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Simultaneous Amino Acid PET/MRI – An Opportunity to Assess True Response in Recurrent High-Grade Glioma after Antiangiogenic Therapy

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Full Text

Sir,

Antiangiogenic therapy (AAT) agents like bevacizumab (BEV) are being explored for glioblastoma (GBM) treatment, which is marked by microvascular proliferation as BEV directly interacts with proangiogenic factors such as vascular endothelial growth factor (VEGF). The Response Assessment in Neuro-Oncology (RANO) group addressed the issue of AAT pseudoresponse (PsR) in 2010 by recommending revised response assessment criteria that included Fluid-attenuated inversion recovery (FLAIR) or T2 signal abnormalities as criteria for determining tumour response or progression (”non-enhancing tumour progression”). Nevertheless, the challenge of reliably identifying the nonenhancing tumors persists; therefore, RANO-PET and the European Association of Neuro-Oncology (EANO) published a guideline for the use of positron emission tomography (PET) imaging in gliomas in 2016.[1]

We report a case of PsR of recurrent GBM after AAT. A 34-year-old male had right cerebellar pilocytic astrocytoma in 2015 and had undergone surgery, but had anaplastic transformation of tumor, which was re-excised, and he received radiation therapy later. In August 2019, local recurrence was observed, which was reoperated and found to be GBM on histopathology. On follow-up magnetic resonance imaging (MRI; Dec 2019), recurrence was suspected again. To confirm, 6-fluoro-(18F)-L-3,4-dihydroxyphenylalanine (18F-DOPA) PET/MRI was done (Jan 2020), which suggested possible recurrence. On follow-up PET/MRI (Mar 2020), disease progression was noted. Patient then received four doses of BEV, and 18F-DOPA PET/MRI (May 2020) was done. In this, we found discordance between MRI contrast enhancement with regression in relative cerebral blood volume (rCBV), which was suggestive of disease regression, that is, PsR, but increased DOPA uptake, in conjunction with increased choline (with reverse Hunter's angle in multivoxel spectroscopy), and low apparent diffusion coefficient (ADC) favored disease progression, all in one single examination, which helped us to conclude that the disease was not responding to therapy. This was corroborated by subsequent clinical follow-up, that is, the patient's condition deteriorated during the period of observation over 6 months and he later reported to succumb to the

disease [Table 1] and [Figure 1].{Table 1}{Figure 1}

Routine MRI alone may not be able to determine whether the reduced enhancement and cerebral edema are due to the tumor's susceptibility to BEV (true response) or due to a treatment-induced alteration in the blood–brain barrier (BBB) (PsR). It is critical to distinguish between the two clinical circumstances at the earliest. Amino acid PET (AA PET) is useful for assessing treatment response to BEV and for evaluating tumor growth regardless of BBB alterations because it depends on increased expression of amino acid transporter system instead of BBB permeability.[2] When MRI and PET results were discordant, AA PET was able to diagnose BEV treatment failure earlier than MRI. It was reported that AA PET in conjunction with MRI, rather than MRI alone, modified the diagnosis or treatment plan in glioma patients and boosted the rate of accurate recurrent high-grade glioma (rHGG) diagnoses in BEV plus irinotecan-treated rHGG patients. This case highlighted that simultaneous AA PET/MRI may be the one-stop modality that is fast and comprehensive to discriminate between PsR from true response, and thus can help in the overall management of glioma patients.[2],[3],[4]

Declaration of patient consent

The authors guarantee that they have all necessary patient consent forms on record.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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Figure 1: Axial postcontrast T1 images (a-c); corresponding section of rCBV map (d-f); ADC map (g- i); fused PET/MRI images (j-l), and spectroscopy (m-o) (first, second: pre-BEV therapy and third: post-BEV therapy). Persisting increased DOPA avidity (through j-l), diffusion restriction (through g-i), and magnetic resonance spectroscopy (MRS) Cho: Cr and Cho: NAA ratios (m-o) between pre- and post-therapy scan images. Decrease in postcontrast enhancement (through a-c) and perfusion (through d-f) between pre- and post-therapy images implied pseudoresponse; but the DOPA uptake, increased choline ratios, and low ADC between pre- and post-therapy images concluded disease progression. BEV = bevacizumab, MRI = magnetic resonance imaging, PET = positron emission tomography, rCBV=relative cerebral blood volume, ADC=apparent diffusion coefficient, Cho=choline, Cr=creatine, NAA=N-acetyl-aspartate

