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Radioguided Intraoperative Detection of Ectopic Adrenocorticotrophic Hormone-Producing Carcinoid Tumor[☆]



Detección intraoperatoria radioguiada de tumor carcinoide productor de hormona adrenocorticotropa ectópica

Carcinoid tumors are malignant neuroendocrine neoplasms that originate in the enterochromaffin cells of the diffuse endocrine system (APUD). The location of about 10% of these tumors is bronchopulmonary, and 1%–2% may be associated with paraneoplastic syndromes like Cushing's syndrome.¹

SRI (¹¹¹In-octreotide) may be indicated for the detection of disseminated carcinoid tumors or millimetric functioning tumors that are difficult to locate with other imaging studies.^{2,3} There are anecdotal reports of its use in the literature, and in our case it was essential for the complete resection of the lesions.⁴

The patient is a 30-year-old male with no medical history of interest who presented symptoms of Cushing's syndrome. Lab analyses showed evidence of hyperglycemia (300 mg/dL with negative ketonuria), elevated glycosylated hemoglobin (6.3%), mild hypokalemia, hypercholesterolemia, and hypercortisolism (3978 µg/day). Treatment was initiated with insulin. Levels of 5-hydroxyindoleacetic acid and chromogranin A were 8.5 mg/24 h and 225 ng/mL, respectively, suggesting carcinoid tumor. The episodic secretions of adrenocorticotrophic hormone (ACTH) were 153 µg and 83.3 µg after 8 and 23 h, respectively, which guided the diagnosis toward an extra-adrenal ACTH-dependent etiology. The absence of dexamethasone suppression and the normal results of a hypophyseal magnetic resonance imaging study led to a diagnosis of ectopic ACTH secretion syndrome.

Thoracoabdominal computed tomography (CT) scan revealed no pathologic findings, but the SRI showed a millimetric pathologic uptake in the right lung hilum (Fig. 1), although no endobronchial lesions were observed on bronchoscopy.

Twenty-four hours after the injection of the radioactive tracer (octreotide), we conducted an exploratory thoracotomy with manual palpation of the lung and scintigraphy scan

using an intraoperative catheter (Fig. 2). In addition to the small quantity of serous pleural fluid, a peripheral nodule measuring 6 mm was found in the RLL along with an interlobar lymph node (both with hyperuptake and value of 34 and 37 over the "pulmonary pool" of 2). Atypical pulmonary resection was performed with systematic mediastinal lymphadenectomy and intraoperative pathology confirmation of the lesions.

The immunohistochemistry study revealed a type 1 neuroendocrine carcinoma. Interlobar lymphadenopathy and the cytology of the pleural liquid were positive for malignancy, corresponding with stage IVa (T1N1M1). No adjuvant therapy was administered. The Cushing's syndrome was resolved after the surgery, and after 5 years of follow-up the patient remains asymptomatic, with no signs of relapse.

15%–20% of cases with Cushing's syndrome can be caused by non-hypophyseal tumors comprised by neuroendocrine tissue.¹ Bronchial carcinoid tumors are the most common cause of ectopic ACTH secretion (25%).¹

In our case, once the hypercortisolism had been confirmed, the differential diagnosis was initiated with Cushing's disease and ectopic Cushing's. After having confirmed the ectopic origin, a thoracoabdominal CT scan showed no lesions.

As reported by certain authors, a considerable number of bronchial carcinoid tumors are undetectable by conventional imaging techniques due to their small size and/or location in the pulmonary hilum, where they are particularly difficult to differentiate from the normal vasculature.² A review by Özkan et al. assessing SRI mentions a series of 90 cases, in which 47% were secondary to intrathoracic tumors and in 19% of cases the lesion was not located.³ More recent publications report the localization of hypersecretory tumors in only 62.5% of

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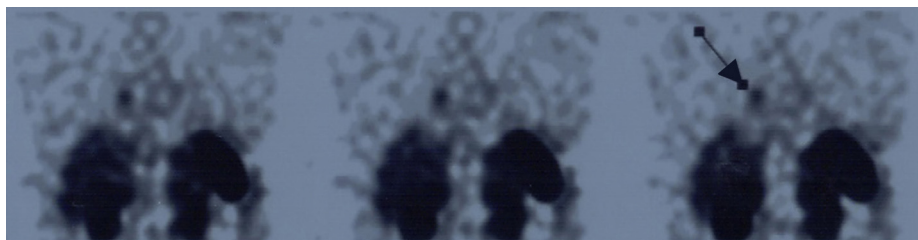


Fig. 1 – Preoperative somatostatin receptor scintigraphy (SRI) (^{111}In -Octreotide) found a millimetric pathologic uptake in the right pulmonary hilum.

cases by means of different imaging tests.³ Although there are controversial results in the literature, SRI with In-^{111} has been proposed to locate ectopic ACTH-secreting tumors that are not visible with conventional techniques.^{2,3}

In the case presented, we used SRI to search for the hypersecretory tumor and found a millimetric lesion with pathologic uptake in the right hilum, corresponding with a lymph node metastasis. The primary lung tumor, which was barely 6 mm, could only be identified by palpation and radioguided exploration. Intraoperative pathology analyses confirmed both lesions, and the definitive study revealed type 1 neuroendocrine cancer in an unusually advanced stage (T1N1M1).

Although they are considered malignant, this type of tumors usually present at initial stages and with a lower metastatic and invasive potential than other pulmonary neuroendocrine tumors.¹ The treatment of choice is complete resection, which has an excellent prognosis, even with lymph node metastases. Lobectomy is the most widely recommended resection, although sleeve resections have also been described in central tumors and sublobar resections in the peripheral lesions with good results.¹ Yendamuri et al., for example, consider that the extension of the surgical resection in this type of tumors is not a prognostic factor.⁵ In our case, as the tumor was millimetric and peripheral, we opted for atypical resection, with excellent results after 5 years of follow-up, in spite of having presented at stage IV. These tumors are relatively resistant to chemotherapy and radiotherapy; therefore, surgical treatment is recommended even in cases of advanced disease.¹ In conclusion, the localization and treatment of ectopic ACTH-secreting tumors is a diagnostic

challenge that requires multidisciplinary management. SRI and radioguided surgery were valuable techniques for this case in which conventional imaging tests were not conclusive.

Conflict of Interest

The authors have no conflict of interests to declare.

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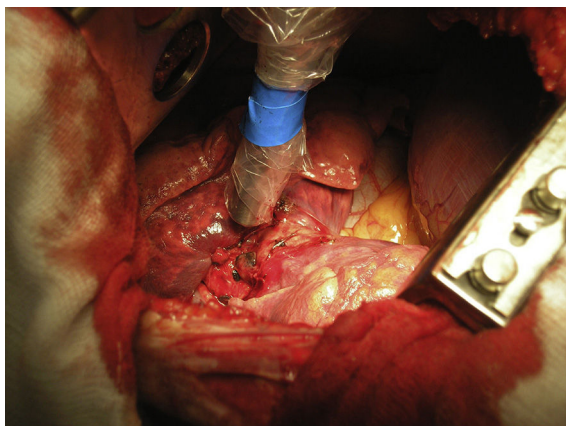


Fig. 2 – Scintigraphy scan of the entire lung with an intraoperative transducer.