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CASE REPORT

# [$^{18}$F]Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography Findings in Anti–Gamma-Aminobutyric Acid B Receptor Encephalitis: A Case Report

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## INTRODUCTION

Encephalitis is a severe inflammatory disorder of the brain that develops as a rapidly progressive encephalopathy and may affect patients of all ages.[1] Autoimmune encephalitis, which is the most common cause of non-infectious encephalitis[2] characterised by the presence of autoantibodies against different neuronal targets, may be associated with various cancers. Anti–gamma-aminobutyric acid B (anti-$GABA_B$) receptor encephalitis is a relatively uncommon entity. Very few have been reported in findings on [$^{18}$F]fluorodeoxyglucose positron emission tomography/computed tomography ([$^{18}$F]FDG PET/CT) and its role in diagnosis and management.[3] We present a patient with anti-$GABA_B$ receptor encephalitis who underwent [$^{18}$F]FDG PET/CT.

## CASE PRESENTATION

A 79-year-old man with a history of hypertension, diabetes mellitus, hyperlipidaemia and gout was admitted for status epilepticus. He had no known history of epilepsy or malignancy and presented with a history of gradual onset slurring of speech and generalised weakness over a few days, followed by repeated seizures and status epilepticus on the day of admission. Cerebrospinal fluid findings following lumbar puncture were not suggestive of infection. Electroencephalogram revealed mild slowing background with excessive slow wave; epileptiform discharge was not detected. CT of the brain revealed no acute intracranial haemorrhage but a hyperdense lesion at the left frontal lobe, suspicious of brain tumour (Figure 1).

Magnetic resonance imaging (MRI) of the brain performed 4 days after admission revealed a small enhancing intra-axial lesion in the left frontal lobe with restricted diffusion and perilesional oedema, likely representing a tumour. Slightly increased fluid-attenuated inversion recovery (FLAIR) signal was also evident in the right hippocampus, suspected to be related to convulsion (Figure 2).

Tumour marker testing revealed elevated carcinoembryonic antigen level at 14.4 ug/L

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Contributors: KLC designed the study, acquired and analysed the data, and drafted the manuscript. WHM and KMM critically revised the manuscript for important intellectual content. All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

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Data Availability: All data generated or analysed during the present study are available from the corresponding author on reasonable request.

Ethics Approval: The study was approved by the Central Institutional Review Board of Hospital Authority, Hong Kong (Ref No.: CIRB-2023-175-1). The patient was treated in accordance with the Declaration of Helsinki. The requirement for patient consent was waived by the Board due to the use of anonymised patient data.

