MedLife Clinics

ISSN: 2689-5943

Case Report

Non-Ionising Medical Image Modality in Brain Tumour

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Abstract

Background: Focal seizures may denote an underlying neurological damage in the brain and may lead to generalized epilepsy if the condition worsens. Therefore, an investigative inquiry is usually needed to determine the extent of disease progression to reduce the impact on the individual's quality of life. In literature, anatomical and functional imaging methodologies have made an extremely significant impact on the diagnosis and management of brain tumours.

Case presentation: This case study presents a 22-year-old female who had a history of Focal Seizures at the age of 9, and medical images show a lesion which is situated deep in the right hemisphere.

Discussion: The patient had several imaging scans over a while, with a late diagnosis of focal changes affecting a small focus within the lesion. This case study reports the interpretations of the various medical images to obtain from the multimodality of images and the management for patient care.

Keywords: Seizures; Medical imaging; Brain tumour; Biopsy; Quality of life; Medical management

Introduction

Medical Management of a patient with a history of brain tumour and neurological pathology requires medical imaging techniques that will help with diagnosis, staging, treatment methods, and monitoring of the therapeutic response of the patient. Modern anatomical and functional brain imaging methodologies have made an extremely great impact on the diagnosis and management of brain tumours [1,2]. A combination of appropriate new medical imaging techniques has led to greater insight into the pathophysiology underlying symptomatic seizures and epilepsy, and this can help elucidate the basic underlying mechanisms of the various forms of epileptic disorders [1]. Medical imaging plays an essential role in the differential diagnosis of brain lesions and seizures. Magnetic Resonance Spectroscopy is known to be useful in the differentiation between brain lesion, abscess, and other cystic masses [3,4].

Seizure

Seizures occur as a result of abnormal paroxysmal discharges in the cerebral cortex, and it is characterized by alteration in behavior, sensation, movement, or consciousness [5] (Figure 1). Table 1 provides a summary of the seizures. Table 2 below provides a summary of some recommendations for Neuroimaging for a patient.

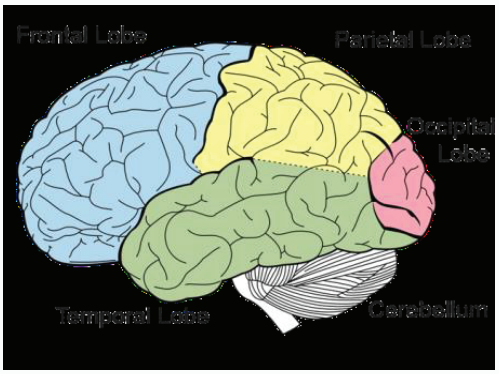

Figure 1: Shows the various lobes of the brain where seizures can affect.

Table 1: Classification for seizures [6].

1. Partial (Focal or Local) seizures
A. Complex Seizure: Characterized by impaired consciousness, with frequent automatisms
B. Simple partial Seizures: Presents with no impairment of consciousness
C. Partial seizure are secondarily generalized
2. Generalized seizures: Patient presents with impaired level of consciousness
A. Absence or the petit mal
B. Myoclonic seizures: Patient presents with short, abrupt muscular contractions
C. Clonic seizures: Characterized by muscle contraction and relaxation
D. Tonic Seizure: Patient presents with abrupt increase muscle tone
E. Tonic-Clonic seizure: There is a quick, bilateral, severe jerking movement
F. Atonic seizures also known as drop attack: Characterized by abrupt loss of muscle
3. Unclassified epileptic seizures: There is an incomplete or inadequate data to identify classification

Citation: Gariba M, Salifu Y, Apiribu F. Non-Ionising Medical Image Modality in Brain Tumour. Med Life Clin. 2020; 2(2): 1016.

Publisher Name: Medtext Publications LLC

Manuscript compiled: July 23rd, 2020

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Table 2: Recommendations for Neuroimaging.

