Dynamic 18F-Fluoro-Ethyl-Tyrosine Positron Emission Tomography/Computed Tomography: A Better Predictor of Isocitrate Dehydrogenase Mutation in Presurgical Evaluations of Glioma

Abstract

The recent WHO classification of gliomas has incorporated molecular markers such as isocitrate dehydrogenase (*IDH*) mutation and 1p/19q co-deletion into the ambit of morphological diagnosis, and 18F-fluoro-ethyl-tyrosine (^{18}F-FET) positron emission tomography (PET) has shown its utility in noninvasive glioma grading and prognosis. Both dynamic and static FET PET parameters may assist in predicting the *IDH* mutational status, but time to peak derived from dynamic data may be a better predictor for *IDH* status. We present a case of left frontal lobe lesion suggestive of high-grade glioma on magnetic resonance imaging and static ^{18}F-FET PET images, however, dynamic FET image was suggestive of low-grade *IDH1*-mutated glioma which was later confirmed on histology and immunohistochemistry.

Keywords: *18F-fluoro-ethyl-tyrosine, glioma, isocitrate dehydrogenase, positron emission tomography/computed tomography*

Kamal Nitheesh Raj Tigapuram, Kirti Gupta[1], Ashwani Sood, Navneet Singla[2], Nivedita Rana, Rakhee Vatsa, Chirag Kamal Ahuja[3], Bhagwant Rai Mittal

Departments of Nuclear Medicine, [1]Histopathology, [2]Neurosurgery and [3]Radiodiagnosis and Imaging, Post Graduate Institute of Medical Education and Research, Chandigarh, India

A 36-year-old man on anti-epileptic treatment for intermittent episodes of generalized tonic–clonic seizures, loss of consciousness, and headache was referred for further work-up. Magnetic resonance imaging (MRI) of brain done revealed a heterogeneous T1 hypointense, T2/fluid-attenuated inversion recovery heterogeneously hyperintense lesion in the left frontal lobe showing increase blood flow, areas of necrosis with significant mass effect-features suggestive of high-grade glioma [Figure 1a]. 18F-fluoro-ethyl-tyrosine (^{18}F-FET) positron emission tomography (PET)/computed tomography (CT) dynamic images were acquired immediately after injection in list mode for 40 min. Dynamic image data were reconstructed with 14 frames comprising 5 frames × 1 min, 5 frames × 3 min, and 4 frames × 5 min, and a static image was reconstructed by summing the images from 20 to 40 min postinjection. The time–activity curve (TAC) from dynamic image showed a delayed time to peak (TTP) and rising curve (Type II curve) suggestive of low-grade glioma with prediction for isocitrate dehydrogenase (*IDH1)*-mutated glioma [Figure 2], though static PET/CT images showed tracer-avid ill-defined enhancing subcentimetric lesion (SUV_{max}: 3.2) in the left prefrontal cortex [Figure 1 b and c]. Histology revealed a diffuse astrocytoma (WHO Grade II) characterized by moderately pleomorphic cells set against a pale fibrillary background. No mitoses, endovascular proliferation, or necrosis was identified. On molecular subtyping, the cells were mutant for *IDH1 R132H* protein with loss of expression for *ATRX* (ATRX-mutant phenotype). No positivity was noted for p53-mutant protein [Figure 3 a-d].

Presurgical evaluation of central nervous system tumors is critical for assessing the lesion for tumor type, grade, and extent. MRI is the primary imaging investigation in the evaluation of brain tumors.[1,2] Recently, the WHO 2016 classification has incorporated *IDH* mutational status in the diagnosis of gliomas which has prognostic implications such that *IDH*-mutant tumors have a more favorable outcome compared to *IDH* wild type.[3,4] The noninvasive techniques to predict the molecular characteristics of tumors are increasingly being explored, and dynamic and static

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Address for correspondence:
Dr. Ashwani Sood, Department of Nuclear Medicine, PGIMER, Sector-12, Chandigarh - 160 012, India.
E-mail: sood99@yahoo.com

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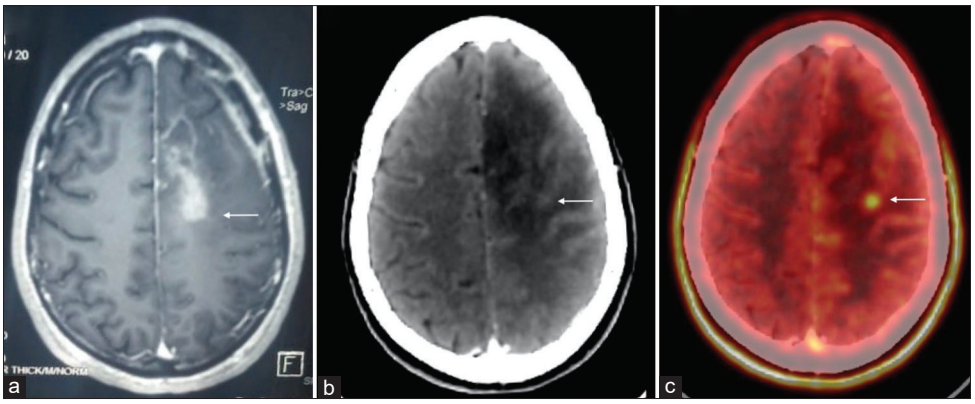