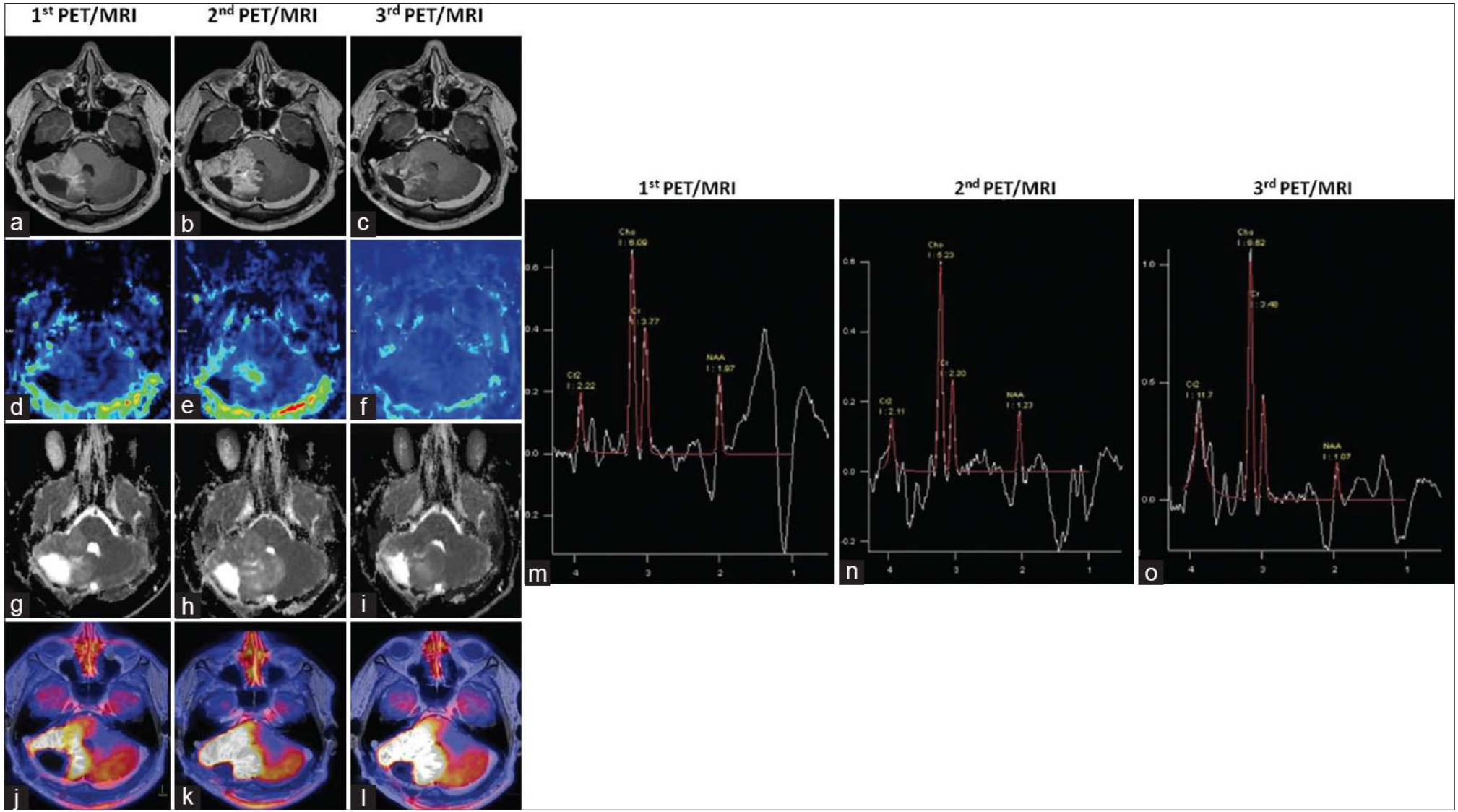

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Table 1: Comparison of different PET/MRI parameters across studies

PET/MRI parameters	First PET/MRI	Second PET/MRI	Third PET/MRI (response evaluation scan)
Lesion size	3.9 (AP)×3.9 (CC)×4.1(TR) cm	5.9 (AP)×4.9 (CC)×5.6 (TR) cm	5.86 (AP)×4.7 (CC)×5.6 (TR) cm
Contrast enhancement	Raised	Raised	Decreased
rCBV	1.90	6.14	5.20
ADC	1151	1094	920
Cho: Cr	1.62	2.38	2.48
Cho: NAA	3.09	4.24	8.06
SUV_{max}	3.73	4.54	4.12
Lesion to striatum ratio	1.61	1.81	1.97
Lesion to gray matter ratio	2.55	2.98	3.4

MRI=magnetic resonance imaging, PET=positron emission tomography, Cho=choline, Cr=creatine, NAA=N-acetyl-aspartate, SUV_{max}=maximum standardized uptake value