cr) (at 3.0 ppm) compared to the other metabolites including N-acetyl aspartate (NAA) (at 2.02 ppm) and choline (at 3.2 ppm).

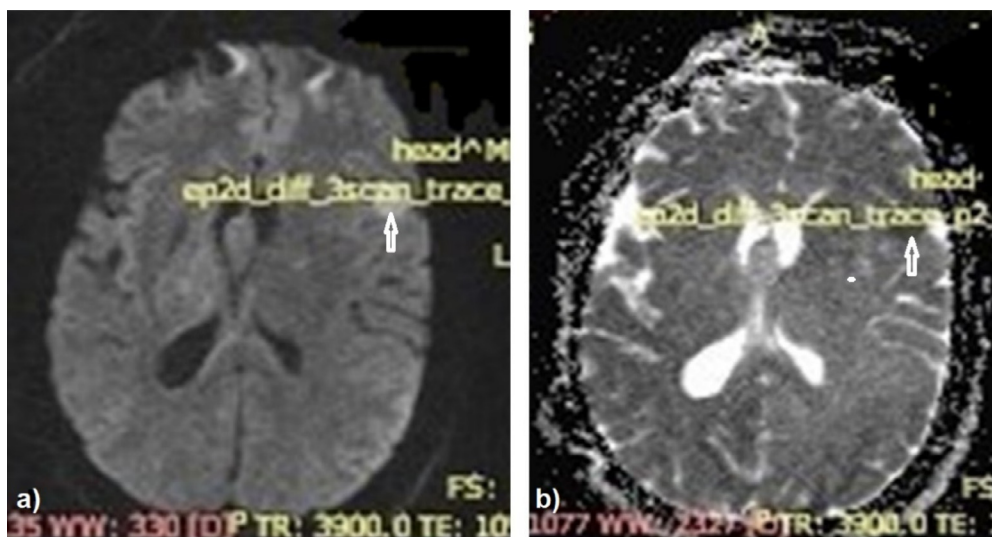
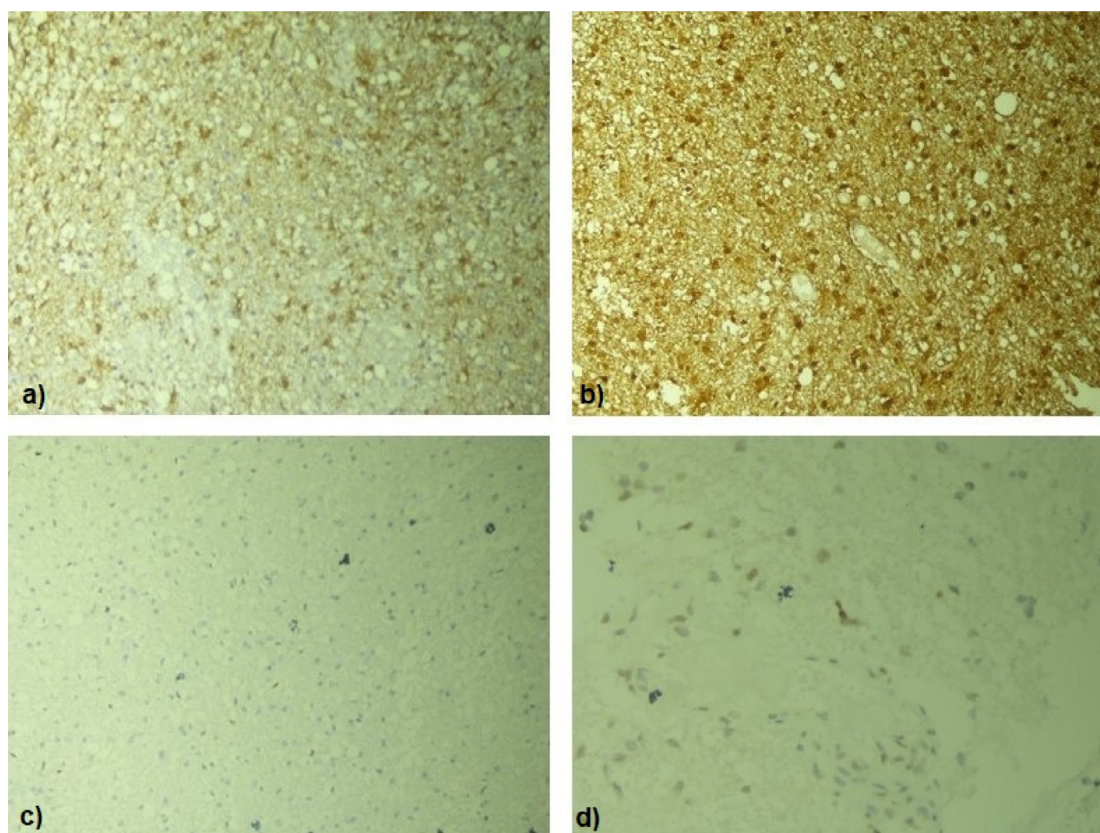


Fig. 6 – Selected images of a) diffusion weighted images (DWIs), and b) apparent diffusion coefficient (ADC) map images of brain MRI showing another small, well-defined lesion in the left temporal lobe with high SI on the DWIs and low SI on the ADC map (arrows).



**Fig. 7 – Selected images of histopathology a) S100 immunostaining and, b) GFAP immunostaining was positive in astrocyte cells, while c, and d) Ki67 immunostaining has less than 5% tumor cells.**

a poor prognostic apart from his histology type. In the present case, the histopathological results confirmed diffuse astrocytoma as the correct diagnosis after the patient had died.

