

[⁶⁸Ga] Ga-Pentixafor diffuse bilateral Adrenal & Breast uptake in a patient with High-grade Glioma: A note of caution on normal variants

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ABSTRACT

[⁶⁸Ga] Ga-labeled C-X-C motif receptor4 as a novel radio-ligand using PET/CT has been investigated for tracing various kinds of solid and hematopoietic malignancies in recent years. High-grade Glioma (WHO classification 2016 grade III and IV) shows elevated levels of CXCR4 ligand expression in the affected tumoral cells. Healthy and non-affected organ cells express low-level CXCR4 ligands density. We performed [⁶⁸Ga] Ga-Pentixafor (Pars-Cixafor™) PET/CT in a patient with high-grade Glioma (anaplastic oligodendroglioma WHO grade III) with no other documented medical condition and history. In addition to the Pentixafor-avid tumor remnant in the PET/CT images, we observed mild symmetrical bilateral uptake in the fibro glandular tissue of the breasts and moderate CXCR4(Pentixafor) avidity in both adrenal glands without any discernable pathology and abnormal density changes in the CT component of the study. Attention should be paid to the interpreting [⁶⁸Ga] Ga-Pentixafor PET/CT examination and its normal uptakes and variants.

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Introduction

[⁶⁸Ga] Ga-labeled C-X-C motif receptor 4 as a novel radio-ligand using PET/CT has been investigated for tracing various kinds of solid and hematopoietic malignancies e.g., High-grade Glioma that shows elevated levels of CXCR4 expression. Information regarding potential pitfalls and various normal variants once interpreting [⁶⁸Ga] Ga-Pentixafor PET/CT are limited.

Case Report

A Thirty-three-year-old woman with a history of treated anaplastic oligodendroglioma (WHO III) in the left occipito-parietal mass with spread to the lateral ventricle and basal ganglia was referred due to worsening headaches and new-onset seizure. She was referred to our department for [⁶⁸Ga] Ga-CXCR4 PET/CT.

Imaging was performed on a 6-slice dedicated PET/CT scanner 60 minutes post-injection of 4.03 mCi (149.11 MBq) of radio-labeled ⁶⁸Ga-CXCR4. Radio-labeling was done under GMP regulations via a fully-automated labeling module with ⁶⁸Ga eluted from PARS-GalluGEN ⁶⁸Ge/⁶⁸Ga generator. Diagnostic CT acquisition (130 Kv, 240mAs, slice thickness 3 mm, 512×512 matrix size, increment of 1.5 mm/s, rotation time of 1.0s, and pitch index of 0.55) was made with no contrast, followed by single bed PET imaging.

Discussion

The scan revealed mild CXCR4 avidity (SUV_{max}: 1.68) in the left occipito-parietal lobe (solid arrow) with evidence of adjacent calcification (dotted arrow) and good tumor-to-background ratio (Figure 1), as we expected in grade III,

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compatible with the tumoral remnant. No abnormal activity in the rest of the brain was noticed.

The acquisition was continued in skull-base to mid-thigh regarding study design with low-dose CT for attenuation correction and anatomical correlation. The whole-body PET/CT

images showed mild diffused-bilateral breast uptake (SUV_{max} : 1.92) corresponding to fibroglandular tissue on CT slices (Figure 2, E, F, G). Moreover, both adrenal glands revealed uniformly elevated CXCR4 avidity (SUV_{max} : 5.82) with no corresponding CT abnormality (Figure 2 A-D).

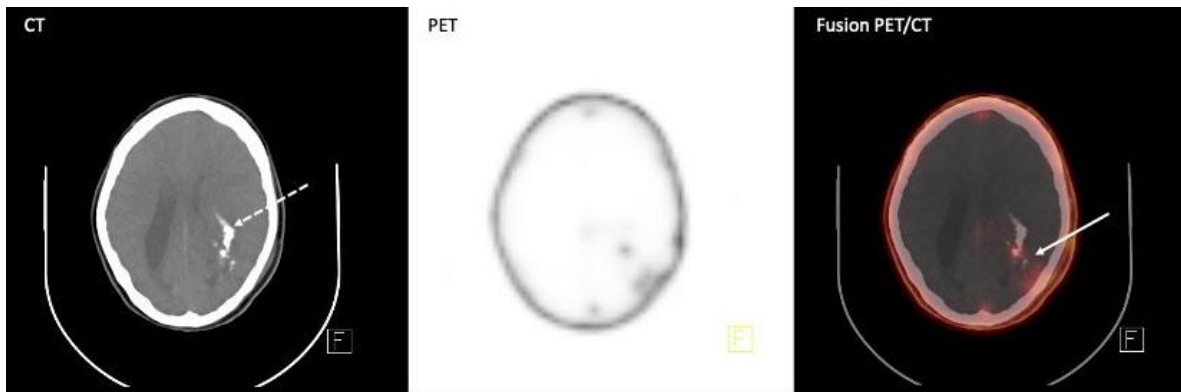


Figure 1. Brain [⁶⁸Ga] Ga-Pentixafor PET/CT. mild CXCR4 avidity (SUV_{max} : 1.68) in the left occipito-parietal lobe (solid arrow) with evidence of adjacent calcification (dotted arrow)

