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18F-DOPA vs. 18F-FDG PET/CT in the ectopic ACTH syndrome due to pulmonary carcinoid tumor



18F-DOPA vs. 18F-FDG PET/TC en el síndrome de producción ectópica de ACTH por tumor carcinoide pulmonar

Overproduction of corticotropin by the pituitary gland or extrapituitary tumors leads to ACTH-dependent Cushing's syndrome; 10% of these are due to ectopic production. These tumors often suppose a difficult diagnostic challenge because of their small size and multiplicity.

The pulmonary neuroendocrine-tumors (NET) originate from the enterochromaffin-cells which are diffusely distributed in the body. Their incidence has increased significantly in recent decades due to the available diagnostic resources; they represent about 1–2% of all lung tumors and 20–30% of all NET.¹

6-Fluoro-(18F)-L-3,4-dihydroxyphenylalanine (18F-DOPA) is an aminoacid-analog for positron emission-tomography (PET) imaging which has been registered since 2006 in several European Union countries and by several pharmaceutical firms. NET imaging is part of its registered indications.

18F-DOPA offers distinct advantage over fluorodeoxyglucose (18F-FDG) for the detection of carcinoids especially since many of these tumors are indolent with low proliferation activity and good differentiation. Furthermore, 18F-DOPA was able to detect more lesions, more positive regions, and more lesions per region than combined somatostatin receptor scintigraphy (SRS) and CT.²

We present the case of a 33-years-old male with a history of ACTH-dependent Cushing's syndrome. Dynamic testing of hypothalamo–pituitary–adrenal axis and high levels of ACTH (131 pg/ml) led to diagnosis of ectopic ACTH secretion. Chest X-ray showed a solitary pulmonary nodule in the anterior-segment of the right-upper-lobe. First PET/CT was performed after injection of 259 MBq of 18F-FDG, and revealed a pulmonary nodule located in the right-upper-lobe (Fig. 1a). The maximum standardized uptake value (SUVmax) measured was 1.9. Furthermore, a second pleural-based pulmonary nodule was observed in the left-upper-lobe with SUVmax 10.3 (Fig. 1b). According to these findings, contralateral or pleural involvement could not be dismissed. In order to better characterize the areas of increased radiopharmaceutical uptake, the patient underwent an 18F-DOPA-PET/CT after the injection of 233 MBq of radiotracer, which revealed a solitary pulmonary node in the right-upper-lobe (Fig. 1d) with SUVmax 1.1. 18F-DOPA-PET/CT

allowed discarding the contralateral and pleural involvement (Fig. 1e).

An atypical resection of the left-upper-nodule was performed by minithoracotomy approach. Lobectomy was discouraged after histopathology revealed alveolar hemorrhage, organizing pneumonia and areas of necrotizing granulomatous inflammation. Right-upper-lobectomy including video-assisted mediastinal lymphadenectomy was performed at a second time. Histology demonstrated a low grade well-differentiated ACTH-producing pulmonary NET with low mitotic and proliferative indices (<2 mitoses per 10 high power fields and Ki67 <1%, respectively), chromogranine/sinaptophysine/CD56 and ACTH positive; TTF1 negative; pT1aN2 stage according to TNM classification. Only 1/8 mediastinal lymph nodes were affected.

The patient recovered rapidly, with normalization of serum ACTH levels. The symptoms of hypercortisolism were resolved 6 months after lobectomy.

Functional imaging based on radiolabeled-analogs targeting overexpressed receptors and transporters is playing a pivotal role in imaging of cancer. SRS, (123I)-metaiodobenzylguanidine (MIBG) scintigraphy and 18F-FDG-PET/CT remain the 3 molecular imaging techniques most widely available and with the most comprehensive clinical experience for NET.³

Published results indicated that 18F-FDG-PET/CT could be valuable for selecting treatment, monitoring therapy and determining prognosis, especially in poorly differentiated NET.⁴ On the other hand, 18F-DOPA has been used for PET imaging in humans for more than two decades, initially for Parkinson's syndrome, and later in oncology for brain tumors or NET; it has proved to be an excellent tool for staging and restaging patients with documented carcinoid tumor.