### Conclusion

In order to avoid fatal complications, full medical imaging and laboratory investigations should be mandatory at first presentation of any brain lesion. Diffuse glioma of the brain can cause clinical and radiological diagnostic dilemmas, and the use of recent diagnostic methods, such as imaging biomarkers and MRS, can help in differentiating between brain lesions.

### Teaching points from this case

- Recently superimposed brain lesions should not distract attention from the potential diagnoses of other more important lesions.
- Due to the potential for bad prognoses, midline brain tumours should be approached seriously when collecting tissue for biopsy.
- Uncommon presentations of common lesions present more frequently than rare lesions.

### Consent statement

Informed consent was obtained for publication of this case report.

### Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.radcr.2020.11.023](https://doi.org/10.1016/j.radcr.2020.11.023).

### REFERENCES

- [1] Mehta S, Lo Cascio C. Developmentally regulated signaling pathways in glioma invasion. *Cell Mol Life Sci* 2018;75(3):385-402.
- [2] Li ZH, Guan YL, Liu Q, Wang Y, Cui R, Wang YJ. Astrocytoma progression scoring system based on the WHO 2016 criteria. *Sci Rep* 2019;9(1):96.
- [3] Kim MM, Parolia A, Dunphy MP, Venneti S. Non-invasive metabolic imaging of brain tumours in the era of precision medicine. *Nat Rev Clin Oncol* 2016;13(12):725-739.
- [4] Louis DN, Perry A, Reifenberger G, Deimling AV, Figarella-Branger D, Gavee WK, et al. The 2016 World Health Organization Classification of Tumors of the Central

- Nervous System: a summary. *Acta Neuropathol* 2016;131(6):803–820.
- [5] Camelo-Piragua S, Jansen M, Ganguly A, Kim JC, Cospser AK, Dias-Santagata D, et al. A sensitive and specific diagnostic panel to distinguish diffuse astrocytoma from astrocytosis: chromosome 7 gain with mutant isocitrate dehydrogenase 1 and p53. *J Neuropathol Exp Neurol* 2011;70(2):110–115.
- [6] Shukla G, Alexander GS, Bakas S, Nikam R, Talekar K, Palmer JD, et al. Advanced magnetic resonance imaging in glioblastoma: a review. *Chin Clin Oncol* 2017;6(4):40.
- [7] Park SE, Choi DS, Shin HS, Baek HJ, Choi HC, Kim JE, et al. Splenial lesions of the corpus callosum: disease spectrum and MRI findings. *Korean J Radiol* 2017;18(4):710–721.
- [8] Li S, Sun X, Bai YM, Qin HM, Wu XM, Zhang X, et al. Infarction of the corpus callosum: a retrospective clinical investigation. *PLoS One* 2015;10(3):e0120409.
- [9] Claes A, Idema AJ, Wesseling P. Diffuse glioma growth: a guerilla war. *Acta Neuropathol* 2007;114(5):443–458.
- [10] Schönfeld MH, Ritzel RM, Kemmling A, Ernst M, Fiehler J, Gellifßen S. Improved detectability of acute and subacute brainstem infarctions by combining standard axial and thin-sliced sagittal DWI. *PLoS One* 2018;13(7):e0200092.
- [11] Sui HJ, Yan CG, Zhao ZG, Bai QK. Prognostic Value of Diffusion-Weighted Imaging (DWI) Apparent Diffusion Coefficient (ADC) in patients with hyperacute cerebral infarction receiving rt-PA intravenous thrombolytic therapy. *Med Sci Monit* 2016;22:4438–4445.
- [12] Drake-Pérez M, Boto J, Fitsiori A, Lovblad K, Vargas MI. Clinical applications of diffusion weighted imaging in neuroradiology. *Insights Imaging* 2018;9(4):535–547.
- [13] White N.S., McDonald C., Farid N., Kuperman J., Karow D., Schenker-Ahmed N.M., et al. Diffusion-weighted imaging in cancer: physical foundations and applications of restriction spectrum imaging [published correction appears in *Cancer Res.* 2014 Nov 15;74(22):6733. McDonald, Carrie R [corrected to McDonald, Carrie]; Kaine, Christopher J [corrected to Kane, Christopher J]]. *Cancer Res.* 2014;74(17):4638–4652.
- [14] Horská A, Barker PB. Imaging of brain tumors: MR spectroscopy and metabolic imaging. *Neuroimaging Clin N Am* 2010;20(3):293–310. doi:10.1016/j.nic.2010.04.003.
- [15] Roldan-Valadez E, Rios C, Motola-Kuba D, Matus-Santos J, Villa AR, Moreno-Jimenez S. Choline-to-N-acetyl aspartate and lipids-lactate-to-creatine ratios together with age assemble a significant Cox's proportional-hazards regression model for prediction of survival in high-grade gliomas. *Br J Radiol* 2016;89(1067):20150502.
- [16] Sarrazin JL, Bonneville F, Martin-Blondel G. Brain infections. *Diagn Interv Imaging.* 2012;93(6):470–90.
- [17] Mohan S, Wang S, Coban G, Kural F, Chawla S, O'Rourke DM, et al. Detection of occult neoplastic infiltration in the corpus callosum and prediction of overall survival in patients with glioblastoma using diffusion tensor imaging. *Eur J Radiol* 2019;112:106–11.
- [18] Tunthanathip T, Ratanalert S, Sae-Heng S, Oearsakul T. Butterfly tumor of the corpus callosum: clinical characteristics, diagnosis, and survival analysis. *J Neurosci Rural Pract* 2017;8(Suppl 1):S57–65.