Recommendations for Neuroimaging of Patient with Seizures or Epilepsy [1]
1. Magnetic Resonance Imaging
2. Magnetic Resonance Spectroscopy
3. Functional Magnetic Resonance Imaging
4. Magnetoencephalography
5. Co-Registration of SPECT/PET with MRI
6. Positron Emission Tomography with Specific Ligands

Patient case report

A 22-years-old female presented at the age of 9-years with focal seizures. Magnetic Resonance imaging scan show a lesion deep in the right cerebral hemisphere.

A followed up annual Magnetic Resonance imaging scans from 2005 to 2014, including regular spectroscopy and perfusion imaging modality. Scans showed no changes over this time. The 2016 scan showed a focal change affecting a small focus within the lesion.

Discussion

Primary brain tumour

A primary brain tumour is a localized intracranial lesion that occupies space within the skull. The following are a variety of physiological changes that occurs in the skull; seizure activity and focal neurological signs, cerebraloedema, increased intracranial pressure, and hydrocephalus [5]. Brain tumours develop from various tissues within the intracranial cavity. An example of this is astrocytoma which originates from the astrocytes [6]. Table 3 below is a classification of primary brain tumour based on the tissue of origin.

The rationale for delayed brain lesion biopsy

Brain lesions can occur at any stage in life; brain lesion growth differs from infants, children, and adults [7,8]; brain development reaches its peak at the age of 22 years and lasts for about five more years [9]. A cardinal sign of brain lesion is seizure [10]. The patient had no biopsy performed when the lesion was identified from the initial medical imaging (MRI) scans may be due to the location, depth of the lesion (deep lesion in the right hemisphere) in the patient brain, the knowledge that patient brain is still developing (age). In addition, the function of the right hemisphere of the brain which is responsible for understanding nonverbal clues, making an inference, for interpretation of languages [11,12].

Reason for interval brain lesion imaging can

Magnetic Resonance Imaging (MRI) is often used to diagnose patients with focal seizures in the region of abnormalities of their presumed focal seizure [13]. The interval for medical imaging for a patient with brain lesion can be based on the treatment guidelines, some brain tumour such as low-grade astrocytoma; low-grade oligodendroglia has a characteristic of slow-growing and well-circumscribed even with endothelial proliferation [14,15]. About 80% of patients with primary brain tumours present with seizures [16], and in others, the slow-growing of the tumours may conceal the diagnosis for years [17]. The decision for the two years interval may be a result of the treatment guidelines and the knowledge of the nature of growth of brain tumour after it has been scan annually for the previous years.

Table 3: Some common primary brain tumours and the tissue of origin [7].

TISSUE ORIGIN	CHILDREN	ADULTS
Meninges	Meningioma in children [56]	Meningioma
Neurons	Medulloblastoma	
Astrocytes	Pilocytic Astrocytoma	Glioblastoma Multiforme
Ependyma	Ependymoma?	
Oligodendrocytes		Oligodendroglioma

Conventional MRI (without contrast-enhanced) and contrast enhance MRI

Magnetic Resonance Imaging (MRI) is a recognized imaging modality for the detection, evaluation, staging, and follow-up of a wide range of disease processes, e.g., brain tumours. The patient had other follow up scan without intravenous contrast because, contrast-enhanced is generally associated with the more aggressive lesion, some brain tumours such as gliomas up to one-third of malignant are non-enhance glioma [18]; suggestive that contrast-enhanced alone is limited in differentiating between low-grade and high-grade gliomas in the patient [19]. Contrast-Enhanced has side effects such as Nephrogenic Systemic Fibrosis and the potential effect of gadolinium accumulation in the brain [20,21]. This shows that the patient had MRI without contrast was to reduce the possibility of missing other differentiated brain tumours and also to prevent side effects of gadolinium. On the other hand, Contrast-enhanced MRI has several advantages over Conventional MR, Contrast-enhanced MRI provides additional information on lesion type, location, staging and diagnosis as well as help treatment planning [22,23]; advances the accuracy of differential diagnosis between tumours, alternative diseases and abscess [24]. Gadolinium contrast-enhanced is vital for the small metastases [25]; helps in the detection of additional lesions compared with non-contrast MRI [26].

