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Incidental Diagnosis of Multiple Paragangliomas by Ga-68 DOTANOC Positron Emission Tomography-Computed Tomography

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ABSTRACT

A 65-year-old man presented with intermittent abdominal pain for three months. Abdominal ultrasonography revealed a mass in the body of the pancreas. Moreover, abdominal contrast-enhancing computed tomography revealed a homogenously enhancing mass in the body of the pancreas. Scan findings were in favor of the neuroendocrine tumor, and the serum chromogranin level was slightly raised (111.9 ng/ml, normal <98). He had no history of vomiting, jaundice, melena, hematemesis, constipation, diarrhea, weight gain, weight loss, loss of appetite, and fever. He also had no symptoms related to the excessive production of catecholamines, such as hypertension. The patient was referred for Ga-68 DOTANOC positron emission tomography-computed tomography (Ga-68 DOTANOC PET-CT) for further evaluation. The scan was done to rule out metastatic disease or other synchronous lesions to plan surgical excision. The Ga-68 DOTANOC PET-CT revealed a pancreatic lesion with no other abdominal lesions. We noted multiple tracer avid soft tissue lesions on both sides of the neck that were not diagnosed previously. This case report demonstrates a rare case with multiple paragangliomas diagnosed by the Ga-68 DOTANOC PET-CT. This finding could lead to changes in patient management.

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Introduction

Paragangliomas (PG) is a rare neuroendocrine tumor of the extra-adrenal paraganglia. They are derived from pluripotent neural crest stem cells associated with the neural crest chromaffin tissues of the autonomic nervous system. The PG may develop at various sites in the body and is usually solitary. The incidence rate of diagnosed PGs is about 0.8/100,000 patients per year (1). Most PGs are non-functioning and do not overproduce nor-adrenalin. Some of them produce epinephrine, norepinephrine, or dopamine in varying proportions and have symptoms (2). They may be multicentric in 10% of sporadic cases and 32% of familial cases (3).

There is a high probability of PGs if the plasma concentrations of normetanephrine, meta-nephrine, and methoxytyramine are more than two-fold above upper cut-offs of reference (4). For localization of the lesion, anatomic imaging, such as ultrasonography (USG), contrast-enhanced computed tomography (CECT), and magnetic resonance imaging (MRI) were utilized. However, for head and neck PGs, small lesions or metastasis, anatomical and functional imaging [Meta I-123 iodobenzyl-guanidine (I-123 MIBG)] have lower sensitivity in comparison to the Ga-68 DOTANOC PET-CT (5).

There is no recommendation for the performance of a biopsy in pheochromocytoma (PCC) and PG. Therefore, biopsy should only be considered in exceptional cases when biochemistry is negative, and it could change patient management (6). It should be emphasized that all patients with a history of

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PCC/PGs are at the risk of recurrence, even after complete resection; moreover, they may have metastatic potential (7). Precise preoperative localization of these tumors is mandatory as surgery is the mainstay of treatment. Undiagnosed functional PGs have high morbidity and mortality and are also challenging for anesthetic management (8).

Case Report

A 65-year-old man presented with intermittent abdominal pain for three months. There was no history of vomiting, jaundice, melena, hematemesis, constipation, diarrhea, weight change, loss of appetite, and fever. Pallor, icterus, clubbing, cyanosis, lymphadenopathy, or edema were absent based on physical examination. Abdominal USG revealed a mass in the body of the pancreas. Results of upper gastrointestinal endoscopy were unremarkable, and abdominal CECT suggested a homogenously enhancing mass in the pancreas that was in favor of neuroendocrine tumor (NET).

The patient was evaluated for 24-h urine 5-hydroxyindoleacetic acid (5-HIAA) and metanephrines with serum chromogranin levels two weeks after stopping proton pump inhibitors. Serum chromogranin level was slightly raised (111.9 ng/ml, normal <98). The 24-h urine metanephrines level was within normal limit (214 mcg/24 h, normal<600).

