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Case Report

Paraneoplastic Cushing Syndrome Secondary to an Atypical Carcinoid Tumor of the Lung: A Rare Diagnostic Challenge

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Abstract

Carcinoid tumors represent approximately 2% of all lung neoplasms and Atypical Carcinoids (ACs) are considerably less common than their typical counterparts. We report the case of a 77-year-old female with a known carcinoid tumor of the right lung who presented with shortness of breath, bilateral lower extremity edema and resistant hypertension. She was initially admitted for presumed heart failure exacerbation. Persistent hypertension, hypokalemia and myopathy prompted further evaluation, revealing hypercortisolism secondary to ectopic Adrenocorticotropic Hormone (ACTH) production from the pulmonary carcinoid tumor. Imaging confirmed a stable right middle lobe mass and endocrine testing demonstrated a non-suppressible cortisol response to both low and high-dose dexamethasone suppression tests. The patient underwent robotic-assisted right middle lobectomy. Histopathology revealed an atypical carcinoid tumor (Grade 2, pT2a N1 M1a) with pericardial and nodal metastases, confirming the diagnosis of paraneoplastic Cushing syndrome due to an ACTH-secreting atypical carcinoid tumor. Postoperatively, blood pressure and potassium levels normalized with medical management including ketoconazole and octreotide.

This case underscores the critical diagnostic element in recognizing secondary endocrine causes of hypertension and in guiding appropriate multidisciplinary consultation. It demonstrates how careful clinical reasoning and persistence in evaluating unexpected findings such as refractory hypertension and persistent hypokalemia can uncover a rare, life-threatening endocrine malignancy. Also, it highlights the importance of close collaboration between Internal Medicine, Oncology and Thoracic Surgery in achieving successful outcomes.

Keywords: Atypical Carcinoid; ACTH-Secreting Tumor; Paraneoplastic Cushing Syndrome; Secondary Hypertension; Neuroendocrine Tumor; Internal Medicine

Introduction

Carcinoid tumors are neuroendocrine neoplasms arising from Kulchitsky cells of the bronchial epithelium, capable of developing in multiple organ systems, most commonly the lungs, appendix, small intestine, rectum and pancreas [1,2]. Pulmonary neuroendocrine tumors are classified by the World Health Organization (WHO) into typical carcinoid, atypical carcinoid, large-cell neuroendocrine carcinoma and small-cell lung carcinoma [3]. Although carcinoid tumors constitute a small fraction of pulmonary malignancies, atypical carcinoids represent an even rarer subset. They predominantly affect middle-aged to older adults, with a modest female predominance [4]. The rising incidence of bronchopulmonary neuroendocrine tumors over recent decades reflects advancements in imaging techniques, refinement of histopathologic criteria and earlier detection [5]. While the majority of pulmonary carcinoids are nonfunctional, a minority secrete biologically active hormones, precipitating distinct paraneoplastic syndromes such as Cushing syndrome due to ectopic ACTH production [6,7]. The clinical manifestations of these functional tumors are often nonspecific and may mimic more common conditions, including resistant hypertension, hypokalemia and proximal myopathy, posing a considerable diagnostic challenge. This case illustrates identifying an uncommon hormonal disorder through the integration of clinical assessment, biochemical testing and multidisciplinary collaboration.

Ethical Statement

The project did not meet the definition of human subject research under the purview of the IRB according to federal regulations and therefore, was exempt.