T2 FLAIR sequences (3D *vs.* 2D)

T2 FLAIR (T2-Weighted Fluid Attenuation Inversion Recovery) is an imaging technique that enables revealing a wide variety of lesions, such as meningeal, cortical, periventricular diseases [27]. The evaluation of the brain and its structures such as nuclei, white matter tract helps with the diagnosis and detection of brain diseases (Figures 2-4). 3D Sequence is an imaging technique that uses high spatial resolution with high signal to noise ratio. 2D Sequence is an imaging technique that utilizes a phase-encoding gradient along slice direction. There are several potential advantages and disadvantages of these sequences over each other, and a summary is provided in Table 4.

Role T1 and T2 Weighted images in characterizing patient lesion

T2 Weighted (T2WI) imaging is a very sensitive imaging

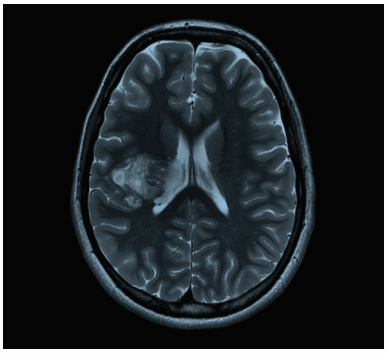

Figure 2: Axial T2 weighted Fast Spin Echo (FSE) images showed high signal intensity and marked perilesional oedema extending into the right ventricle of the right hemisphere and a hypo intense necrotic core.

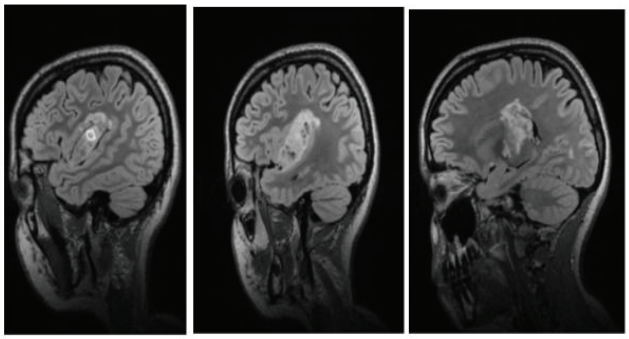

Figure 3: Sagittal 3D T2 weighted FLAIR reveals a hyper intense lesion with a hypo intense centre (necrotic) and surrounding perilesional oedema.

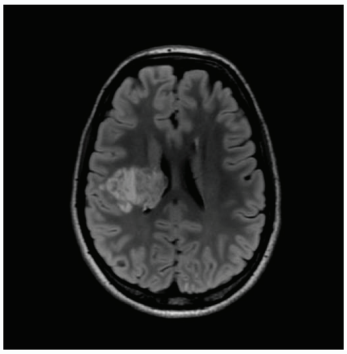

Figure 4: Axial T2 Weighted FLAIR MPR shows a lesion characterized with perilesional oedema extending into the ventricle of the right hemisphere (i.e., compression of the right ventricle).

technique for the detection of hyper intense regions in the white matter of the brain [34]; hyper intense showed by the T2WI may be due to a widespread of brain pathology such as oedema and demyelination (mild) lesions characterized by replacement of the glial cell replaced by necrotic or scar glial [35,36] (Figure 5). T1Weighted Imaging (T1WI) with gadolinium-enhanced may suggest an acute inflammation, serving as a marker of disease activity [37]. Images from T2 Weighted were compared to T1 weighted images in other to help confirm the diagnosis. Table 5 provides a summary of the T1, T2 Weighted sequence, and T2*Weighted Sequence.

Table 4: Advantages.

