False Positive or False Negative PET Scan?

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Abstract

Background: Presentation of paraganglioma can be often very puzzling and localizing the site of extra catecholamine production can be very exhausting especially in a very unusual circumstance.

Case Presentation: This is case of 51 years old man with history of anxiety attacks, hyperhidrosis, flushing, palpitation, occasional hypertension and dizziness which had repeated elevated 24 hours’ urine metanephrine and positive PET scan (Figure 1) then PET scan was negative after he took phenoxybenzamine for 8 weeks.

Conclusion: Based on the clinical and paraclinical data patient most probably had paraganglioma and the reason for the negative second PET scan was due to him taking phenoxybenzamine (for 8 weeks) which is an α blocker and blocks or at least decreases cellular glucose uptake of the tumor cells.

Key Worlds: GLUTs; Paraganglioma; PET scan; Phenoxybenzamine

Introduction

Presentation of paraganglioma can be often very puzzling and localizing the site of extra adrenal gland catecholamine production can be very exhausting. The current available advance technology significantly improved the diagnosis of paraganglioma/pheochromocytoma, however, every test should be performed on an appropriate condition, otherwise may not be beneficial or even may become confusing.

Case Report

A 51 years old man was referred to the endocrine clinic for further evaluation of episodic anxiety attacks accompanied with hyperhidrosis, flushing, palpitation and hypertension with systolic blood pressure that occasionally would increase up to 180s to 200s. He had history of grade 3A follicular lymphoma treated with chemotherapy 3 years prior to these events, he also has history of diet controlled Type 2 Diabetes Mellitus (T2DM), hypertension (sub optimally controlled with amlodipine and Lisinopril), bipolar, anxiety disorder (on cetirizine10 mg/day, fluoxetine 20mg/day and temazepam 30 mg at bed time) and hypogonadism (on testosterone cypionate 100mg/week, intramuscular). He demonstrated biochemical evidence of urinary normetanephrine hypersecretion on four separate occasions, in the absence of any interfering medication at least in couple occasions; 1174, 1719, 1562, 1541 (44 - 540mcg/24h). However, serum normetanephelines and serum and urine metanephrines levels, all were within normal levels. Chromogranin A level was 132ng/ml (1.9-15ng/mL) and urinary 5-HIAA and serum dopamine levels were within normal limit. MRI of the neck, chest, abdomen, pelvis and colonoscopy also did not yield more information. CT of chest and abdomen was negative for adrenergic or extra-adrenal mass and 123I-MIBG were also negative. However, 18F-FDG whole body PET/CT scan showed focal uptake along a short length of the terminal ileum a few centimeters from the cecum, max SUV of 11 (Figure 1). Given the history of follicular lymphoma, oncology service was also consulted. Although follicular lymphoma is PET avid, oncology service deemed it would be very unusual for isolated lymphoma recurrence on the wall of small bowel and agreed with current working clinical diagnosis of paraganglioma. In addition, there were no signs of any inflammatory process or malignancy in the bowel based on the most recent colonoscopy. It is important to add that during these studies patient was on only cetirizine10mg/day and fluoxetine 20mg/day.

Therefore, based on clinical symptoms, elevated urinary normetanephrines on multiple occasions and positive whole body 18F-FDG PET/CT scan, patient was diagnosed of having paraganglioma possibly located on the bowel wall. Patient was started on phenoxbenzamine in preparation for surgery. Surgery service, however, later for the sake of more clear localization repeated 18F-FDG PET/CT while patient on cetirizine10mg/day and fluoxetine 20mg/day and tramadol 25 mg 3-4 times/day in addition to phenoxbenzamine 10 mg every 6-8 hours (for almost 8 weeks). The second 18F-FDG PET/CT scan fails to show any uptake. Therefore, the surgery was cancelled and dose of phenoxbenzamine was gradually decreased and he was on a “maintenance” dose to keep his blood pressure under control. Unfortunately, he was found dead in his restroom few weeks later and there was no autopsy performed and we will never know whether

Abbreviations

AR: Adrenalin Receptor
CT: Computed Tomography
DM: Diabetes Mellitus
18F-FDG: 18F- Fluorodeoxyglucose
GLUTs: Glucose Transporters
5-HHIA: 5-Hydroxy Indoleacetic Acid
MRI: Magnetic Resonance Imaging
123I-MIBG: 123I-Metaiodobenzylguanidine
PET: Positron Emission Tomography

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had paraganglioma and/or the cause of his sudden death. Now, our question is; did he have paraganglioma? Was his first 18F-FDG PET/CT scan a false positive test or his second 18F-FDG PET/CT scan was a false negative test?