Case Presentation

A 77-year-old female with a significant past medical history of gastroesophageal reflux disease, hypothyroidism, hypertension and a carcinoid tumor of the right lung. Her lung mass was diagnosed in February 2024, when a right middle lobe mass was incidentally discovered during hospitalization for biliary pancreatitis. This prompted further imaging, including a CT scan, which revealed a 3 cm mass in the Right Middle Lobe (RML). A subsequent PET/CT (PET (Positron Emission Tomography/Computed Tomography) scan showed that the right middle lobe mass was metabolically active and biopsies confirmed the presence of a carcinoid tumor with a Ki-67 index of 2-3%, indicating low proliferative activity. However, her diagnosis became more complicated when a planned robotic-assisted lobectomy in March 2024 was aborted after multiple pleural and pericardial lesions were visualized, suggestive of metastatic disease. A pleural biopsy confirmed metastasis from the carcinoid tumor, leading to a staging of at least Stage IVA. Over the following year, the patient managed her condition through a combination of monitoring and conservative treatments. However, in May 2025, her clinical condition worsened. She arrived at the hospital with symptoms of heart failure exacerbation, including shortness of breath, bilateral lower extremity edema and rapid weight gain. Her hypertension remained difficult to control and laboratory tests showed persistent hypokalemia, elevated troponin and increased BNP (B-type Natriuretic Peptide), indicating heart failure possibly caused by an underlying endocrine disorder. On admission, her blood pressure was 180/90 mmHg, oxygen saturation was 98% on room air and physical examination revealed bilateral pitting edema without acute respiratory distress. Laboratory studies showed troponin 69 ng/L (normal: 0 to 0.06 nanograms per milliliter (ng/mL), BNP 599 at pg/mL, (below 100 picograms (pg)/mL) and persistent hypokalemia (K^+ 3.1 mEq/L). She was admitted with a diagnosis of heart failure exacerbation and started on intravenous diuretics and spironolactone. Despite therapy, hypertension and hypokalemia persisted. Further evaluation revealed elevated cortisol levels (58.5 μg/dL) (normal morning cortisol 5 to 25 (micrograms) μg/dL) and ACTH (Adrenocorticotropic Hormone) of 113 pg/mL (normal morning ACTH 10 and 60 pg/mL). A low-dose Dexamethasone Suppression Test (DST) showed cortisol that was not suppressed (35 μg/dL), (For a low-dose overnight DST, a fasting cortisol level of less than 1.8 μg/dL at 8 am is considered normal) and a high-dose test also failed to suppress, suggesting ectopic ACTH (Adrenocorticotropic Hormone) production. MRI (Magnetic Resonance Imaging) of the pituitary was unremarkable, revealing an empty sella. Chest X-ray (Fig.1) and CT scan (Fig. 2) of the chest showed a stable right middle lobe mass consistent with the previously known carcinoid tumor.