Advantages of 3D Sequence over 2D	Advantages of 2D Sequence over 3D
3D imaging technique improves the detection of different brain lesions (especially in the brain of multiple sclerosis patients) when compared to the 2D sequence [28,29].	A 2D sequence is quicker compared to the 3D sequence, which has an increase in the number of images leading to more time consuming [30].
3D sequence imaging techniques are effective due to the smaller slice thickness compared to the 2D sequence [31].	Image quality in a 3D sequence is relatively poor when compared to the 2D sequence [32].
Image resolution can be increased in a 3D sequence, but not applicable in a 2D sequence.	Coverage can be increased in a 2D sequence without loss of spatial resolution by separating the slice, but this is not applicable in the 3D sequence.
Multiplanar reformatting is applicable in 3D sequence. 3D sequence reduces pulsations and blood flow artifacts in brain imaging [33].	When the dynamic range of the signal is less than the receiver, the 2D sequence might give higher sensitivity when compared to the sensitivity of 3D.

Perfusion MRI imaging techniques

Perfusion imaging technique helps to assess conditions such as brain tumours and other path physiologic parameters using a non-invasive MRI [38]. Perfusion MRI techniques utilize high-quality contrast media to detect, characterize, and monitor diseases of the central nervous system [39,40]. Perfusion MRI can be used to measured cerebral perfusion with a different technique, which includes Dynamic Susceptibility Contrast (DSC) MRI perfusion (Figure 6), Dynamic Contrast-Enhanced (DCE) MRI perfusion, and Arterial Spin Labeling (ASL) MRI perfusion. DSC perfusion MRI utilizes the susceptibility effect of gadolinium contrast, DCE perfusion MRI uses the relativity effects of gadolinium contrast and ASL perfusion MRI operates with water as an endogenous contrast agent in measuring cerebral perfusion [38]. These cerebral perfusion techniques have advantages over one and another, as summarized by Table 6.

Susceptibility weighted imaging

Susceptibility Weighted Imaging (SWI) is a highly sensitive 3D high-resolution technique with a gradient-echo sequence that uses phase data and magnitude to enhance information about local tissue susceptibility [34]; it provides new techniques for enhancing contrast in MRI imaging (Figure 7). Susceptibility weighted imaging is very sensitive to iron i.e., in the form of hemosiderin, ferritin, and deoxyhemoglobin [34,43].

The phase image of SWI in characterizing patient lesion helped to distinguish between haemorrhage (paramagnetic), which appeared hypo intense and calcification (diamagnetic), which appeared hyper intense on SWI phase images [44]. SWI minimum Intensity Projection (mIP) has a high resolution (i.e., from multiplying of phase and magnitude images) provide better visualization of a small blood vessel; a hypo intense area was observed SWI minimum Intensity Projection (mIP) in the patient suggestive micro bleed, that is in the SWI shows a linear structure showing signal loss in keeping with the increased venous flow in the area of the tumour.

MR tractography images from Diffusion-Tensor Imaging (DTI)

MR tractography helps to deduce 3D of the white matter through a combination of the estimate of the underlying continuous fibre orientation field measured non-invasively with diffusion tensor imaging [45]. Diffusion-Tensor Imaging (DTI) provides additional information into brain microstructure at a scale that is not easily accessible with other imaging modality techniques in MRI [46]; it sometimes improves the detection and characterization of brain abnormalities in the white matter. MR tractography can be derived from the DTI because DTI provides information needed to construct a diffusion ellipsoid with the image volume from each voxel. MR Tractography provides useful information on brain pathology and anatomy information [47]; which may not be available from MRI images [48]; and can be used as a pre-surgical planning tool [49]; in this patient to help identify and preserve critical white matter tract, e.g., arcuate fasciculus during surgery (Figure 8).

MR spectroscopy in brain lesion

MR spectroscopy is a non-invasive technique that provides metabolic information of tissues; this technique is required for

Table 5: Weighted sequence.