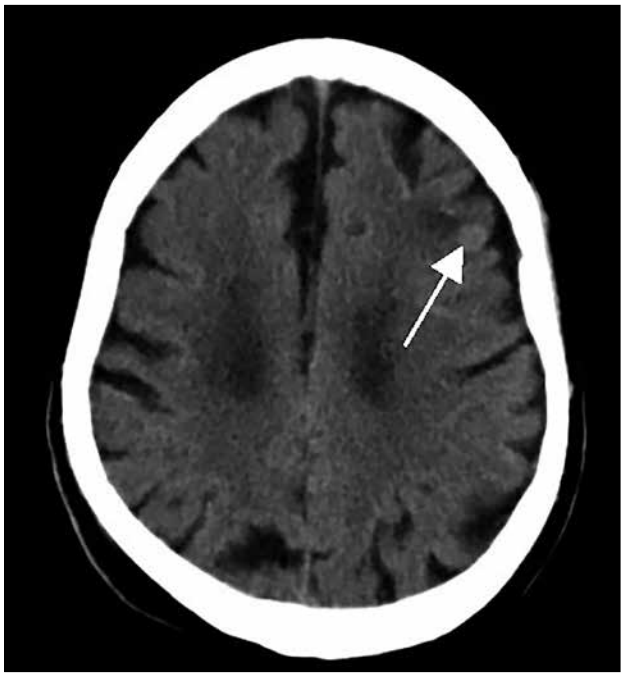

**Figure 1.** Computed tomography of the brain showing left frontal lesion (arrow).

(reference interval, ≤ 5.0). Paraneoplastic markers (anti-Hu/Yo/Ri) were negative. Autoimmune markers (anti–NMDA [N-methyl-D-aspartate] receptor, anti-CASPR2 [contactin-associated protein-like 2], anti-AMPA1/2 [alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid 1/2], anti-LGI1 [leucine-rich-glioma-inactivated 1] and anti-DPPX [dipeptidyl-peptidase-like protein 6] antibodies) were negative except anti-$GABA_{B1}$/ anti-$GABA_{B2}$ receptors that were positive. MRI of the brain was repeated 1 month after admission and revealed the increased FLAIR signal at the right hippocampus to have become slightly more conspicuous (Figure 3).

[$^{18}$F]FDG PET/CT was performed the day after the second MRI of the brain. A hypermetabolic lung mass was found in the apicoposterior segment of the left upper lobe as well as multiple hypermetabolic mediastinal, hilar and cervical lymph nodes (Figure 4). Findings raised suspicion of an underlying primary lung tumour with multiple nodal metastases. Focal hypermetabolism observed in the right hippocampus was consistent with limbic encephalitis. Nonetheless no overt hypermetabolism was observed in the left frontal lobe brain lesion (Figure 5).

The patient underwent plasmapheresis with substantial improvement in neurological symptoms. Incisional biopsy of the right submandibular cervical lymph node confirmed small-cell lung carcinoma. Chemotherapy and radiotherapy were planned, but the patient developed a severe hospital-acquired chest infection and sepsis with rapid deterioration of his condition despite antibiotics. Oncological treatment was suspended and the patient eventually succumbed.