The efficacy of 18F-DOPA-PET imaging in identifying carcinoid tumors depends on the ability of tumor cells to uptake, decarboxylate, and store aminoacids. 18F-FDOPA offers distinct advantages over 18F-FDG for detection of carcinoids, especially since many of these tumors are indolent, with low proliferation activity and good differentiation.⁵

18F-DOPA-PET is useful for detecting primary and metastatic neoplasia with neuroendocrine differentiation, such as carcinoid, gastroenteropancreatic tumors, glomus tumors, medullary thyroid cancer, small cell lung cancer, and pheochromocytoma/paraganglioma.^{6,7}

When compared with other available functional imaging, 18F-DOPA-PET/CT was able to detect more lesions, more positive regions, and more lesions per region than combined SRS and CT in catecholamine-producing tumors with a low aggressiveness and in well-differentiated tumors.^{2,8}

While the practice of 18F-FDG-PET/CT is fully standardized, up to now this has not been accomplished for

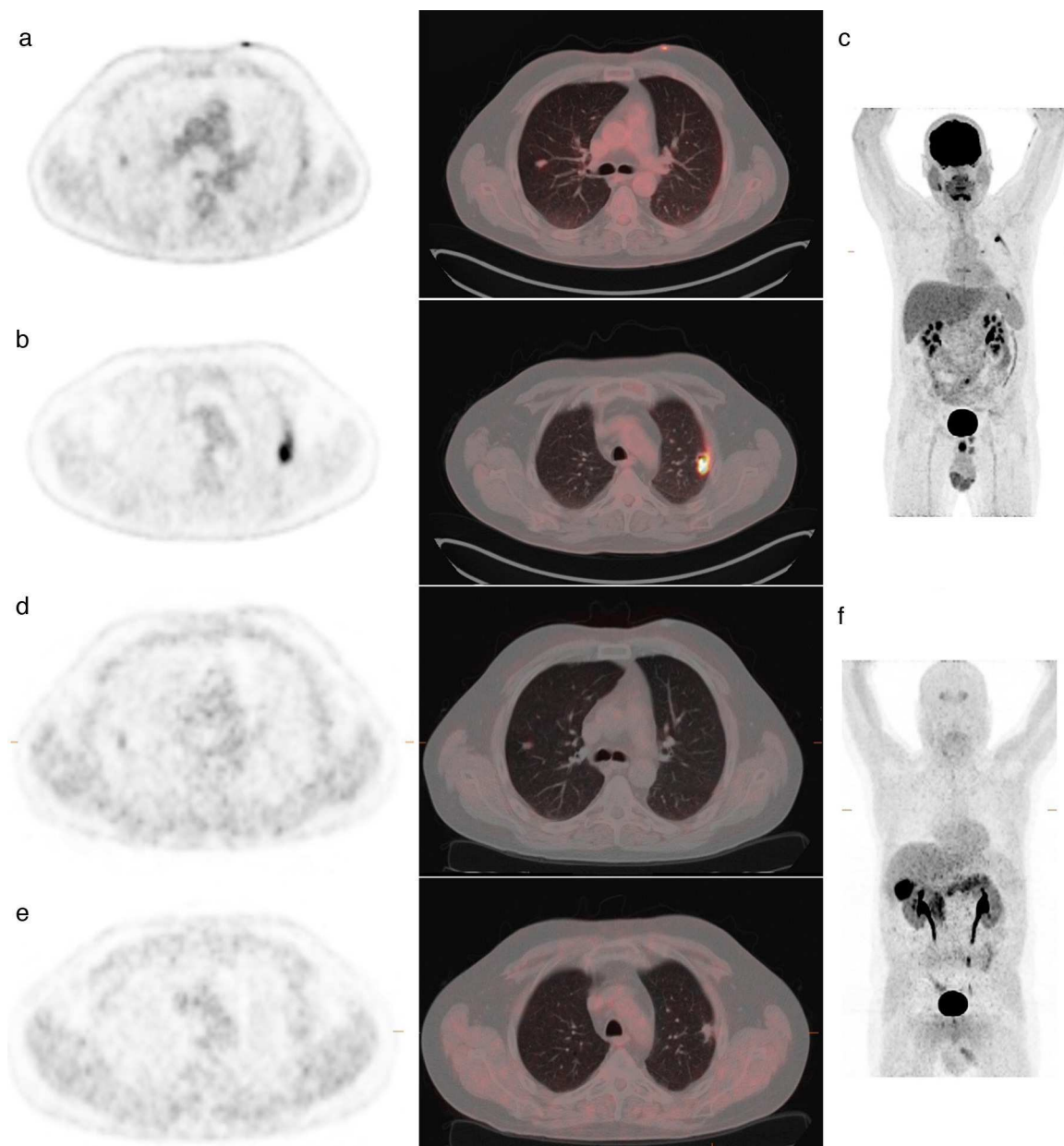


Figure 1 Upper panel. 18F-FDG-PET/CT performed after the injection of 259 MBq of radiotracer. (a) Pulmonary nodule located in the right-upper-lobe with SUVmax 1.9. (b) A second pleural-based pulmonary nodule was located in the left-upper-lobe with SUVmax 10.3. (c) Maximum intensity projection of 18F-FDG-PET/CT scan. Lower panel. 18F-DOPA-PET/CT acquired after the injection of a dose of 233 MBq. (d) Solitary pulmonary node showed in the right-upper-lobe with SUVmax 1.1. (e) 18F-DOPA-PET/CT allowed discarding the contralateral and pleural involvement. (f) Maximum intensity projection of 18F-DOPA-PET/CT scan revealing pancreatic physiological uptake due to no administration of carbidopa before the injection of radiotracer.

