A Stressful Cough; A Pain in the Back.

Joint AACE and AAES Interesting Case Session

Vikram Krishnamurthy MD,
Melissa Boltz DO,
Carol Farver MD,
Allan Kennedy MD,
***and* Allan Siperstein MD**
from the
Endocrine & Metabolism and Pathology Institutes,
The Cleveland Clinic

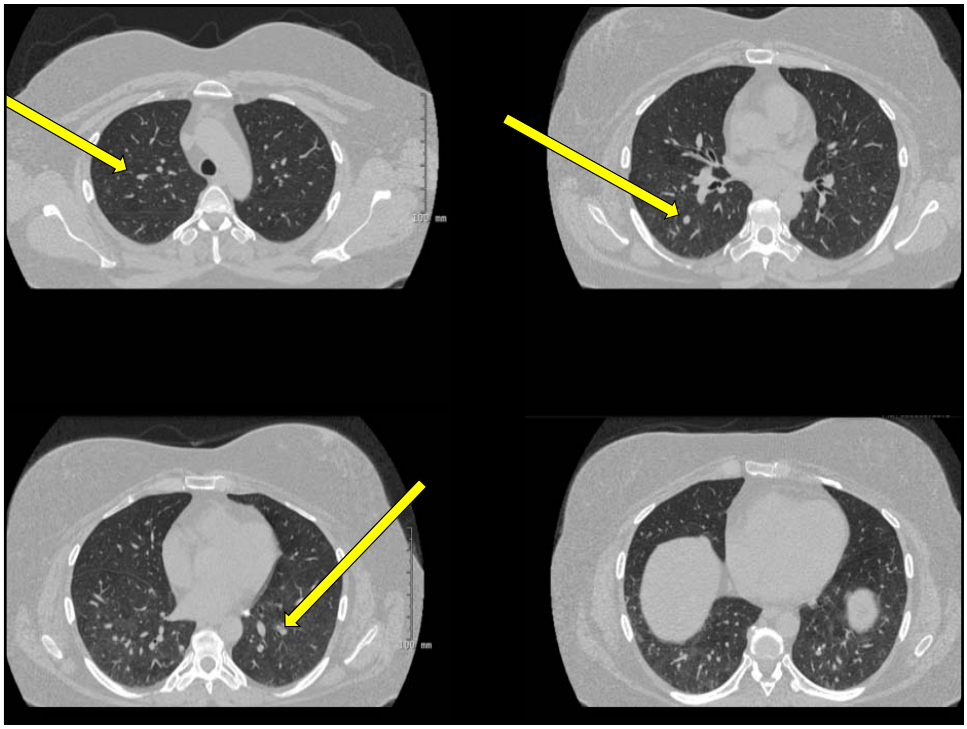
No Disclosures

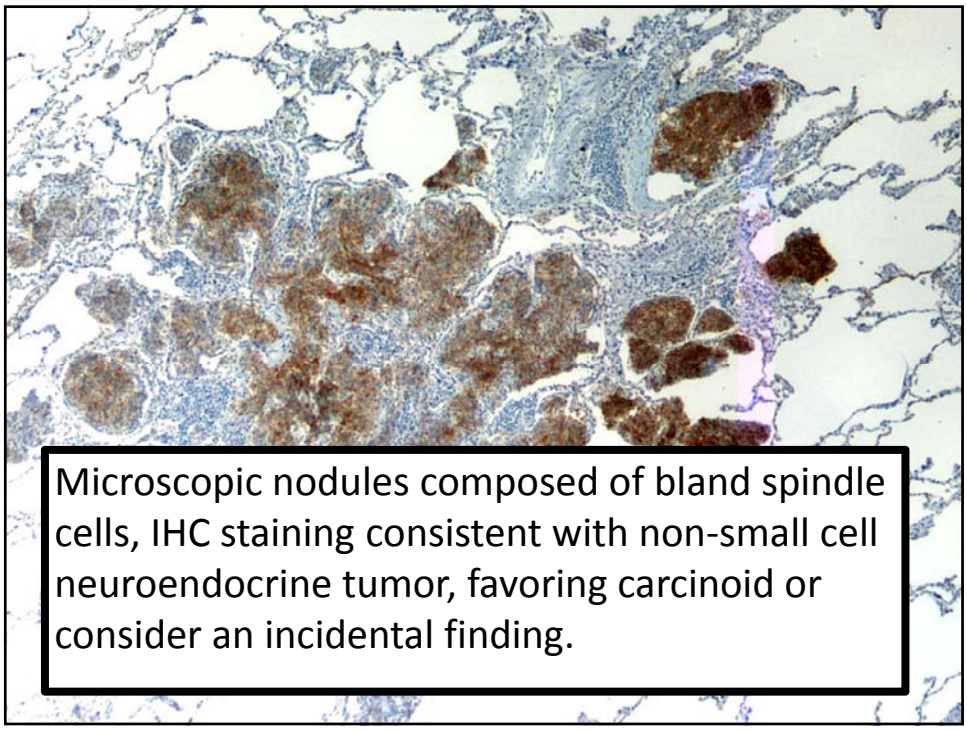
CASE PRESENTATION

- **In 2006, 47 year old female presented to her primary care physician with a nagging, dry cough.**
- **No prior history of lung disease.**
- **Non-smoker.**
- **Chest X-ray was unrevealing.**