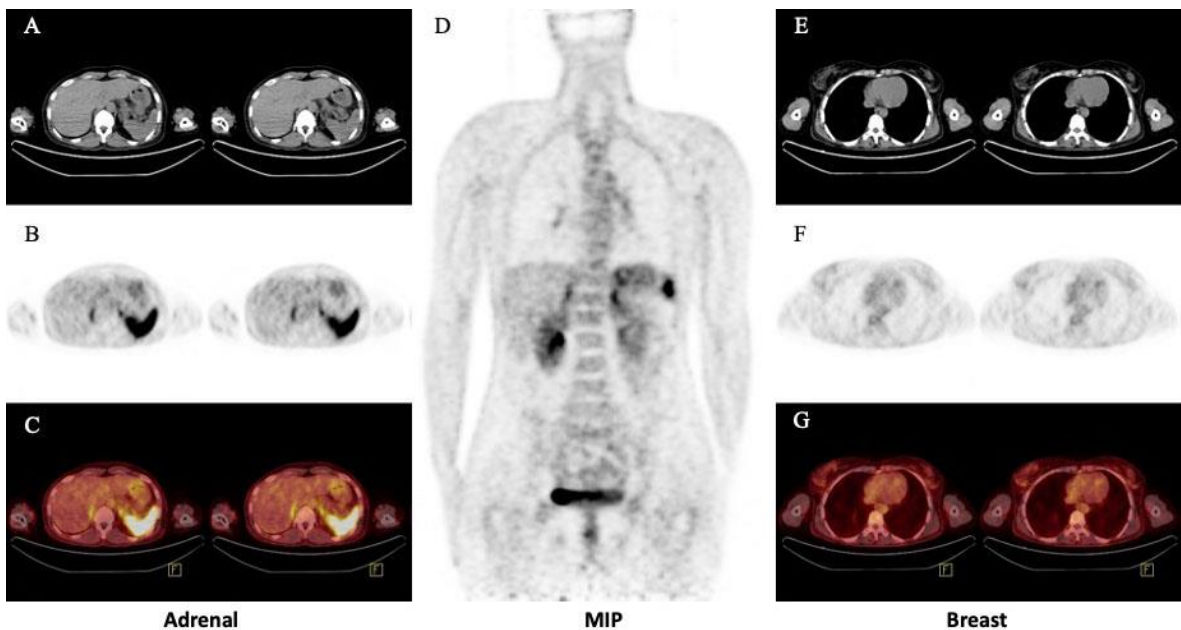


Figure 2. [⁶⁸Ga] Ga-Pentixafor PET/CT. depicting slices of adrenals and breasts normal uptake

[⁶⁸Ga] Ga-labeled CXCR4-directed PET/CT imaging in high-grade Glioma has shown promising information regarding residual remnant and aggressiveness of tumor (1, 2).

[⁶⁸Ga] Ga-labeled C-X-C motif receptor4 as a novel radio-ligand using PET/CT has been investigated for tracing various kinds of solid and hematopoietic malignancies (3, 4).

Although breast cancer has shown over-expression of CXCR4; normal healthy breast tissue expressed low-density CXCR4 receptors (5- 7).

Low level over-expression of CXCR4 ligands in the fibroglandular tissue of our case can be due to hormonal stimulation and during the menstrual cycle (our patient was in the follicular phase; day 3).

In contrast to normal adrenal tissue, significantly elevated levels of CXCR4 have been reported in cortisol-producing and aldosterone-producing adenomas, as well as adrenal hyperplasia (8-10). Nevertheless, our patient had no prior history of hypertension, neither relevant family nor drug history. The blood lab

data (Potassium, Sodium levels and Bicarbonate) were within normal limits as well. To sum up, tracer uptake in both breasts and adrenals can be considered normal variants. Thus, attention should be paid to these normal uptakes while interpreting [⁶⁸Ga] Ga-CXCR4 PET/CT examination.

Compliance with ethical standards

The patient was enrolled in a clinical trial of CXCR4-targeted PET/CT in vivo assessment of high-grade gliomas (Ir. MUMS. Medical. REC. 1399.734). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Conflict of interest

The authors declare that they have no conflict of interest.

Informed consent

Written Informed consent was obtained from our patient.

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