RESEARCH ARTICLE

LUNG NODULE PRESENTING AS CUSHING’S SYNDROME: CASE REPORT AND REVIEW OF LITERATURE

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Abstract

The early diagnosis of Cushing’s syndrome is very important. We present here a case of adrenocorticotropic hormone-dependent Cushing’s syndrome caused by a carcinoid lung nodule in a young patient who presented with the clinical and biochemical features of Cushing’s syndrome; this was successfully diagnosed by endobronchial biopsy and treated by surgical resection, with excellent recovery.

Introduction:

Adrenocorticotropic hormone (ACTH)-dependent Cushing’s syndrome is noted in approximately 80% of all patients with Cushing’s syndrome (1). Although Cushing’s syndrome triggered by bronchopulmonary carcinoids (BCs) is very rare, BCs account for the most common ectopic ACTH-releasing tumors (2) (3). The early diagnosis of this condition is challenging; however, it is crucial since it can avoid adrenalectomy and other unnecessary procedures.

Case report:

A 29-year-old woman presented to our hospital complaining of generalized fatigability, increase in weight, and generalized body ache since two years. Notably, the patient’s complaints started after the delivery of her second child. A history of irregular menses was also noted following the second delivery. In addition, the patient’s weight began to increase. She also reported progressive darkening of the skin and the occurrence of acne. She denied having cough, hemoptysis, or dyspnea, and no history suggestive of connective tissue disease was elicited. The patient was on antidepressant medications and using an acne cream. The patient was observed to be anxious and easily provoked even by trivial issues. On clinical examination, she was conscious, alert, and well oriented. Her blood pressure was 149/90 mm Hg, the pulse was 100 bpm, the respiratory rate was 18 bpm, and the oxygen saturation was 95% at room air. The patient had a moon face (round facies), acne, visible facial hair, and a buffalo hump. No lymphadenopathy or thyroid swelling was noted. She also showed proximal muscle weakness. Further, her skin appeared to be thin with multiple bruises, and she had a distended abdomen with red purple striae.

Laboratory investigations revealed the following findings: normal complete blood count, high random blood sugar, and normal biochemistry and liver function values, apart from severe hypokalemia (potassium was 1.7 mmol/L). The morning serum cortisol level was 1640 nmol/L (171–536 nmol/L). The 24-h cortisol level 1560 nmol/L. The serum ACTH level was very high at 2216 pg/ml (normal: 10–65 pg/ml). Magnetic resonance imaging (MRI) of the brain revealed no significant abnormality. Computed tomography (CT) scans of the chest, abdomen, and pelvis showed a solitary, well-defined mass in the left lower lobe of the lung measuring about 2 × 2 cm, abutting the central left hemidiaphragm (Fig. 1), associated with the small left hilar lymph node. The adrenal glands showed...
bilateral hyperplasia. Endobronchial biopsy was performed for the pulmonary mass (Fig. 2), and immunohistochemical staining was positive for thyroid transcription factor-1 (TTF-1), chromogranin, cytokeratin 7, and synaptophysin, confirming the diagnosis of carcinoid tumor. The patient underwent left lower lobe resection with good outcome.

**Abbreviation List:**
ACTH: Adrenocorticotropic hormone  
BC: Bronchopulmonary carcinoids  
CRH: Corticotropin-releasing hormone  
CT: Computed tomography  
IPSS: Inferior petrosal sinus sampling  
MRI: Magnetic Resonance Imaging  
TTF-1: Thyroid transcription factor-1