T2 Weighted sequence	T1 Weighted Sequence	T2 *Weighted Sequence
Axial T2 Weighted Fast Spin Echo (FSE) images showed high signal intensity and marked perilesional oedema extending into the right ventricle of the right hemisphere and a necrotic.	Axial IR-FSPGR + Contrast also showed a hypo intense lesion with perilesional oedema and a ring-enhancing lesion with a hypo intense necrotic centre with contrast.	Axial Dynamic susceptibility contrast rCBV and rCBV fused with post-contrast image showed an area of increased blood flow and a ring enhanced lesion with a hypo intense necrotic centre on post-contrast imaging.
Axial T2 Weighted FLAIR MPR images which confirm oedema due to fluid also extending to the right ventricle of the right hemisphere of the brain.	T1 Spin Echo, with contrast, also confirmed a hyper intense ring enhanced lesion with a hypo intense necrotic centre.	SWI map shows a linear structure showing a signal loss in keeping with the increased venous flow in the area of the tumour.
Apparent Diffusion Coefficient (ADC) b=1000 mm^2s^{-1} The image showed a hyper intense area due to reversible oedema.	Fractional Anisotropy (FA) map shows the amount of anisotropy or "enlongatedness" of diffusion characterized by hypo intense area in the right hemisphere.	3D ASL CBF reveals high signal intensity suggestive of cerebral blood flow using endogenous contrast (water) media at the right hemisphere compared to the contralateral side.
Axial diffusion tensor imaging (DTI) image showed a hypo intense area indicating reduce diffusivity.		
Sagittal 3D T2 Weighted FLAIR reveal hyper intense lesion with a hypo intense centre (necrotic) and surrounding perilesional oedema		

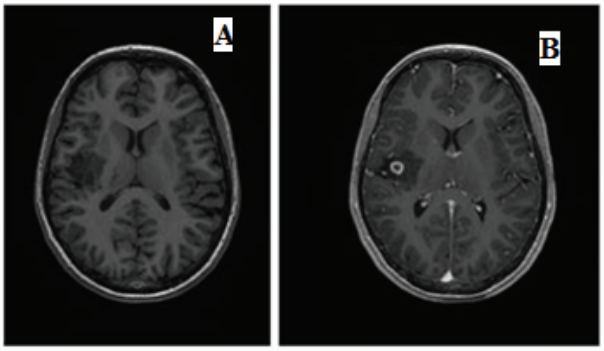

Figure 5: Axial IR-FSPGR ± Contrast reveal an area of the hypo intense lesion with surrounding oedema with a necrotic core (A) and a hyper intense ring enhanced lesion and perilesional oedema on the post-contrast with a hypo intense necrotic core (B).

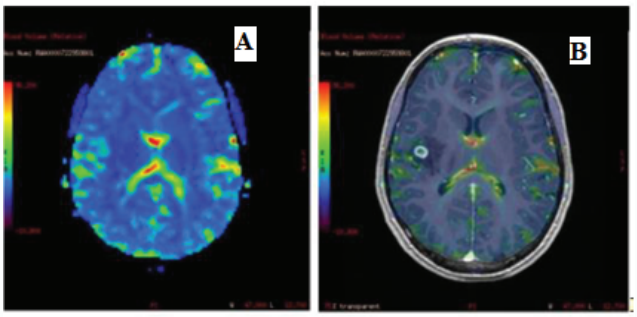

Figure 6: Axial DSC. rCBV and rCBV fused with post-contrast imaging; (A) an area of the relative increase in blood flow in the right hemisphere compared to its contra lateral part and (B) a ring enhanced lesion around an area of hypo intensity with a necrotic core on the post-contrast.

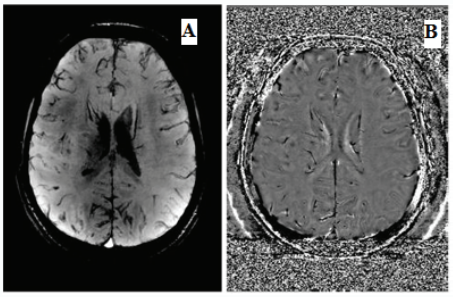

Figure 7: Axial SWI mIP and phase map: (A) reveal a linear structure showing signal loss in keeping with the increased venous flow to the area of tumour suggestive of haemorrhage or micro bleed and (B) showed a hypo intense spot in the right hemisphere confirm haemorrhage and a hyper intense surrounding white matter suggestive of calcification.