Finally, the patient underwent Ga-68 DOTANOC PET-CT for diagnosis and detection of potential disease burden. It revealed an avid tracer mass in the pancreatic body (maximum standardized uptake value [SUV_{max}]= 32.02). Furthermore, multiple previously undiagnosed tracer avid soft tissue lesions were seen on both sides of the neck. They were situated just above the carotid bifurcation (SUV_{max}=42.40) on both sides at the left carotid bifurcation and in the left pyriform fossa region (Figure 1). This case report demonstrates a rare case with multiple non-functioning PGs disclosed by the Ga-68 DOTANOC PET-CT. These findings could lead to changes in the surgical management of such patients.

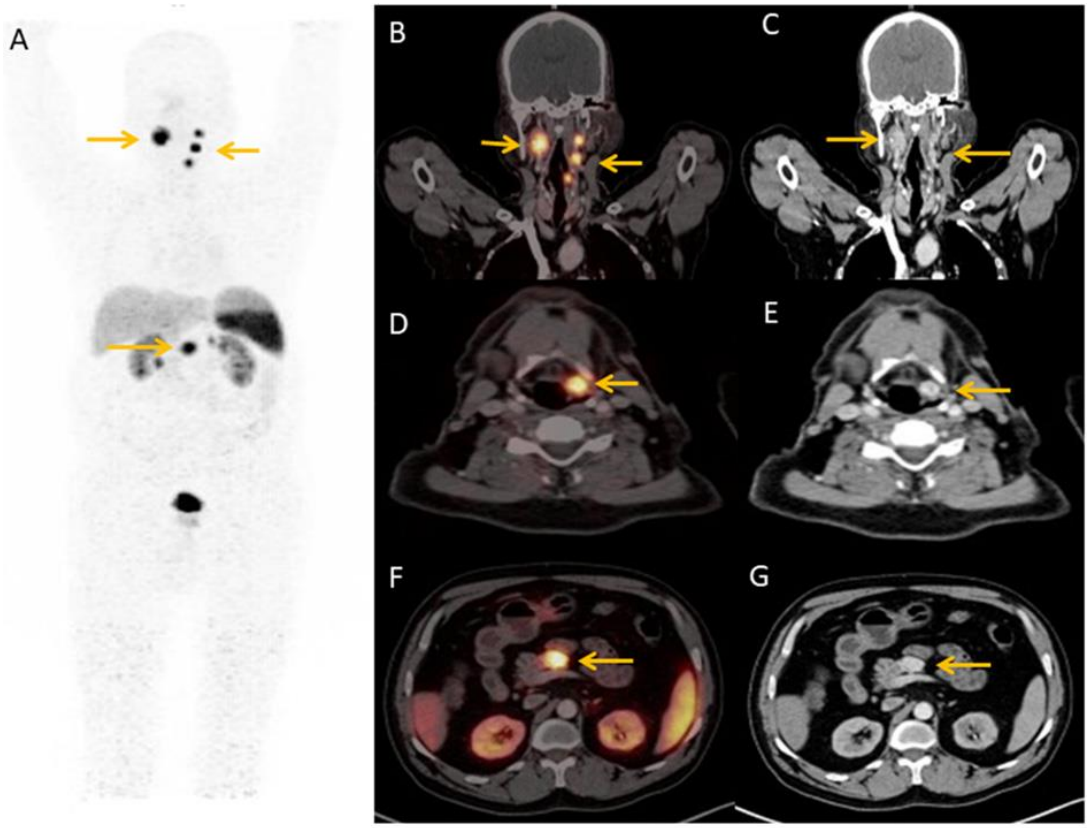

Figure 1. A) Maximum intensity projection image revealing avid multiple tracer avid lesions in the neck and abdomen. **B** and **C**) Coronal image of the neck showed tracer-avid (maximum standardized uptake value=42.40) enhancing several lesions on both sides of the neck in the carotid space, the largest of which was 2.0×2.2 cm. **D** and **E**) Trans-axial images at the pyriform fossa level reveal an enhancing lesion in the left pyriform fossa region. **F** and **G**) It shows tracer-avid enhancing lesion in the body of the pancreas (maximum standardized uptake value=32.02) with the size of 2.0×2.6 cm

Discussion

Neural crest cells constitute a multipotent population from numerous cellular lineages. It includes melanocytes, craniofacial cartilage, bone, smooth muscle, neurons, and glia. In addition, multiple tumors, such as PCC/PGs and neuroblastomas, arise from neural crest cells (9). Para-ganglia cells also originate from the neural crest but differentiate into sympathetic and parasympathetic subtypes that can give rise to PGs. Sympathetic PGs secrete norepinephrine; in contrast, parasympathetic PGs are non-secretory and typically occur in the head and neck .