Figure 1: Magnetic resonance imaging axial section of the brain revealing a heterogeneous T1 postcontrast heterogeneously enhancing lesion in the left frontal lobe (a). Static images of computed tomography and fused positron emission tomography/computed tomography showing tracer-avid ill-defined enhancing subcentimetric lesion (SUVmax: 3.2) in the left prefrontal cortex (b and c)

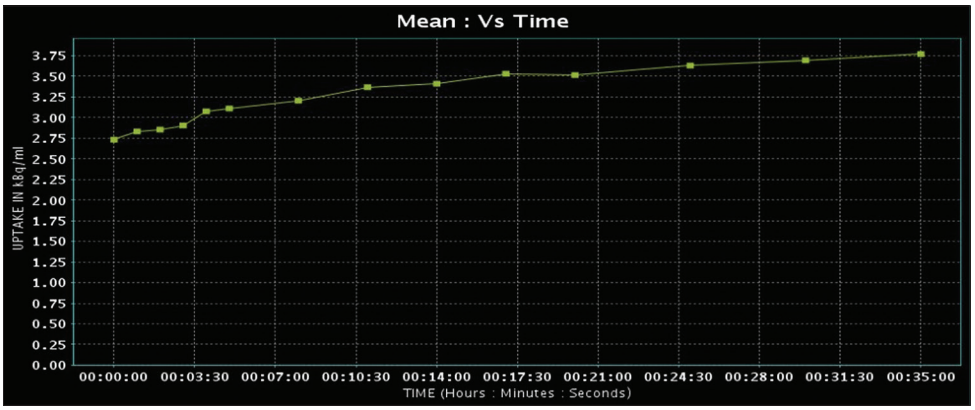

Figure 2: Time–activity curve from dynamic image showing a delayed time to peak and rising curve (Type II curve) suggestive of low-grade glioma with prediction for isocitrate dehydrogenase 1-mutated glioma

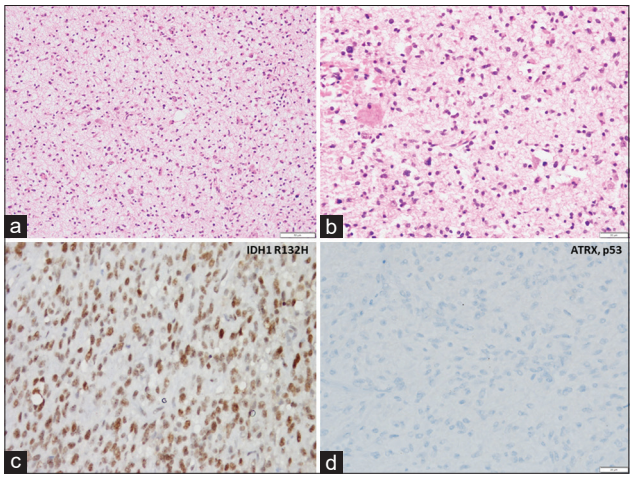

Figure 3: Histopathology revealing a diffuse astrocytoma (WHO grade II) characterized by moderately pleomorphic cells set against a pale fibrillary background. No mitoses, endovascular proliferation, or necrosis is identified (a, H&E x200; b, H&E x400). c: Neoplastic cells revealed immunoreactivity for IDH1 R132H mutant protein; d: Loss of expression for ATRX protein (mutant phenotype). (c,d: immunoperoxidase x400)

FET PET images have shown promising results.[5,6] For primary diagnosis, a cutoff threshold for SUV_{max} >1.6–1.8 using FET has been suggested to differentiate between high versus low-grade tumors. Increased tracer uptake is reported to have a high positive predictive value for high-grade lesions, though low-grade lesions, especially oligodendroglioma, may even show high uptake.[7]

Recently, new EANM/RANO guidelines for PET imaging in gliomas suggested that dynamic parameters from FET PET/CT with assessment of TTP by measuring the time of tumor peak uptake can help in distinguishing the grade of gliomas better than static images.[7] In a study, more patients with *IDH* wild-type gliomas showed FET positivity (TBR_{max} > 1.6) with higher median TBR_{max} than patients of *IDH*-mutant gliomas, but reliable cutoff could not be achieved because of high overlap. However, dynamic data showed significantly shorter TTP for *IDH* wild-type gliomas with high positive predictive value.[8] The shape and TTP in the TAC on dynamic images may be indicative of tumor grade. The continuous increasing uptake in TAC is frequently observed in Grade I/II gliomas, though this pattern may also be seen in radiation-induced changes, inflammatory lesions, hematoma, or infarction.[7] In the index case, MRI and high SUVmax on static FET imaging were indicative of high-grade glioma, while dynamic FET imaging suggestive of low-grade correlated

with histopathological findings suggesting that dynamic data may be more useful in predicting the molecular characteristics.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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