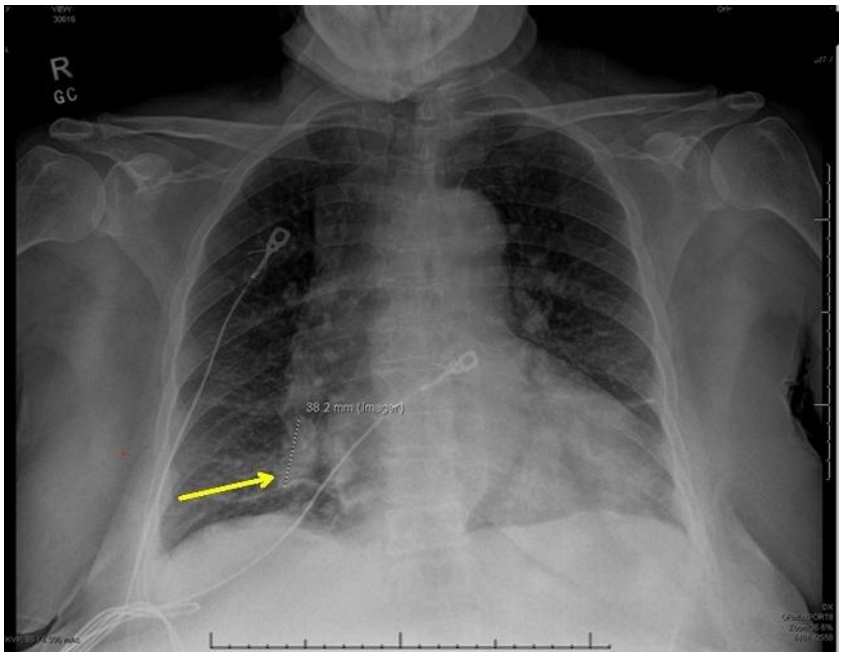

Figure 1: Chest X-ray before surgery. A 3.8 cm ovoid mass in the right middle lobe is at the yellow arrow. Linear atelectatic changes in both lower lobes. Stable cardiomegaly with mild vascular congestion.

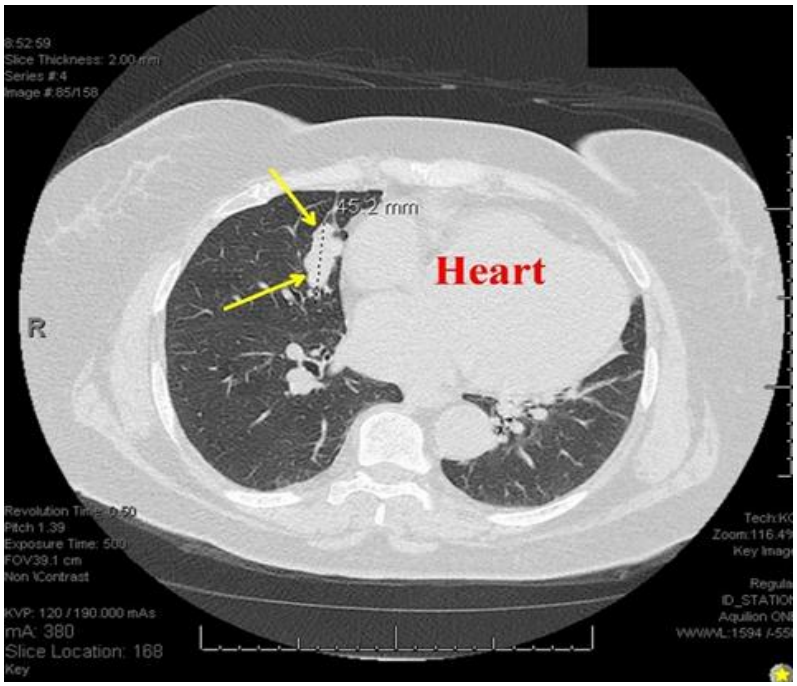

Figure 2: Stable ovoid 37 x 33 x 15 mm mass in the medial segment of the right middle lobe consistent with carcinoid (yellow arrows). Broad medial pleural attachment to the epicardium. Minimal bibasilar pulmonary scarring.

A working diagnosis indicated that the hypokalemia and hypertension were secondary to paraneoplastic Cushing syndrome caused by an ACTH-secreting pulmonary carcinoid tumor. She was empirically treated with ketoconazole 200 mg twice daily, octreotide 300 mcg subcutaneously every 8 hours, potassium chloride supplementation (40-60 mEq daily) and furosemide was discontinued due to electrolyte imbalance. After a multidisciplinary discussion between Internal Medicine, Oncology and Thoracic Surgery, the patient underwent robotic-assisted right middle lobectomy with tumor debulking on May 26, 2025. The histopathological results revealed a Grade 2, 3.7 cm atypical carcinoid with pleural invasion (Fig. 3) and 3/3 lymph nodes positive for metastatic neuroendocrine tumor. There was a pericardial implant of neuroendocrine tumor consistent with atypical carcinoid (Fig. 4). Bronchial and vascular margins negative; parenchymal margin focally involved. The final diagnosis was stage: pT2a N1 M1a (American Joint Committee on Cancer 8th Edition).