Our patient presented with just intermittent abdominal pain. He had no other symptoms due to the secretory function of PGs. Results of routine blood tests, including the levels of hemoglobin (12.3 gm/dl), white blood cell (8200 per microlitre), and platelet count (140000 per microlitre) were unremarkable. The results of other investigations, such as renal and liver function tests, were also within the normal limits .

As it is traditionally known, PCC is described by the rule of 10. Metastasis, bilaterality, familial, and extra-adrenal (PG) involvement with no hypertension is noted in 10% of PCC patients. It should be mentioned that the rule of 10 is helpful in many cases. The current research has stressed the increased importance of genetic predisposition in such cases. However, in our case, there was no familial predisposition. His clinical examination was unremarkable, and he was found to be normotensive on various occasions (10).

The frequency of metastases varies generally depending on the tumor origin. Only 2–10% of PCC metastasize contrasted with 20–70% of extra-adrenal PGs (11). Our case had a solitary pancreatic lesion with no other abdominal or systemic metastases. However, he had multiple lesions in the neck carotid regions, which is a rare condition (12).

The majority of PCC/PGs are active endocrine tumors and cause symptoms by secreting excessive amounts of catecholamine (epinephrine, norepinephrine, and dopamine) and their inactive metabolites (metanephrines, normetanephrines, 3-metoxythromine). The classical symptom triad of headache, perspiration, and palpitations is seen in 25% of the patients (13). Nevertheless, our patient had no sign and symptom related to their excessive secretion .

Non-functional PGs may exhibit regional compression symptoms which could be the reason for his intermittent abdominal pain. It must be noted that due to their small sizes, variable locations, and low metabolic rates, conventional imaging of these tumors is challenging. Therefore, the CECT, USG, and MRI are sometimes unable to detect such tumors (14).

Imaging of patients with a PG is essential at every step of their management. Anatomic imaging is usually sufficient to locate a solitary tumor and proceed to surgery. However, when combined with functional imaging, there is an improvement in the specificity and sensitivity of the detection of metastases and multifocality. Functional imaging also provides a road map to the targeted radionuclide therapy .

Even though MRI and CT have excellent sensitivity (90-100%) (15), they are less specific regarding the differentiation of PCC from other abdominal lesions (16). A recent study has demonstrated the wide range of possible manifestations of PCC/PGs on MRI. The author has emphasized their low specificity and questioned the relevance of finding the 'classical' hyper-intense PCC image T2 weighted MRI. It signifies the insufficiency of "area-limited" imaging in these patients whose multifocal, extra-adrenal, and metastatic disease cannot be quickly ruled out (17).

The Ga-68 DOTANOC PET-CT is useful for the baseline evaluation of the head and neck PG and can reveal synchronous PG and distant metastases. It is superior to I-123 MIBG scintigraphy and conventional imaging for this purpose (18). The patient reported in this case study highlights this matter based on the findings of the imaging, excision of all the lesions and a serial follow-up studies .

As standard treatment for PGs is surgical resection, the assessment of baseline disease burden is crucial. After complete resection of the primary tumor, patients are at risk of recurrence; therefore, long-term follow-up is recommended in patients who were operated on for PGs, along with various serum and urinary tumor markers .

Performance of an imaging test is recommended after three months in patients with functional PGs. High-risk patients (i.e., young patients and those with a genetic disorder and high disease burden at baseline) should be offered lifelong annual follow-up. Biochemical tests should be performed every year to screen for local or metastatic recurrences or new tumors. Imaging should be performed every 1–2 years in patients with biochemically inactive PGs to screen for local or metastatic recurrences or metachronous tumors (7).

Conclusion

Functional imaging plays a crucial role in the management of NET. The PET-CT with Ga-68

labeled somatostatin analogs has shown excellent results for the imaging of NET. It is superior to conventional anatomical images and somatostatin receptor-based scintigraphy. It accurately and specifically localizes lesions throughout the body as a single imaging modality of choice. Therefore, it could lead to a change in the management of patients. In this regard, this case highlights the value of Ga-68 DOTANOC PET-CT in the management of patients with multiple non-functioning PGs.

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