Post-treatment Assessment of Glioblastoma Multiforme: Imaging with Fluorodeoxyglucose, Sestamibi, and Choline

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Abstract

Glioblastoma multiforme (GBM) is the most common primary brain tumor in adults, and is generally of poor prognosis. The post-treatment assessment of GBMs is a known diagnostic issue, with problems in the differentiation of viable remnant tumor and post-treatment inflammatory changes. We present a case where various molecular tracers (fluorodeoxyglucose, choline, and methoxyisobutylisonitrile) were used in the post-treatment assessment of a patient with histologically proven GBM.

Key words: Choline, fluorodeoxyglucose, glioblastoma multiforme, molecular imaging, sestamibi

Introduction

Glioblastoma multiforme (GBM) can be treated with surgery, chemotherapy, and radiotherapy. Post-treatment imaging with computed tomography (CT) and magnetic resonance imaging (MRI) shows soft tissue changes with enhancement. Serial CT or MRI scans may be required to differentiate between post-treatment inflammation or residual tumor, delaying appropriate therapy. Molecular imaging has higher sensitivity and specificity for residual tumor, and is useful in post-treatment management of gliomas.

Case Report

The patient is a 17-year-old man, without significant previous medical history, presenting with headaches, blurred vision, and left upper limb weakness that developed over 2 months.

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On admission, MRI scan of the brain [Figure 1] showed a 4 cm rim-enhancing mass in the right cerebrum. There was mass effect, effacing the right lateral ventricle, and causing midline shift. The mass extended inferiorly to compress the suprasellar cistern resulting in obstructive hydrocephalus.

Transcallosal tumor biopsy was performed, and histology confirmed the diagnosis of GBM.

As the tumor was deemed unresectable, it was treated with intensity-modulated radiation therapy and temozolomide. Initial post-treatment MRI scan showed slight reduction in size of the mass, with improvement in hydrocephalus.

However the patient's headache worsened after another 5 months and a second post-treatment MRI scan was performed [Figure 2]. It was not possible to conclude from this MRI scan if features were of residual tumor or postradiation therapy inflammatory changes.

^{18}Fluorine-fluorodeoxyglucose (FDG) PET/CT and ^{18}fluorine-fluorocholine (FCH) PET/CT were performed [Figures 3 and 4], both showing uptake of tracer around the mass and central photopenia. No tracer uptake was

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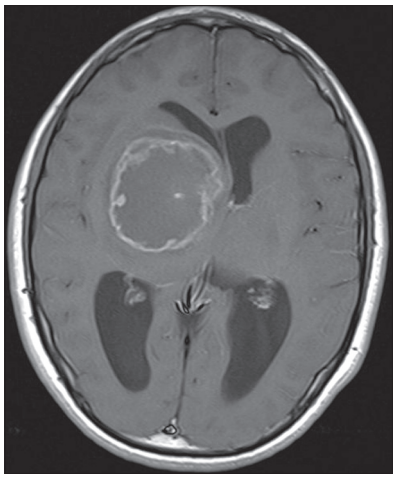

Figure 1: Pretreatment MRI scan with intravenous gadolinium shows a mass in the right lentiform nucleus and internal capsule, with rim enhancement. Wall irregularity is more prominent along the medial aspect

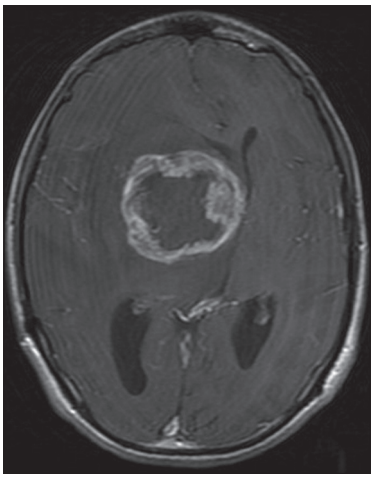

Figure 2: Second post-treatment MRI scan with intravenous gadolinium enhancement shows increased wall thickness, with enhancement. These could represent viable tumor or postradiation therapy inflammation. The first post-treatment MRI scan (not shown) had demonstrated reduction in tumor size and hydrocephalus. An enhancing nodule has developed along the medial wall of the mass. The enhancing area is concordant with the PET scans [Figures 3-5]

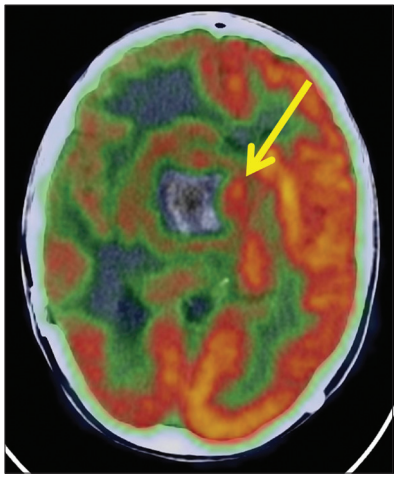

Figure 3: PET/CT with ^{18}FDG shows diffuse physiologic uptake in the normal brain cortex, and abnormal uptake in the wall of the right basal ganglia mass, especially along the medial aspect