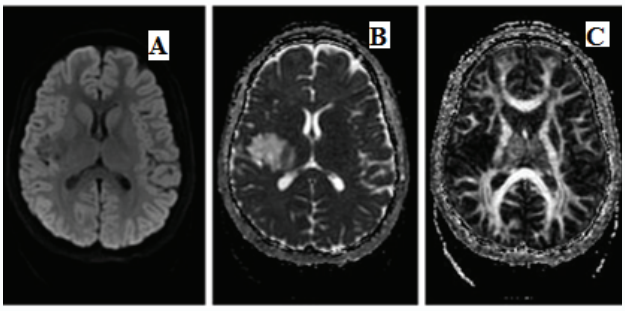

Figure 8: Axial DTI. b=1000 mm2s-1, ADC and FA maps: (A) image showed a hypo intense area indicating reduce diffusivity; the (B) image showed a hyper intense area due to reversible oedema, (C) shows the amount of anisotropy or "enlongatedness" of diffusion characterized by hypo intense area in the right hemisphere.

the diagnosis of a brain tumour [50,51]; image acquisition in MR Spectroscopy can be either single voxel or multiple voxel spectroscopy. Table 7 shows key metabolites, their normal range, and properties.

MR spectroscopy has 90% sensitivity in bilateral lobe abnormalities providing more useful information in the patient who has otherwise normal MRI scan [52]. MR spectroscopy (i.e., multiple voxel spectroscopy) added to the MRI used in this patient provided useful lateralization of metabolic dysfunction (in the right hemisphere) which shows an increased choline level, a drop in N-acetyl aspartate and normal level of creatine, suggestive of a possible low-grade glioma (e.g., low-grade astrocytoma, and low-grade oligodendroglia) (Figures 9-11).

Further Patient Management with Biopsy and Interval Imagings

Biopsy

Brain biopsy can be performed using a computer-assisted stereotactic, which enables the diagnosis of a deep-seated brain tumour [5]. Biopsy in this patient will help provide insight into the staging of the disease, and this can be used to indicate prognosis and

Table 6: Summary.

Summary of the various Perfusion MRI Techniques in terms of their advantages over the other
In ASL (uses water as endogenous contrast), no gadolinium contrast agent is required compared to DSC and DCE perfusion MRI that requires gadolinium with a risk of side effects such as nephrogenic systemic fibrosis [20,21].
DSC and DCE perfusion MR allows quantification and visualization of the whole brain due to high signal to noise ratio compared to ASL, which uses the low signal to noise ratio [41,42].
In determining absolute quantification of cerebral blood flow is better in ASL than in DSC MR Perfusion, which lacks a direct linear relationship between contrast concentration and signal changes [38].
ASL is considered as complete independence in its operation [42], compared to DSC and DCE perfusion MRI which relies on gadolinium contrast.

Table 7: Key metabolites and properties.

Metabolite	ppm	Properties
Myo-inositol	3.5	Glial call maker, osmolyte hormone receptor mechanism
Choline	3.2	Cell membrane marker
Creatine	3	Engery Metabolism
Glutamine/GABA	2.2-2.4	Neurotransmitter
N-acetyl aspartate (NAA)	2	Neural Marker
Lactate	1.3	Product of Anaerobic glycolysis
Lipids	0.9-1.4	Products of brain destruction

Table 8: Biopsy.

BIOPSY	PROCEDURE
1. Needle biopsy	A burr hole (small cut and a hole) is made into the skull. A sterile needle is then inserted through the hole to remove tumour tissue.
2. Stereotactic Biopsy	Involves a similar procedure as the needle biopsy, but a biopsy is obtained by a computer-assisted guidance system that helps in the location and diagnosis of the tumour tissue. The computer uses information from the MRI, or CT scan to provide the exact details on tumour tissue location and position.
3. Open Biopsy	The procedure involves taking tumour during an operation where the tumour is exposed.

Table 9: Other alternative management option for a patient with brain lesion.

