Incremental Utility of Tc-99m Glucohepatonate Single-Photon Emission Computed Tomography over ^{18}F-Flourodeoxyglucose Positron Emission Tomography in Diagnosis of Brain Tumor Recurrence – Old is Gold

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Abstract

Detection of recurrence of a brain tumor after treatment is one of the most important and challenging diagnostic problems in neuro-oncological practice. In spite of technical advances in imaging modalities, sometimes, certain clinical presentations and manifestations can lead to a diagnostic dilemma even with the best of the technical know-how. We present a case of recurrence of anaplastic oligoastrocytoma (World Health Organization Grade III), where the patient's initial clinical presentation and the F-18 flourodeoxyglucose positron emission tomography (PET) magnetic resonance imaging findings were suggestive of stroke-like migraine attacks after radiation therapy syndrome. Due to a seizure episode before PET image acquisition, intense gyral uptake was noted in the left parietal lobe which made it difficult to ascertain the presence of a tumor recurrence. However, Tc-99m glucohepatonate single-photon emission computed tomography done after 1 week revealed radiotracer uptake within the site corresponding to the primary tumor, and a diagnosis of recurrence was made.

Keywords: *F-18 flourodeoxyglucose positron emission tomography magnetic resonance imaging, recurrence, stroke-like migraine attacks after radiation therapy syndrome, Tc-99m glucohepatonate single-photon emission computed tomography-computed tomography*

Introduction

High-grade glioma is a term which encompasses World Health Organization (WHO) Grade III and Grade IV tumors.[1] In modern neuro-oncology practice, surgical resection followed by chemotherapy and radiotherapy is considered as standard of care in the treatment of high-grade glioma.[2] When a patient comes for follow-up imaging after treatment of a high-grade glioma, and an enhancing lesion is found at the site of the primary tumor, the differential diagnosis is between the recurrence of the tumor and treatment-related changes. Among the treatment-related changes, radiation necrosis, pseudoprogression, and pseudoresponse are the most commonly encountered in clinical practice.[2] Stroke-like migraine attacks after radiation therapy (SMART) syndrome is a rare delayed complication of brain irradiation.[3] The patients with SMART syndrome present with features of cortical dysfunction with clinical symptoms manifesting as seizures, migraine-like headache, hemiparesis, confusion, visuospatial defects, etc.[3,4] Among the various pathophysiological mechanisms, the role of radiation-induced endothelial dysfunction, direct injury to the neurons, and other inflammatory, metabolic, and genetic factors has been suggested.[5] On magnetic resonance imaging (MRI), unilateral temporoparietal cortical involvement with postcontrast enhancement is described in the literature.[3-5]

Case Report

A 30-year-old man diagnosed high-grade anaplastic mixed oligoastrocytoma (WHO Grade III) underwent a gross total resection of the tumor 3 years back followed by concurrent chemoradiotherapy. After the completion of the chemoradiotherapy, the patient was asymptomatic. However, 8 months later, he presented with complaints of headache and recurrent episodes of vomiting. The patient also had developed right hemiparesis.

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With the suspicion of tumor recurrence or radiation necrosis, F-18 flourodeoxyglucose (FDG) positron emission tomography PET/MRI was sought by a treating neurosurgeon. On the day of PET/MRI examination, the patient had an episode of focal motor seizure involving the right upper limb with vomiting which occurred few minutes after the administration of F-18 FDG. MRI showed evidence of T2/fluid-attenuated inversion recovery (FLAIR) hyperintense signal conforming to the gyri in the left parietal lobe, and postcontrast T1 images showed few patchy focal areas of postcontrast enhancement [Figure 1a]. On PET images, intense tracer uptake was noted along the gyri only in the areas corresponding to hyperintensity, and there was no tracer uptake in the foci which showed postcontrast enhancement [Figure 1b] or the cortex surrounding the postoperative cavity. A clinical suspicion of SMART syndrome was considered; however, we could not rule out recurrence of tumor on the basis of F-18 FDG PET findings. In view of inconclusive imaging findings, the patient underwent Tc-99m glucohepatonate (GHA) single-photon emission computed tomography-computed tomography (SPECT-CT), the following week. Early 1 h and delayed 3 h images showed focal abnormal increase in tracer uptake corresponding to areas of contrast enhancement on MRI, which in turn corresponded to the site of the primary lesion [Figure 2]. The cortical metabolic changes visualized on PET which were caused by the ictus were not appreciated on SPECT images.