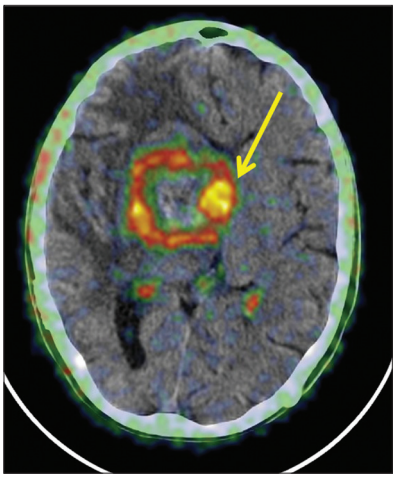

Figure 4: PET/CT with ^{18}FCH shows selectively increased uptake in the wall of the mass, more prominent along the medial aspect. Normal brain parenchyma does not show uptake. Slight physiological uptake is seen in the choroid plexus

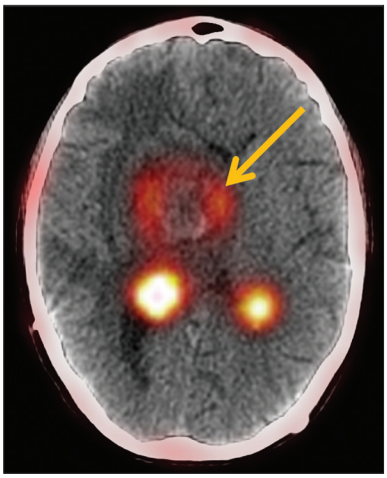

Figure 5: PET/CT with ^{99}Tc-MIBI shows similar distribution of uptake to ^{18}FCH, without uptake by normal brain parenchyma. Physiological uptake by the choroid plexus is more prominent

seen in the cerebral cortex, in keeping with known patterns of uptake.

^{99m}Technetium methoxyisobutylisonitrile (MIBI) SPECT/CT [Figure 5] was performed and correlated with the FDG and FCH PET/CT scans, and also showed tracer uptake in the periphery of the mass with central photopenia.

Overall, all three functional imaging modalities indicated the presence of viable tumor in the periphery of the mass, with a necrotic center.

A short course of dexamethasone was administered, followed by bevacizumab. Subsequent MRI scans

showed that the tumor size decreased slightly, with subsequent plateau. The patient remains alive 18 months after diagnosis of GBM.

Discussion

GBM is the most common primary brain malignancy in adults, and is the highest grade form of glioma (World Health Organization classification Grade IV).[1] Prognosis is poor, with 75% mortality within 18 months.[1]

MRI is the standard imaging modality for GBM,[1] but is limited in differentiating between residual or recurrent brain tumor and postradiation therapy necrosis.[2]

FDG is the most commonly used positron tracer in clinical practice, with wide applications in a variety of tumors. Although its use in the imaging of brain gliomas may be limited by normal physiological cortical uptake that may obscure uptake by lesions, there is possible prognostication value, where higher FDG avidity suggests high-grade malignancies and hence poorer prognosis.[3] For post-therapy assessment, FDG PET may be effective in differentiating recurrent tumor from post radiation changes for high grade (III and IV) tumors, but has limited value in defining the extent of tumor involvement and recurrence of low-grade lesions.[4]

Gliomas have been reported to show elevated choline levels, attributed to increased cell membrane turnover and cellular proliferation with over-expression of choline transporters and choline kinase enzymes.[5] The ^{18}fluorine-labeled choline derivative FCH has demonstrated potential utility for imaging of a variety of neoplasms, including those of the breast, prostate, liver, and brain.[6] Due to lack of confounding uptake in normal brain cortex and inflammatory uptake, FCH offers a potential advantage over FDG in the imaging of gliomas, especially in post-therapy settings.[7] FCH can also distinguish between high grade gliomas, metastases, and benign lesions, with increased peritumoral uptake characteristic of high-grade gliomas.[8]

Similar to FCH, there is no uptake of MIBI in normal brain parenchyma. Physiological uptake is seen in the scalp, choroid plexus, and pituitary gland.[9] MIBI single photon emission computed tomography (SPECT) has been shown to be a highly sensitive and specific modality in assessing patients with suspected glioma recurrence after radiation therapy, with the ability to differentiate between areas of radiation necrosis and tumor recurrence.[9,10] With SPECT/CT hybrid imaging, the role of MIBI is enhanced with improved anatomic localization, as shown in this case.

Conclusion

We present a case of glioblastoma multiforme where various molecular tracers were used to evaluate and characterize the tumor following external beam radiotherapy, and highlight the role and potential management impact of functional imaging in the post-treatment assessment of gliomas.

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