Methods	Procedures
Lumbar Puncture	The patient had characteristic perilesional oedema extending to the right ventricle (seen in Axial T2 Weighted FLAIR, Axial T2 and Weighted FSE) can suggest cancer cells spreading to the cerebrospinal fluid; lumbar puncture help determine to extend of the tumour with analysis of cerebrospinal fluids [54].
Blood and urine test	Blood and urine tests can help diagnose brain tumours extending to areas like the pituitary gland [55,56].
Surgery	Involves a surgical removal of brain lesion, e.g., Endonasal Endoscopy, Neuroendoscopy, craniotomy.
Radiotherapy	Treatment involves the use of high beam radiation, which is directed on cancer cells. E.g., Stereotactic radiotherapy, Proton Beam Therapy, Image-guided radiotherapy.
Chemotherapy	Involves the use of anti-cancer medication for patient treatment.eg. Temozolomide, Procarbazine
Medication to control symptoms	Steroids may be used to reduce inflammation around brain tumours, e.g., Betamethasone, Prednisolone. Anticonvulsants medications to help control seizures, e.g., Carbamazepine, Clobazam, phenobarbital. Analgesic to ease any headache, e.g., paracetamol plus codeine.

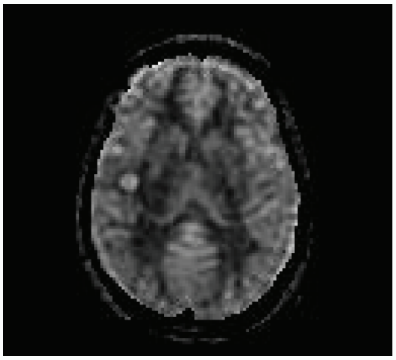

Figure 9: 3D ASL CBF reveals high signal intensity suggestive of cerebral blood flow using endogenous contrast (water) media at the right hemisphere compared to the contra lateral side.

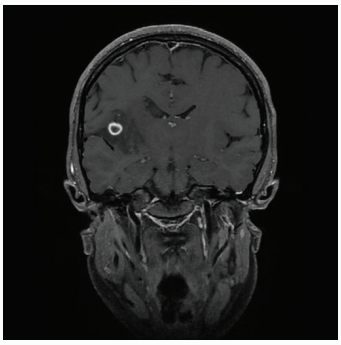

Figure 10: 3D T1 SE +C T1 Spin Echo with contrast shows a hyper intense ring enhanced lesion with a hypo intense necrotic centre and perilesional oedema.

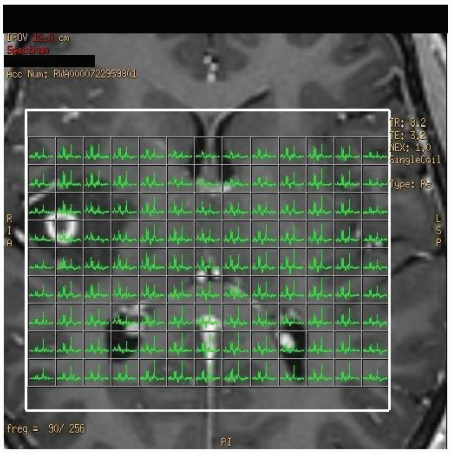

Figure 11: Axial MRSI. TE=144ms fused with post-contrast imaging showing a ring of enhancement around an area of hypointensity with a necrotic core with a map of decreased N-acetyl aspartate, a normal level of creatine and an increased level of choline at the right hemisphere compared to it contra lateral part.

guide a treatment plan. Some possible effects that can occur during brain lesion biopsy include infections, blood clots, temporary neurological deficits, seizures [53]. Table 8 below provides some examples of brain tumours biopsies.

Interval imaging

Interval imaging used in patient condition can help with the continuous monitoring of lesion and treatment planning, as some

brain tumour (e.g., low-grade oligodendroglia) are slow-growing and well-circumscribed [14,15]. The possible effect that may arise from interval imaging may be a delay in treatment. Alternative management for the patient with brain lesion includes lumbar puncture, blood and urine test surgery, radiotherapy, chemotherapy, and medications for symptoms are tabulated (Table 9).

Statement of Ethics

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

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