Revealing subependymal giant cell astrocytoma with multimodal positron emission tomography: illustrative cases

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BACKGROUND There is limited literature on the use of positron emission tomography (PET) for benign tumors originating in the brain ventricles, and the use of multiple tracers for subependymal giant cell astrocytoma (SEGA) has not been reported. The authors compared the PET findings in two SEGA cases with past reports and literature, exploring the distinctive characteristics of SEGA on PET.

OBSERVATIONS In a 21-year-old female with SEGA, the authors utilized 18F-fluorodeoxyglucose (18F-FDG), 11C-methionine (11C-MET), 18F-fluorothymidine (18F-FLT), 18F-fluoromisonidazole, and 11F-THK5351 tracers. Additionally, in a 6-year-old girl, the authors performed 11C-MET PET.

LESSONS The results indicated the accumulation of all tracers except 18F-FDG, with particularly intense accumulation noted with 18F-FLT. In particular, 18F-FLT demonstrated accumulation comparable to that observed in malignant tumors. This study suggests that multiple PET tracers can provide valuable insights into the characterization of SEGA, with 18F-FLT showing particular promise as a distinctive marker of blood-brain barrier disruption. Further research in larger cohorts may enhance our understanding of metabolic patterns in SEGA and aid in its diagnosis and treatment.

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KEYWORDS SEGA; subependymal giant cell astrocytoma; meningioma; central neurocytoma; PET; positron emission tomography; radiology

Positron emission tomography (PET) is a valuable tool in the field of medical imaging, providing insights into various aspects of tumor biology and metabolism. However, while PET has been extensively used to characterize malignant brain tumors such as gliomas, its application to benign brain tumors is more limited, particularly in the context of tumors originating in the brain ventricles. Subependymal giant cell astrocytoma (SEGA) is one such benign tumor that primarily develops in the lateral ventricles.

There is relatively little medical literature on the characterization of SEGA through PET imaging. Existing studies often focused on the use of a single PET tracer, limiting our understanding of the metabolic and physiological aspects of these tumors. This gap in knowledge prompted our investigation into the utility of multiple PET tracers for assessing SEGA.

In our clinical practice, we routinely perform PET scanning with various radionuclides for brain tumors, including gliomas, primary central nervous system lymphomas, meningiomas, and metastatic brain tumors. The diagnosis of 2 patients with SEGA, which is relatively rare in our caseload, presented a unique opportunity to explore the potential of multiple PET tracers for characterizing this benign tumor.

In this study, we present findings from 2 SEGA cases, one assessed using multiple PET tracers and one assessed using 11C-methionine (11C-MET) PET. We compare our results with previous reports and the literature on SEGA, as well as with other benign tumors with similar imaging characteristics, such as meningiomas and central neurocytomas (CNs). Through this comparative analysis, we aimed to uncover distinctive features of the PET findings of SEGA, which may contribute to improved diagnosis and management of this condition.

ABBREVIATIONS 11C-MET = 11C-methionine; 18F-FDG = 18F-fluorodeoxyglucose; 18F-FLT = 18F-fluorothymidine; 18F-FMISO = 18F-fluoromisonidazole; BBB = blood-brain barrier; CN = central neurocytoma; MRI = magnetic resonance imaging; PET = positron emission tomography; SEGA = subependymal giant cell astrocytoma; SUVmax = maximum standardized uptake value; T/N = tumor-to-normal cortex.

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Illustrative Cases

Case 1
A 21-year-old female diagnosed with Crohn’s disease presented with persistent headaches. Subsequent imaging revealed a tumorous lesion occupying the right cerebral ventricle. At the initial visit, she exhibited full consciousness with no notable neurological deficits. Neuroimaging revealed a tumor approximately 3 cm in size, originating near the foramen of Monro within the right lateral ventricle. This tumor caused compression of the third ventricle, leading to hydrocephalus. The tumor displayed calcification in the lateral regions and demonstrated homogeneous low density on computed tomography scans. On magnetic resonance imaging (MRI), we noted a contrast-enhancing mass obstructing the right foramen of Monro, resulting in hydrocephalus and dilatation of the right lateral ventricle (Fig. 1A).

A PET examination was performed using 5 different tracers. $^{18}$F-fluorodeoxyglucose ($^{18}$F-FDG) revealed low glucose metabolism within the tumor, with a maximum standardized uptake value (SUVmax) of 3.69 (tumor-to-normal cortex [T/N] ratio 0.23; Fig. 1B). The $^{11}$C-MET SUVmax was 6.35, with a T/N ratio of 4.92 (Fig. 1C). $^{18}$F-fluoromisonidazole ($^{18}$F-FMISO) displayed modest accumulation, with an SUVmax of 1.57 and a T/N ratio of 1.55, suggesting hypoxic conditions within the tumor (Fig. 1E). Finally, $^{18}$F-THK5351 showed an SUVmax of 1.03 and a T/N ratio of 1.03 (Fig. 1F).