![Figure 1](image-url): 18F FDG whole body PET scan shows a focal uptake along the short length of the terminal ileum a few centimeters from the cecum, Max SUV11.

**Discussion**

This case was suspected to have excess secretion of catecholamine’s based on his clinical symptoms of episodic anxiety attacks accompanied with hyperhidrosis, flashing, palpitation and hypertension. The clinical diagnosis of paraganglioma/pheochromocytoma was supported by finding of almost 3-fold increase in urinary normetanephrine (in every occasion that we have studied the urine). As per the reported study the measurements of urine fractionated metanephrine (in every occasion that we have studied the urine). The key to successful PET imaging is adequate preparation of suspected patient to minimize the appearance of potential artefactual uptake patterns that may make interpretation difficult. It is important that the patient be relaxed at the time of injection since muscle uptake of 18F-FDG increases after exercise in the hours leading up to the scan. Chewing, talking and muscle tension are forbidden at least 30 minutes before 18FDG injection. This will keep circulating insulin levels low and minimize uptake of 18FDG into muscle, fat and the myocardium [7]. Diet-controlled diabetic individuals can be treated similarly to nondiabetics [7]. However, diabetic patient’s blood glucose should be normalized as much as possible since high glucose levels reduce 18F-FDG uptake [7]. The short acting insulin should be stopped at least 4 hours before the injection and long acting insulin should be safely decreased over the past few days while keeping blood sugar close to normal levels and metformin is preferred to be stopped few days before the test, since both insulin and metformin utilize GLUTs and decrease uptake of 18F-FDG [7,8]. Furthermore, fluoxetine increases mRNA of GLUTs 1&10 in the neuronal tissue and may also interfere with uptake of 18F-FDG [9] and he was taking fluoxetine during both tests however, he was on much smaller dose of fluoxetine on the first study. Our medical center observes all these criteria and this patient had diet control diabetes mellitus.

As we have stated earlier paraganglioma cells has neuronal origin and it is well accepted that glucose is almost the main source of energy for neuronal cells/paraganglioma cells. Glucose enters neuronal cells via various Glucose Transporters (GLUTs) that mediate the sodium-independent facilitated transport of glucose to the cells [9]. Receptors for catecholamine’s (Adrenalin receptor= AR) are widely distributed on neuronal cells [10-12]. ARs are classified into 3 main subgroups α1, α2 and β all are distributed on the cells membrane, these ARs are functional receptors and are stimulated or blocked by ARs agonist or antagonist. Moreover, it has been shown that adrenalin and noradrenaline mediate the entry of the glucose to the neuronal cells [13], therefore, it is conceivable that administration of AR blocker can decrease neuronal cell glucose uptake [13]. Consequently, administration of phenoxybenzamine that blocks both α1 and α2 AR scan also block the entry of glucose as well as 18F-FDG to the paraganglioma cells. Based on this information blocking the ARs may result in converting a positive 18F-FDG PET/CT to a negative test. This patient was taking phenoxybenzamine 30-40mg for 8 weeks prior to the second test which could have blocked the entry of 18F-FDG to the paraganglioma cells and converted a positive test to a negative test as it had probably occurred in this case.

In summary, it is plausible to assume the first PET/CT was posi-
tive and the second PET scan was negative due to patient taking rather large dose of phenoxybenzamine for 8 weeks which had blocked glucose uptake by the tumor cells and converted a positive scan to a negative scan. However, this is only a hypothesis and we do not have a clinical data in this case to prove that.

Author’s Contribution

Nasrin Azad studied Patient’s data, studied the literature and prepared this manuscript.

Competing Interests

The author declares that they have no competing interests.

References