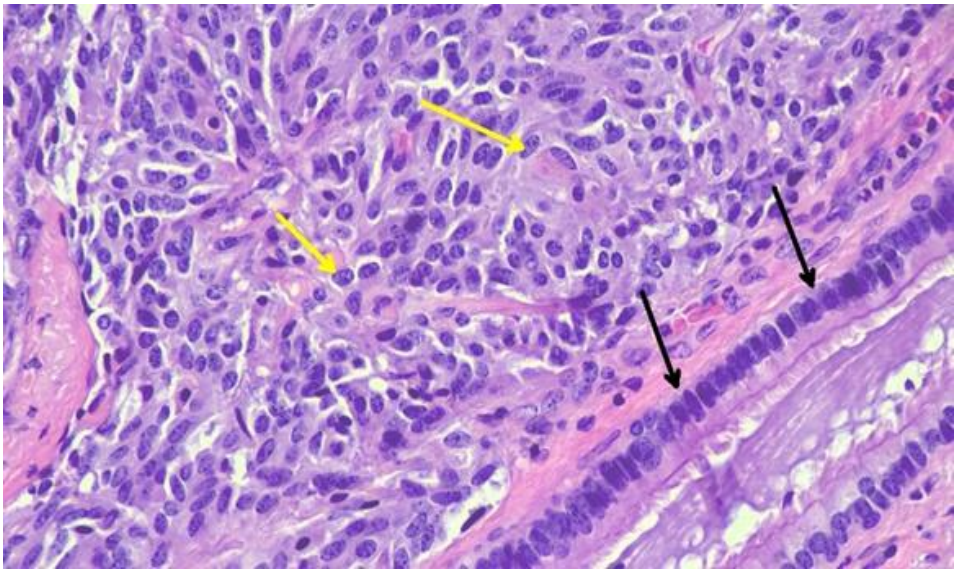

Figure 3: Tumor with adjacent bronchial epithelium (black arrows). The tumor cells are relatively uniform in size and shape (yellow arrows) and display oval nuclei with the typical salt-and-pepper chromatin, inconspicuous nucleoli and a moderate amount of cytoplasm.

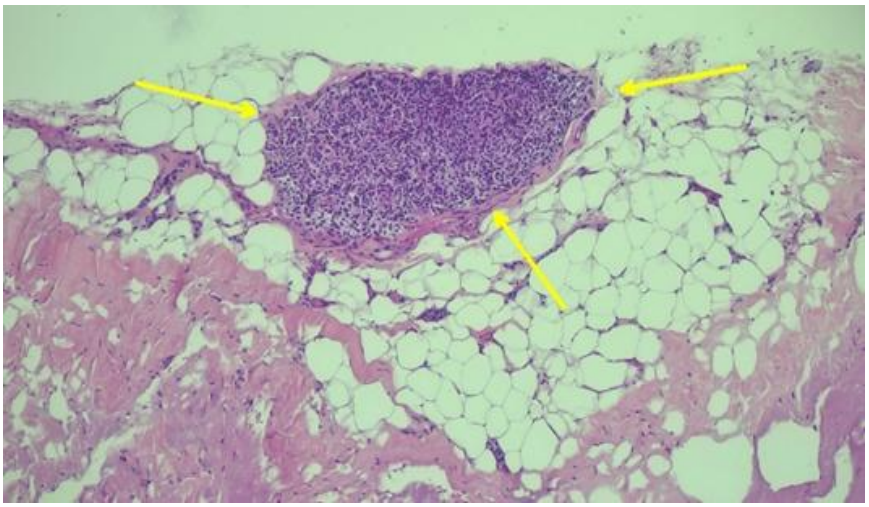

Figure 4: Pericardial biopsy shows tumoral cells (yellow arrows) invading the fibroadipose tissue.

By postoperative day 9, the patient's blood pressure had normalized, serum potassium had stabilized and cortisol levels had decreased. She was discharged on June 4, 2025, in improved condition with outpatient follow-up.

