Interactive CardioVascular and Thoracic Surgery 2022, 35(3), ivac130
https://doi.org/10.1093/icvts/ivac130 Advance Access publication 16 May 2022

Cite this article as: Chen X, Zhang Y, Lin J, Li H . An ACTH-secreting tumour hidden in a congenitally hypoplastic left lung. Interact CardioVasc Thorac Surg 2022; doi:10.1093/icvts/ivac130.

An ACTH-secreting tumour hidden in a congenitally hypoplastic left lung

Xueyu Chen[a,†], Yajie Zhang[a,†], Jules Lin[b] and Hecheng Li [a,*]

[a] Department of Thoracic Surgery, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, Shanghai, China
[b] Section of Thoracic Surgery, University of Michigan Medical School, Ann Arbor, MI, USA

* Corresponding author. Department of Thoracic Surgery, Ruijin Hospital, Shanghai Jiaotong University School of Medicine, 197 Ruijin Er Road, Huangpu District, Shanghai 200025, China. Tel: +86-21-64370045 Ext 666113; e-mail: lihecheng2000@hotmail.com (H. Li).

Received 5 April 2022; accepted 13 May 2022

Abstract

Ectopic adrenocorticotrophic hormone (ACTH) syndrome has historically been a therapeutic challenge because of the difficulty localizing occult ACTH-secreting tumours. Here, we report a case of a 67-year-old woman with ectopic ACTH syndrome and had an ACTH-secreting tumour hidden within a congenitally hypoplastic left lung. A satisfactory therapeutic outcome was obtained after left pneumonectomy was performed on patient in this case.

Keywords: Ectopic ACTH syndrome • Congenital pulmonary hypoplasia • Pneumonectomy

INTRODUCTION

Ectopic adrenocorticotrophic hormone (ACTH) syndrome (EAS) is due to the specific secretion of biologically active ACTH by tumour tissues located outside the pituitary, which stimulates renal epithelial hyperplasia to produce excessive cortisol leading to Cushing's syndrome [1]. Accurate imaging localization and resection of ectopic ACTH-secreting tumours are key to the successful treatment of patients with EAS but can be challenging. Herein, we report a rare case of a patient with an occult ectopic ACTH-secreting tumour hidden in a congenitally hypoplastic left lung who presented with the clinical symptoms of EAS.

CASE PRESENTATION

In June 2020, a 67-year-old woman presented with elevated blood pressure came to our hospital for examination. The patient also has the clinical manifestations of a rounded face, low frontal hairline, lower extremity oedema and high blood ACTH. An 8-mg dexamethasone suppression test showed that the patient's blood cortisol was suppressed, suggesting that the patient suffered with ACTH-dependent Cushing's syndrome. We subsequently performed a BIPSS (Bilateral inferior petrosal sinus sampling) test, which showed no increase in central ACTH secretion (IPS/Peripheral vein ratio 1.19). Although the patient's pituitary magnetic resonance imaging revealed a suspicious microadenoma (size in 6.2×4.2 mm), the elevated ACTH was not felt to be from the pituitary lesion because of the negative BIPSS test. Enhanced chest computed tomography (CT) showed congenital hypoplasia of the left lung, left mediastinal shift and partial herniation of the right lung into the left chest (Fig. 1A and B). There were no obvious lesions in the thymic region or right lung parenchyma. An 18F-FDG positron emission tomography–CT (PET-CT) was performed and still found no definite lesions. After discussion with a multidisciplinary team including thoracic surgeons, radiologists and endocrinologists, the patient was felt to have an occult ACTH-secreting lesion. Therefore, the patient underwent a 68Ga-DOTATATE PET-CT scan and a 10 mm DOTA-positive lesion was identified within the congenitally hypoplastic left lung (Fig. 1C).

Due to the hypoplastic left lung, the patient consented to a left pneumonectomy. Intraoperative exploration revealed that the left lung was completely atrophied to the size of a fist with severe left mediastinal shift and contraction of the chest cavity (Fig. 1D). Because of the severe congenital deformity and insufficient chest volume, we decided to proceed with a traditional thoracotomy rather than video-assisted thoracoscopic surgery (Fig. 1E). On postoperative pathology, the size of the left congenitally hypoplastic lung was $11.0 \times 4.5 \times 2.0$ cm. A nodule was found in left lung which measured $1.3 \times 1.0 \times 1.0$ cm in size. Immunohistochemistry was AE1/AE3 (+), CD56 (+), Syn (+), ACTH (about 35% +), TTF-1 (+), Napsin A (-), P40 (-), P63 (-) and Ki67 (about 1% +). Based on histology and immunohistochemistry, the

[†]The first two authors contributed equally to this work.