Discussion

Tc-99m GHA has been described as poor man's F-18 FDG.[6] Tc-99m GHA imaging was introduced in the 1970s by Dr. Henry Wagner where he and his colleagues used it for myocardial imaging.[6] The first use of Tc-99m GHA for brain scanning is credited to Léveillé *et al*., who proposed an active transport mechanism of uptake of Tc-99m GHA in metabolically active tumor cells.[7] GHA acts as an analog of glucose and may utilize GLUT-1 and GLUT-4 transporters for active transport into the metabolically active cells.[6,7] It has also been shown that hypoxia may induce increased expression of GLUT1 receptors on the cell membrane, and thus, hypoxic cells may also take up GHA.[6] Tc-99m GHA SPECT-CT could be used as an alternative imaging modality equally efficacious as N-13 ammonia PET-CT[8] or F-18 dihydroxyphenylalanine (DOPA)[9] in detecting recurrent glioma, particularly in our part of the world, where financial constraints may play an important factor while choosing the imaging modality. Some studies have also reported Tc-99m GHA as a better imaging modality than F-18 FDG PET/CT for the detection of recurrent gliomas.[10]

In our case, the patient had clinical symptoms which were suspicious of SMART syndrome. Further, on structural MRI, the pattern of FLAIR hyperintensity and diffusion restriction was suggestive of SMART syndrome. The patient had a seizure episode few minutes after the injection of F-18 FDG; hence, the imaging findings on PET were akin to that of an ictal PET where the radiopharmaceutical was taken up preferentially by the ictal zone in the left parietal cortex due to elevated metabolic demand, thus masking the uptake in the recurrent tumor. One week later, when the patient was effectively in an interictal period, the Tc-99m GHA SPECT revealed the presence of a recurrent tumor which was evident by progressive uptake of Tc-99m GHA on 1 h and delayed (3 h image).

The recurrent tumor may be co-existent with treatment-related changes. In such a situation, like in our case, this seeming co-existence may alter the metabolic milieu in brain and thus may alter the structural and metabolic imaging findings, which may in turn pose a diagnostic dilemma. In such a situation, follow-up imaging may help uncover the tumor recurrence. In this regard,

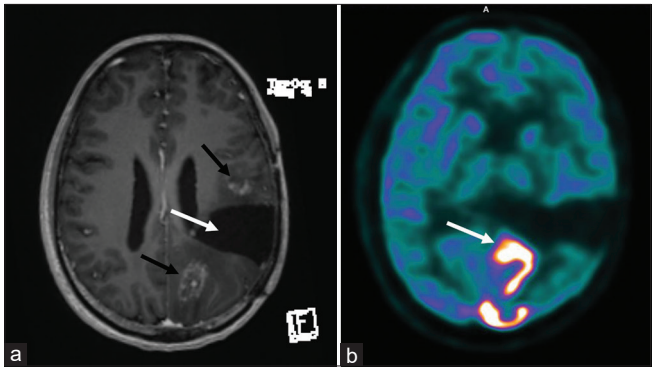

Figure 1: Hybrid magnetic resonance-positron emission tomography imaging at the initial presentation 8 months after completion of the chemoradiotherapy. (a) Contrast-enhanced magnetic resonance imaging showing evidence of patchy areas of enhancement (black arrow) adjacent to the postoperative cavity (white arrow). (b) F-18 flourodeoxyglucose positron emission tomography image showing intense gyral uptake in the left parietal lobe (white arrow). Note that the uptake on F-18 flourodeoxyglucose is not corresponding to the areas of contrast enhancement

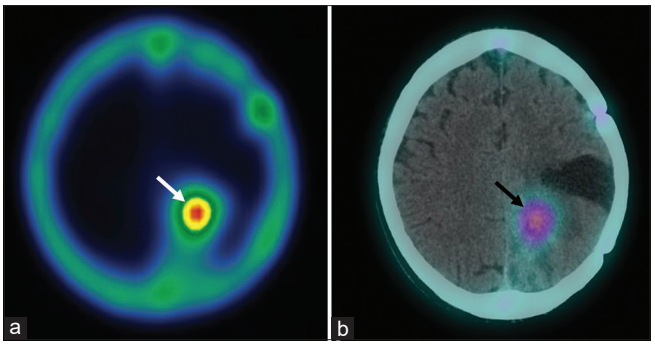

Figure 2: Tc-99m glucohepatonate single-photon emission computed tomography done after 1 week of magnetic resonance-positron emission tomography. Single-photon emission computed tomography image (a) and fused single-photon emission computed tomography/computed tomography (b) acquired post-Tc-99m glucohepatonate injection showing uptake corresponding to the areas of enhancement on magnetic resonance imaging (white arrow in a and black arrow in b). Note that the areas of gyral uptake seen on positron emission tomography images are no longer appreciated

Tc-99m GHA is of particular use and interest as it is cost-effective, more readily available, and affordable for the patient.

Conclusions

Differentiating recurrence of a tumor from treatment related changes may be difficult, particularly when both co-exist. Even in the era of PET/CT or PET/MRI and with the advances in newer molecular probes, this case appraises the diagnostic value of Tc-99m GHA. This investigation can be easily and routinely done in many centers across the country and is cost-effective.

Declaration of patien consent

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

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Conflicts of interest

There are no conflicts of interest.

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