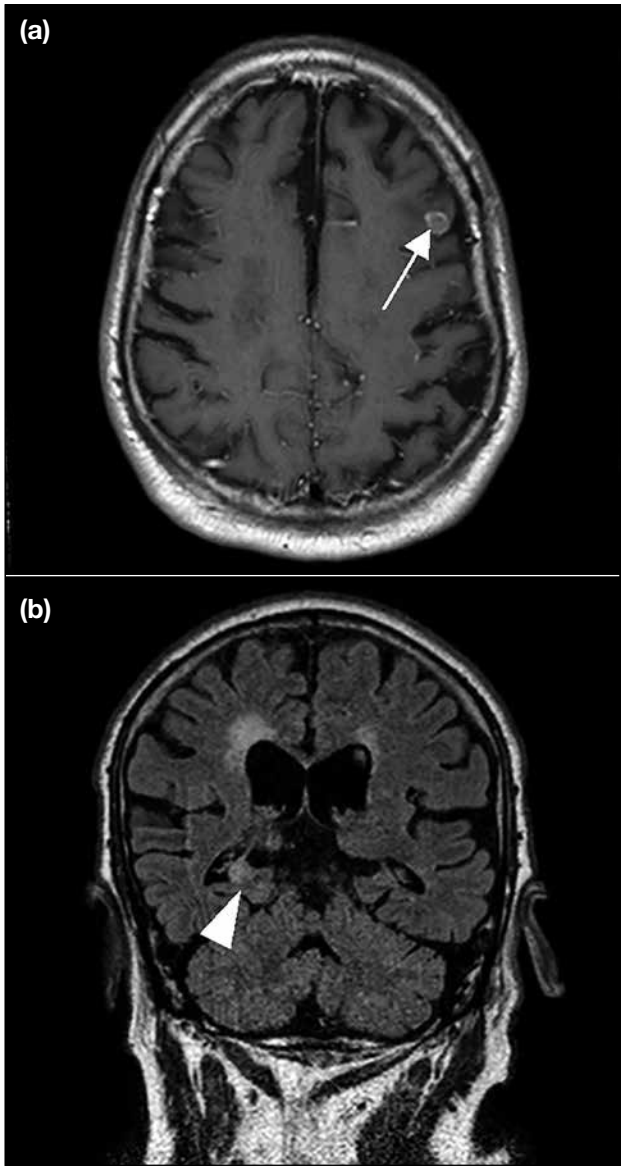


**Figure 2.** Magnetic resonance imaging of the brain 4 days after admission. (a) T1-weighted image with contrast demonstrating an enhancing left frontal lobe lesion likely representing a tumour (arrow). (b) Coronal fluid-attenuated inversion recovery image demonstrating slightly increased signal at the right hippocampus (arrowhead) suspected to be related to convulsion.

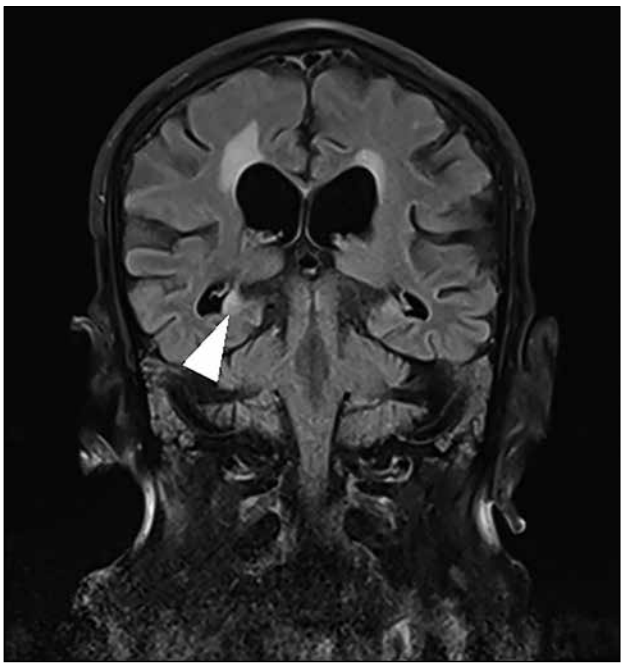

**Figure 3.** Magnetic resonance imaging of the brain 1 month after admission. The increased fluid-attenuated inversion recovery signal at the right hippocampus had become slightly more conspicuous (arrowhead).

## DISCUSSION

According to the diagnostic criteria of autoimmune encephalitis proposed by Graus et al,[1] the diagnosis of anti-GABA$_B$ receptor encephalitis could be established in the patient presented here. Autoimmune encephalitis is an emerging neurological disease associated with neuronal autoantibodies against various neuronal targets. Encephalitis with autoantibodies against GABA$_B$ receptors is an uncommon entity with an estimated relative frequency of 5%.[4] GABA receptors play an important role in neuronal activity associated with learning, memory and cognitive functions[5] and have been found to cause limbic encephalitis.[6]

Limbic encephalitis refers to inflammation of the limbic system and is considered a classic paraneoplastic syndrome. Common malignancies associated with limbic encephalitis include lung tumours (especially small-cell lung cancer), seminoma, thymoma, breast cancer, and lymphoma. Patients with limbic encephalitis typically present with memory loss, confusion, hallucinations, personality change, and seizures. Prompt diagnosis and management are essential for neurological recovery. Nevertheless the initial diagnostic tests currently utilised are mainly cerebrospinal fluid analysis,