**Figure Legends:**

**Fig. 1:** Solitary, well defined mass lesion seen in the left lower lobe of the lung measuring 2 × 2 cm.

**Fig. 2:** Bronchoscopic view of the endobronchial extension of the carcinoid nodule.
Discussion:
Previous reports of Cushing’s syndrome caused by BCs have included presentations of Cushing’s features (3) (4) (5), hypertension (4), diabetes (4) (6), and psychiatric problems (4). These patients rarely present with a clinical picture of systemic endocrine dysfunction pertaining to a hormone-secreting tumor (2), and all reported cases have included patients within their forties (3) (7). Abnormal laboratory findings in these patients have included hypokalemia (8) (4) (5) and metabolic alkalosis (8). Although some cases reported a positive response of ACTH or cortisol to the corticotropin-releasing hormone (CRH) test, they showed no positive gradient on inferior petrosal sinus sampling (IPSS) (4). In contrast, other cases with plasma ACTH and cortisol levels responsive to CRH have shown a positive gradient of plasma ACTH on IPSS after CRH stimulation (6). Non-suppressibility of ACTH and cortisol after high-dose dexamethasone was reported in some cases (6), while suppression was noted in others (1) (5). Suppression following octreotide administration has been reported in some cases (6) (9). These contrasting findings indicate that biochemical studies should not be the only basis for diagnosing Cushing’s syndrome caused by BCs (10). For accurate localization of the carcinoid tumor, CT studies are needed (8) (4) (6) (5). Surgical treatment is indicated in these patients, and it has been shown to be an effective treatment modality (3) (4) (5). Adjunctive radiotherapy is indicated if there is lymph nodal metastasis (4), which is a poor prognostic factor. Prognosis is generally favorable (7).

Conclusion:
ACTH-dependent Cushing’s syndrome related to a carcinoid lung nodule can be diagnosed by endobronchial biopsy, and early detection and surgical resection are important for appropriate management of this lesion.

References:
1. Fuentes Tudanca S, Ortiz de Urbina PM, De Dios LM, Gallego Rodriguez S, Perez Pelayo M, Del Olmo Garcia D. ACTH-dependent Cushin syndrome, a diagnostic challenge. Endocrinol Nutr. 2009;56(4):205-8.
2. Sutton BJ, Parks GE, Manavi CK, Palavecino EL, Geisinger KR. Cushing’s syndrome and nocardiosis associated with a pulmonary carcinoid tumor: report of a case and review of the literature. Diagn Cytopathol. 2011; 39(5): 359-62.
3. Lococo F, Margaritora S, Cardillo G, Filosso P, Novellis P, Rapicetta C, et al. Bronchopulmonary Carcinoids causing Cushing Syndrome: Results from a Multicentric Study Suggesting a More Aggressive Behavior. Thorac Cardiovasc Surg. 2015.
4. Tsirona S, Tzanela M, Botoula E, Belenis I, Rondogianni D, Tsagarakis S. Clinical Presentation and Long-Term Outcome of Patients with Ectopic Acth Syndrome Due to Bronchial Carcinoid Tumors: A One-Center Experience. EndocrPract. 2015;21(10):1104-10.
5. Limper AH, Carpenter PC, Scheithauer B, Staats BA. The Cushing syndrome induced by bronchial carcinoid tumors. Ann Intern Med. 1992;117(3):209-14.
6. Tani Y, Sugiyama T, Hirooka S, Izumiyama H, Hirata Y. Ectopic ACTH syndrome caused by bronchial carcinoid tumor indistinguishable from Cushing's disease. Endocr J. 2010;57(8):679-86.
7. Bodaert G, Grand B, Le Pimppe-Barthes F, Cazes A, Bertagna X, Riquet M. Bronchial carcinoid tumors causing Cushing's syndrome: more aggressive behavior and the need for early diagnosis. Ann Thorac Surg. 2012;94(6):1823-9.
8. Dal Verme A, Cejas C, Margan M, Siguelboim D, Canosa V, Peralta C. ACTH's ectopic secretion in a patient with precedents of Cushing's disease. Medicina (B Aires). 2015;75(4):218-20.
9. McDermott JH, Thabit H, Hickey N, Thompson C, Gaffney E, Young V, et al. ACTH-secreting bronchial carcinoid: a diagnostic and therapeutic challenge. Ir J Med Sci. 2008; 177(3):269-72.
10. Amer KM, Ibrahim NB, Forrester-Wood CP, Saad RA, Scanlon M. Lung carcinoid related Cushing’s syndrome: report of three cases and review of the literature. Postgrad Med J. 2001; 77(909):464-7.