Following the examination, a craniotomy was performed, and the tumor was completely resected. Hematoxylin and eosin staining revealed tumor cells with eosinophilic cytoplasm arranged in circular patterns, exhibiting eccentrically located nuclei (Fig. 2A). These tumor cells were surrounded by capillary fractions, with some regions showing avascular zones. Immunohistochemical staining was negative for glial fibrillary acidic protein and synaptophysin (Fig. 2B). However, subsequent staining for SOX2 and nestin was positive for both, supporting the diagnosis of SEGA and consistent with a 2021 World Health Organization grade 1 tumor. A 1-year follow-up neuroimaging examination showed no evidence of tumor recurrence or hydrocephalus.

Case 2
A 6-year-old girl presented with fever and headaches, leading to a visit to her local clinic. MRI revealed a contrast-enhancing lesion near the foramen of Monro in the left lateral ventricle, accompanied by hydrocephalus (Fig. 3A). Following referral to our hospital, an $^{11}$C-MET PET examination was performed (Fig. 3B). She was subsequently transferred to another hospital where surgery was successfully conducted, resulting in complete removal of the tumor. Pathological examination confirmed the diagnosis as SEGA, and symptoms of tuberous sclerosis were also observed in skin lesions. Remarkably, there has been no recurrence even after 15 years of follow-up.

Patient Informed Consent
The necessary patient informed consent was obtained in this study.

Discussion

Observations
SEGA, a benign tumor often associated with tuberous sclerosis, primarily develops within the lateral ventricles. While SEGA shares MRI characteristics similar to those of other benign ventricular tumors, such as meningiomas or central nervous system tumors, its characterization through PET has been limited. In this study, we aimed to...
resembling those seen in malignant glioma. A high degree of BBB disruption or its potential absence, with values indicative of the presence of reactive astrocytes. 

Tumors of particular interest was the substantial accumulation of 

Our findings revealed distinctive features of SEGA in comparison with both literature reports \(^1,2\) and other benign tumors. Notably, our study indicated limited \(^{18}\)F-FDG uptake, consistent with previous case reports, whereas \(^{11}\)C-MET exhibited substantial accumulation in both of our SEGA cases, suggestive of amino acid metabolism within the tumors. Of particular interest was the substantial accumulation of \(^{18}\)F-FLT, a tracer often associated with blood-brain barrier (BBB) disruption. \(^3\) The elevated \(^{18}\)F-FLT uptake in one of our SEGA cases suggests a high degree of BBB disruption or its potential absence, with values resembling those seen in malignant glioma. \(^4\) Additionally, \(^{18}\)F-FMISO showed modest accumulation indicating hypoxic conditions within the tumor, \(^5\) while \(^{18}\)F-THK5351 demonstrated slight tau accumulation, indicative of the presence of reactive astrocytes. \(^6\)

To provide a broader context, we compared SEGA with other benign tumors that exhibit similar imaging characteristics, namely meningiomas and CNs. Our findings suggest that \(^{18}\)F-FDG uptake

in SEGA resembles that of low-grade meningiomas, \(^7,8\) whereas \(^{11}\)C-MET accumulates regardless of malignancy grade in meningiomas. \(^9\) Furthermore, \(^{18}\)F-FLT accumulation in one of our SEGA cases significantly surpassed that reported for meningiomas, potentially serving as a point for differentiation. \(^8,10\) Both our SEGA cases exhibited \(^{11}\)C-MET T/N ratios similar to those of CN, and the case with multiple tracers also showed a similar \(^{18}\)F-FDG T/N ratio, indicating minimal accumulation. \(^11\)

This comparative analysis underscores the potential of multiple PET tracers for characterizing SEGA and distinguishing it from other benign ventricular tumors. The findings obtained from this case suggest that distinguishing SEGA from other benign tumors such as \(^{18}\)F-FMISO and \(^{18}\)F-THK5351 has not been addressed, making it difficult to completely differentiate it from other tumors at the present time. Further research with larger cohorts may enhance our understanding of the metabolic patterns of SEGA, ultimately aiding in its diagnosis and management.

**Lessons**

Our case report highlights the utility of multimodal PET imaging in the diagnosis of SEGA. The use of various PET tracers provided valuable insights into the metabolic patterns of SEGA, aiding in its differentiation from other ventricular tumors. This approach offers a promising avenue for improving SEGA diagnosis and management. Further research with larger cohorts and long-term follow-up is warranted to validate our findings and enhance our understanding of this rare benign brain tumor.

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**FIG. 2.** Case 1. Cells with large eccentrically located nuclei were observed with hematoxylin and eosin staining (A). Immunohistochemical findings: synaptophysin was negative (B), nestin was positive in the cytoplasm (C), and SOX2 was positive in the nucleus (D). Original magnification ×400.

**FIG. 3.** Case 2. Admission gadolinium-enhanced T1-weighted MRI (A). Admission \(^{11}\)C-MET PET (B).

Disclosures
The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Supplemental Information
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