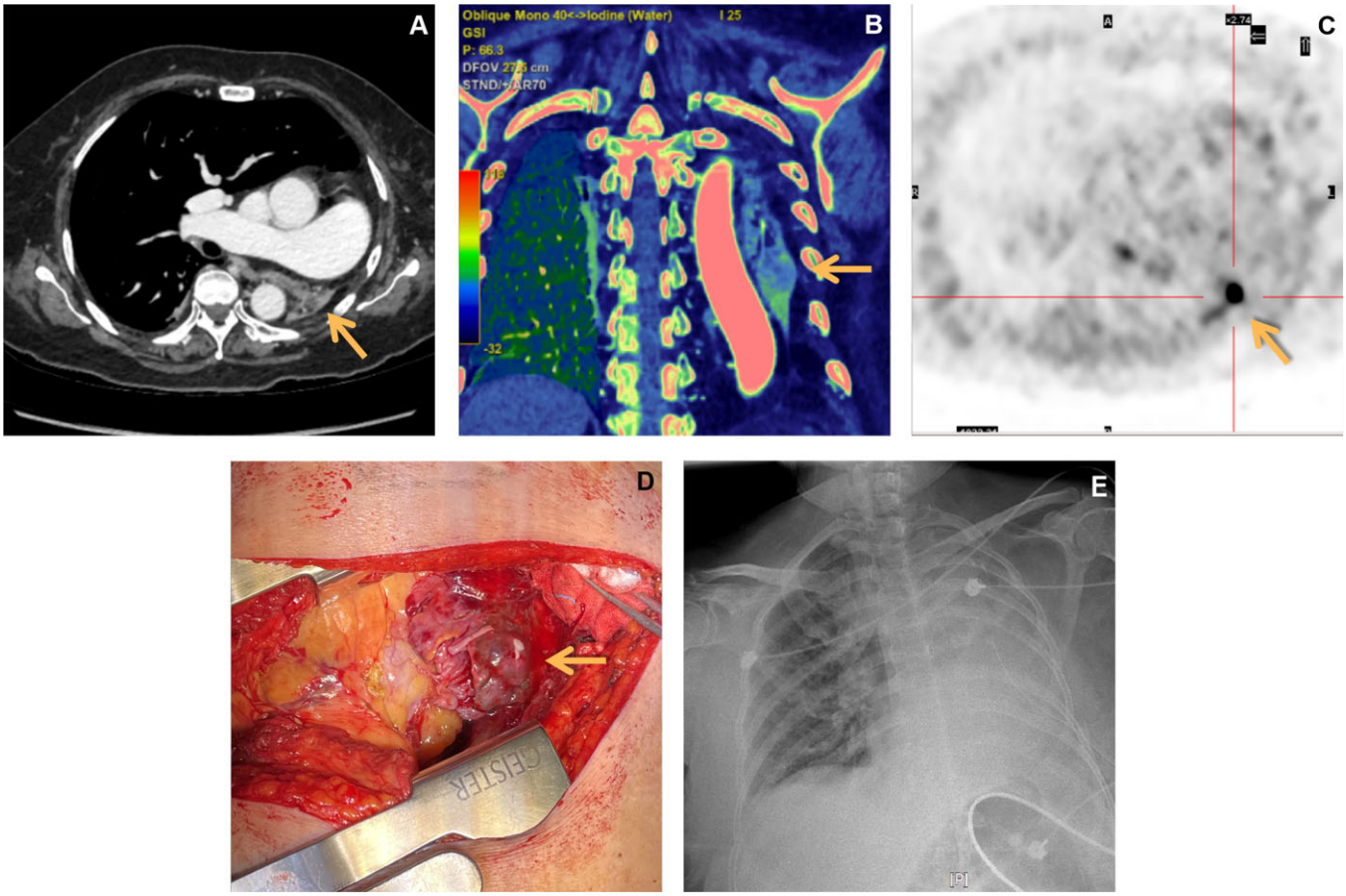

Figure 1: There was severe contraction of the left chest cavity with the congenitally hypoplastic left lung (arrow) compressed between the heart and the descending aorta (**A**). Spectral computed tomography imaging of the congenitally hypoplastic left lung with decreased perfusion (arrow) compared to the right lung (**B**). The adrenocorticotrophic hormone-secreting tumour appears hyperintense on 68Ga-DOTATATE positron emission tomography–computed tomography (arrow) and could be detected easily (**C**). Diffuse consolidation and significant atrophy were observed in the left lung with congenital hypoplasia intraoperatively (arrow) (**D**). A chest radiography of the patient after the operation (**E**).

nodule was identified as an ACTH-secreting carcinoid tumour. The patient was discharged on the 10th postoperative day. At 3-month follow-up, lab results showed stable adrenocortical function, and the clinical manifestations of EAS were controlled and improved. We learned that the patient had only mild hypertension at present, and other EAS symptoms had resolved completely compared with those before the operation.