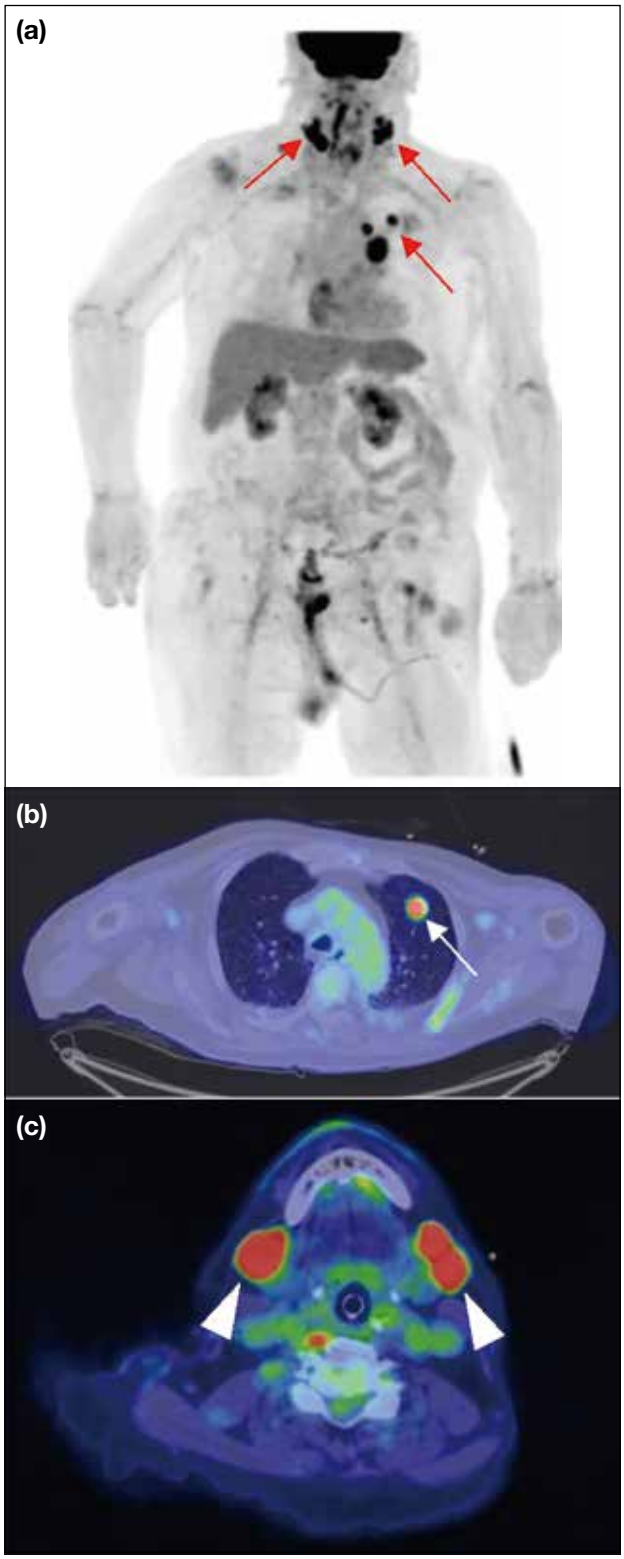


**Figure 4.** [$^{18}$F]fluorodeoxyglucose positron emission tomography/computed tomography of the body. (a) Maximum intensity projection image demonstrating hypermetabolic left upper lobe lung mass with suspected mediastinal, hilar and bilateral cervical nodal metastases (red arrows). (b) Fusion image of the left upper lobe lung mass (white arrow). (c) Fusion image of suspected bilateral submandibular nodal metastases (arrowheads) later biopsy proven to be small-cell lung carcinoma.