Discussion

Atypical Carcinoid Tumors (ACTs) of the lung are rare, intermediate-grade neuroendocrine neoplasms that typically exhibit more aggressive behavior compared to typical carcinoids, with a higher potential for metastasis and a worse overall prognosis [2,3]. These tumors are often hormonally active, with approximately 5-10% secreting ACTH, leading to ectopic Cushing syndrome, a rare but significant paraneoplastic manifestation [6,8]. The diagnosis of hormonally active ACTs presents a challenge, as their systemic endocrine symptoms can easily be misinterpreted as common conditions such as heart failure or hypertension. In the current case, the patient's presentation initially appeared to be heart failure, characterized by dyspnea, bilateral edema and uncontrolled hypertension. However, persistent hypokalemia and resistance to standard therapy prompted further investigation. The medical team's persistence in exploring alternative causes led to the diagnosis of ectopic ACTH secretion, secondary to a right middle lobe atypical carcinoid tumor. This case underscores the critical role of modern collaboration between services in considering endocrine etiologies when cardiopulmonary diagnoses fail to explain unexplained metabolic or biochemical abnormalities. The differential diagnosis in our case was challenging because the patient's clinical picture was marked by systemic manifestations of hypercortisolism (i.e., resistant hypertension, hypokalemia and edema) and was more suggestive of an endocrine disorder than a primary cardiopulmonary condition. Hormonal evaluation, including elevated cortisol and ACTH levels, along with non-suppressible cortisol in the dexamethasone suppression tests, confirmed ectopic ACTH production. This was further supported by imaging, which identified the mass in the right middle lobe with metastatic spread to the pleura, pericardium and lymph nodes, confirming Stage IV disease (pT2a N1 M1a). A similar case was reported by Garg, et al., in which a 50-year-old woman with a left mediastinal mass and non-functional atypical carcinoid was treated with chemotherapy after surgery was not possible [9]. However, several important differences between this case and ours illustrate the heterogeneity of atypical carcinoids. First, the age and presentation were markedly different: Garg, et al., patient was much younger and presented with localized thoracic symptoms, whereas our patient, at 77 years old, displayed systemic symptoms of hypercortisolism without respiratory complaints. Second, the functional nature of the tumor in our patient was pivotal to the diagnosis-hormonal evaluation was crucial in detecting the underlying cause. In contrast, Garg, et al., patient had a non-functional tumor, which was detected incidentally in imaging. Additionally, management strategies and outcomes in these two cases diverged. While chemotherapy was employed as a palliative measure in the earlier case due to the unresectable nature of the tumor, our patient benefited from a combination of surgical resection and medical therapy aimed at controlling hypercortisolism. Surgical resection of the primary tumor, followed by pharmacologic management with ketoconazole and octreotide, led to complete biochemical remission, a significant improvement in the patient's clinical status and normalization of her blood pressure and electrolyte balance. This case highlights the importance of early recognition of endocrine dysfunction in patients with atypical carcinoid tumors. Despite the advanced stage of disease, a coordinated, multidisciplinary approach involving Internal Medicine, Oncology and Thoracic Surgery resulted in improved clinical outcomes. Timely identification and management of the hormonal component of this tumor were key to stabilizing the patient's condition.

Conclusion

In conclusion, atypical carcinoid tumors present with considerable clinical variability from non-secretory lesions to hormonally active tumors that cause significant endocrine disturbances. The current case emphasizes the need for heightened clinical awareness of paraneoplastic syndromes, particularly in the setting of unexplained systemic symptoms. It also illustrates how a collaborative, multidisciplinary approach can dramatically alter the prognosis, even in cases with advanced metastatic disease.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Financial Disclosure

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Consent To Participate

The authors certify that they have obtained all appropriate patient consent.

Data Availability and Consent of Patient

The patient provided informed consent for publication of this report.

Author's Contribution

All authors had access to the data and a role in writing the manuscript.

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