DISCUSSION

As early as 1928, a possible connection was reported between the clinical manifestations of Cushing's syndrome and oat cell lung cancer [2]. The diagnostic rate of lung ectopic ACTH-secreting tumour on conventional chest CT scans is only 52–66% [3], and about 20% of EAS cases cannot be localized on conventional CT scans [4]. Therefore, all efforts should be made to localize the source of the ectopic ACTH simultaneously while endocrine therapy is started. Resection of the ectopic ACTH-secreting tumour can prevent EAS patients from undergoing an adrenalectomy due to uncontrollable high blood cortisol, and early resection may also reduce the incidence of tumour metastasis. The patient was initially diagnosed with hypertension by a local hospital, ignoring other diseases that may lead to secondary hypertension. With the growth of ectopic ACTH-secreting tumour, the patient's EAS symptoms appeared and hypertension began to deteriorate and difficult to control, so she was admitted to our hospital. This might explain the reason that the patient's tumour and symptoms were not detected until the age of 67. Congenital pulmonary dysplasia might be misdiagnosed as atelectasis caused by inflammation or sputum thrombus. It also needs to be differentiated from pulmonary sequestration, especially in patients who have a partial pulmonary hypoplasia. An obvious undeveloped bronchial blind end can be observed in patients with congenital pulmonary dysplasia through fibre-optic bronchoscopy examination which is quite different from atelectasis. This is consistent with the fibrous bronchoscopy result of the patient in this case. Patients with pulmonary sequestration can be diagnosed by an enhanced chest CT which can identify the existence of anomalous systemic arterial supply to the lung. In our case, with the abnormal volume and morphology of the hypoplastic left lung, even an enhanced high-resolution chest CT scan with a 1-mm slice thickness would have difficulty detecting the occult ectopic ACTH-secreting tumour. Meanwhile, the tumour also failed to be localized by 18F-FDG PET-CT due to the low-grade, less-invasive nature of the tumour, which was consistent with the findings reported by Nilica *et al.* [5]. Eventually, a 68Ga-DOTATATE PET-CT scan successfully confirmed an ectopic

ACTH-secreting tumour located in the congenitally hypoplastic left lung. Functional PET-CT examination using gallium 68 radiolabeled somatostatin analogues was verified to be significantly superior in the detection of neuroendocrine tumours compared to other examinations.

To our knowledge, this is the first reported case of an ectopic ACTH-secreting tumour hiding in a congenitally hypoplastic left lung and causing the manifestations of EAS. Successful localization of the ectopic ACTH-secreting tumour by 68Ga-DOTATATE PET-CT was critical to the treatment in this case. At subsequent follow-up, clinical manifestations of EAS were completely resolved. However, long-term therapeutic efficacy and prognosis still require continued observation. We believe that this particular EAS case will provide significant diagnostic and therapeutic experience for subsequent similar cases.

Conflict of interest: none declared.

Data availability statement

The data underlying this article will be shared on reasonable request to the corresponding author.

Reviewer information

Interactive CardioVascular and Thoracic Surgery thanks Fikret Kanat, Katrin Welcker and the other anonymous reviewer(s) for their contribution to the peer review process of this article.

REFERENCES

[1] Boscaro M, Barzon L, Fallo F, Sonino N. Cushing's syndrome. Lancet 2001;357:783–91.

[2] Brown WH. A case of pluriglandular syndrome—diabetes of bearded women. Lancet 1928;212:1022–3.

[3] Isidori AM, Sbardella E, Zatelli MC, Boschetti M, Vitale G, Colao A *et al.*; ABC Study Group. Conventional and nuclear medicine imaging in ectopic Cushing's syndrome: a systematic review. J Clin Endocrinol Metab 2015;100:3231–44.

[4] Ilias I, Torpy DJ, Pacak K, Mullen N, Wesley RA, Nieman LK. Cushing's syndrome due to ectopic corticotropin secretion: twenty years' experience at the National Institutes of Health. J Clin Endocrinol Metab 2005; 90:4955–62.

[5] Nilica B, Waitz D, Stevanovic V, Uprimny C, Kendler D, Buxbaum S *et al.* Direct comparison of (68)Ga-DOTA-TOC and (18)F-FDG PET/CT in the follow-up of patients with neuroendocrine tumour treated with the first full peptide receptor radionuclide therapy cycle. Eur J Nucl Med Mol Imaging 2016;43:1585–92.