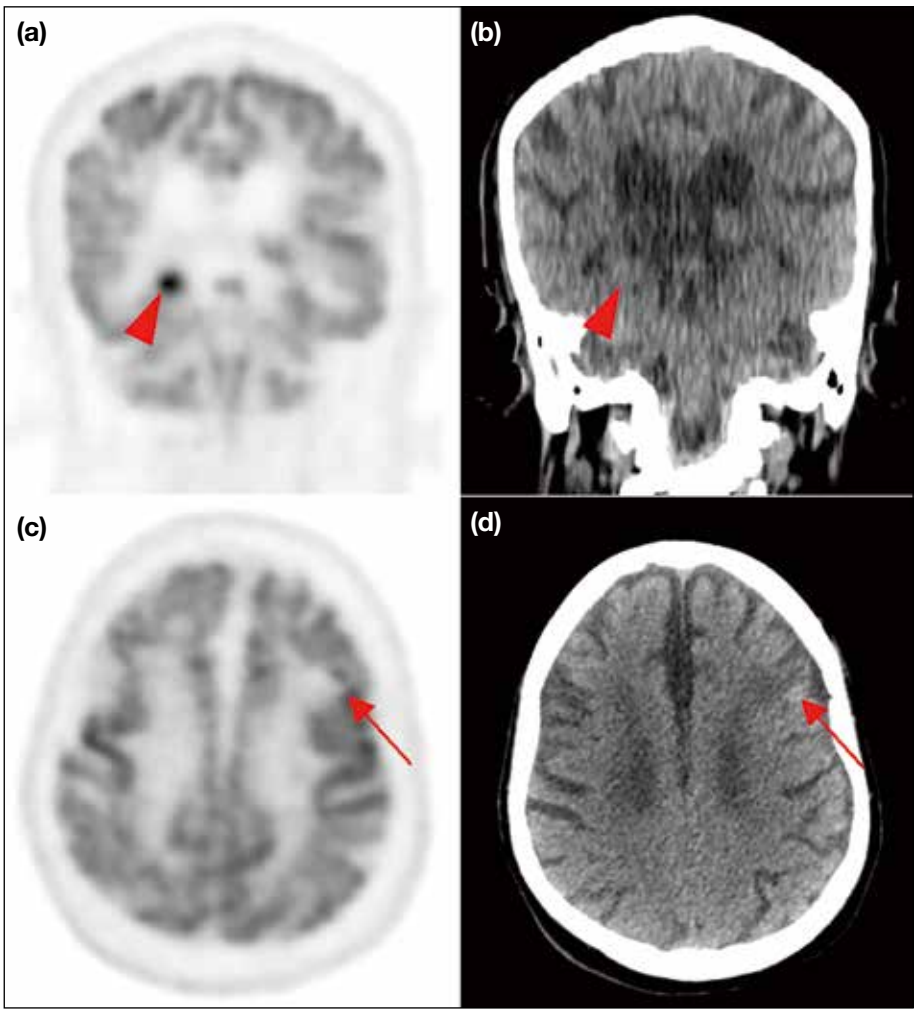


**Figure 5.** [$^{18}$F]fluorodeoxyglucose positron emission tomography/computed tomography of the brain. (a, b) Focal hypermetabolism in the right hippocampus consistent with limbic encephalitis (arrowheads). (c, d) No overt hypermetabolism was observed in the left frontal lobe lesion (arrows).

electroencephalogram, and MRI of the brain.[1] The role of [$^{18}$F]FDG PET/CT remains unclear, despite being a sensitive functional brain imaging technique. Baumgartner et al[7] reported a higher sensitivity of [$^{18}$F]FDG PET/CT in detecting limbic encephalitis–associated pathological findings than MRI. [$^{18}$F]FDG PET/CT offers information on the neuronal metabolic activity that increases in the presence of brain inflammation. In the case we present, the FLAIR signal abnormality was very subtle on MRI of the brain.

According to a case series by Höftberger et al,[8] 50% of patients had small-cell lung carcinoma. They also demonstrated that a patient may have neurological improvement with oncological treatment alone. Therefore, the clinical outcome for patients with anti-$GABA_B$ receptor encephalitis and underlying small-cell lung carcinoma is dictated by successful treatment of the tumour. [$^{18}$F]FDG PET/CT is also a sensitive oncological diagnostic tool in addition to functional brain imaging. Our patient underwent [$^{18}$F]FDG PET/CT following equivocal results of other investigations and consequent diagnosis weeks after initial presentation. Unfortunately, our patient succumbed and was not able to receive timely oncological treatment. We suggest that incorporation of [$^{18}$F]FDG PET/CT in the initial assessment may benefit the diagnosis and subsequent initiation of oncological treatment in patients with underlying tumour as well as their clinical outcome.

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