18F-DOPA-PET/CT protocol for NET. A 4h fast is recommended by all groups. The oral premedication with the carbidopa, which was introduced to block the aromatic aminoacid-decarboxylase enzyme, is less common than for brain 18F-DOPA imaging. Furthermore, the range of injected activity of 18F-DOPA is 2–4 MBq/kg of body mass. The 18F-DOPA uptake by most organs and target lesions has been described as a plateau between 30 and 90 min post-injection.

In the case we describe, both PET/CT were performed according to the scientific community

recommendations. Concordantly, we do not consider the administration of carbidopa before the injection of 18F-DOPA, so pancreatic physiological uptake can be observed (Fig. 1f). Both scans were acquired 60 min post-injection of radiotracer in a Biograph-16-PET/CT camera (Siemens/CTI).

The increasing number of therapeutic options and diagnostic procedures available for this disease requires a multidisciplinary approach and decision-making in tumor committees to ensure a personalized treatment. Whenever possible, once hypercortisolemia is under control with

medical therapy, the final treatment consists in the surgical excision of the tumor.

Surgery is the mainstay of treatment, based on the general principle of complete resection with preservation of as much normal lung tissue as possible. The treatment of choice for carcinoid tumors remains surgery and consists of a lobectomy supplemented by lymph node dissection.⁹

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Lactococcus lactis thyroid abscess in an immunocompetent patient[☆]



Absceso tiroideo por *Lactococcus lactis* en paciente inmunocompetente

Case report

Acute suppurative thyroiditis (AST) is an uncommon, potentially serious disease occurring mainly in children. The low prevalence of thyroid abscess is related to thyroid gland resistance to infection due to its fibrous capsule, high blood perfusion, high iodine contents, and significant lymphatic drainage, and to anatomical separation of the gland from the airway.¹

AST may arise from hematogenous or lymphatic dissemination, continuity from adjacent organs, or direct inoculation after fine needle aspiration (FNA).² The predisposing factors vary depending on age at presentation. In children, the most common predisposing factor is a pyriform sinus fistula (PSF), which is due to the abnormal development of the third or fourth branchial arch. The condition occurs on the left side in 87–95% of cases. This is explained by the asymmetry of the fourth branchial arch.^{3,4} PSF is

uncommon in adults, in whom other factors such as prior thyroid disease (Hashimoto's thyroiditis, differentiated thyroid cancer, multinodular goiter) and immunosuppression, which promotes in turn infection by uncommon microorganisms, are more relevant.⁵

We report the case of a 17-year-old female patient with a history of anorexia nervosa who attended the emergency room for fever, pain in the anterior aspect of the neck, and increased size of the left thyroid space. Subacute thyroiditis was clinically suspected, and anti-inflammatory treatment (ibuprofen 600 mg/8 h) was started. Six days later the patient returned to the emergency room reporting no improvement. Prednisone (30 mg/24 h) was therefore added in a tapering scheme, and the patient was referred to the endocrinology department due to the persistence of the condition.

Physical examination revealed left thyroid lobe enlargement with pain and a palpated mass and increased temperature.

Laboratory tests results included: leukocytosis (WBC: 13,500 mm⁻³, with 79.3% neutrophils) with elevated acute phase reactants (C-reactive protein: 108.40 mg/L) (range: 0.1–10.0) and ESR: 122.00 mm (range: 0.0–25.0) with normal thyroid function (TSH: 1.97 μIU/mL) (range: 0.35–5.0), free T4 1.40 ng/dL (range: 0.7–1.98) and free T3 2.54 pg/mL (range: 2.3–4.2) and negative thyroid autoimmunity.

A thyroid ultrasound examination showed three hypoechogenic collections suggesting thyroid abscess. A culture of purulent material collected by FNA revealed the presence of penicillin-sensitive *Lactococcus lactis*. Blood cultures were negative. Barium esophagogram revealed a fistula in the left

[☆] Please cite this article as: Campos R, Pérez B, Armengod L, Muñoz E, Ramos A. Absceso tiroideo por *Lactococcus lactis* en paciente inmunocompetente. *Endocrinol Nutr*. 2015;62:204–206.