CASE PRESENTATION

- **She was treated for reactive airway disease then for GERD.**
- **No relief for several years with standard asthma therapies or antacids.**
- **In 2008, a CT chest was obtained…**

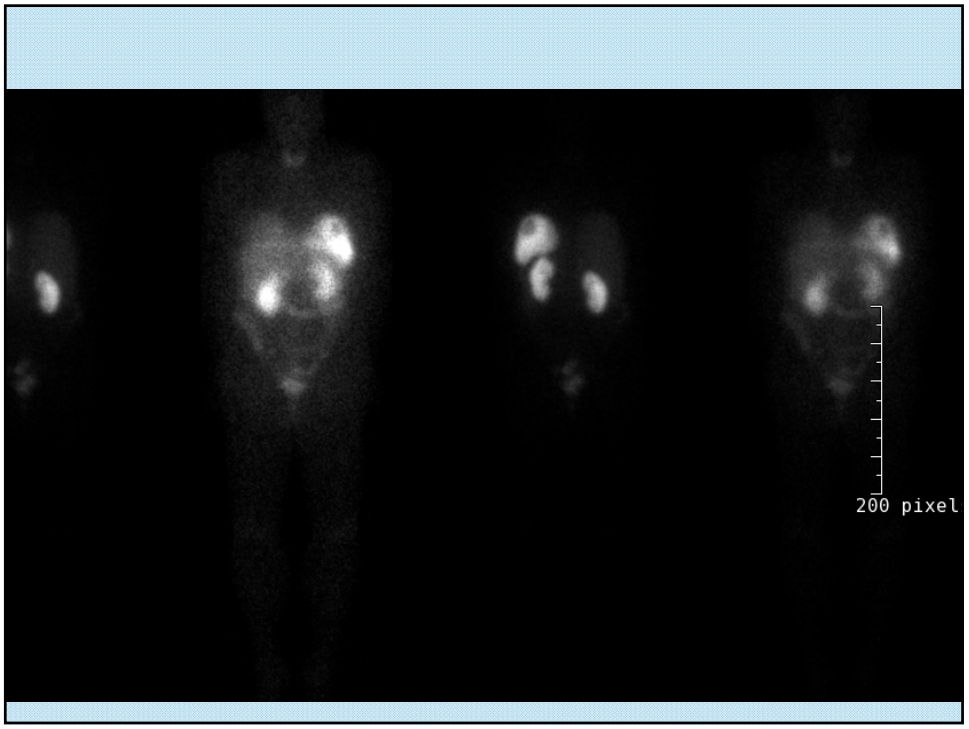




Microscopic nodules composed of bland spindle cells, IHC staining consistent with non-small cell neuroendocrine tumor, favoring carcinoid or consider an incidental finding.

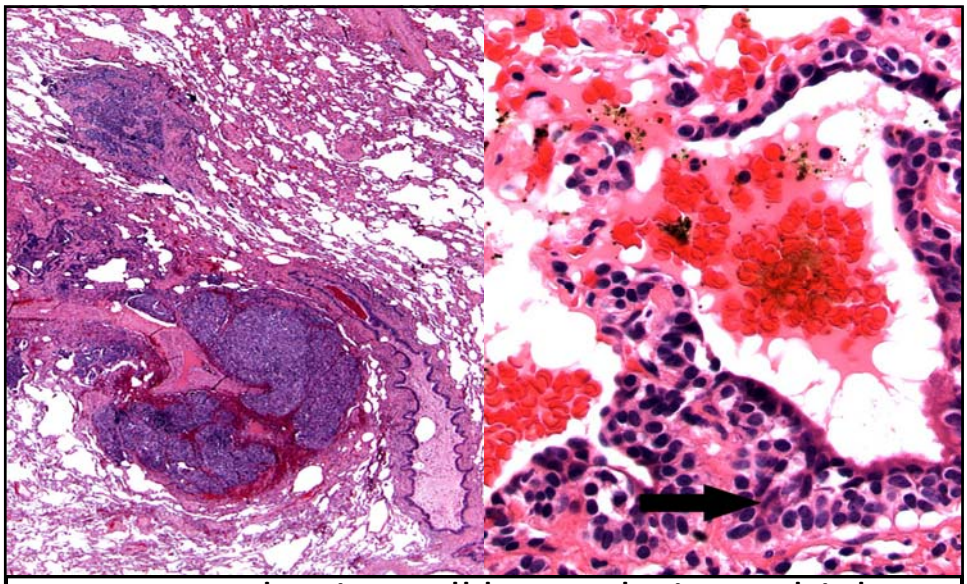
INVERSTIGATION

- **Serum Chromogranin A:**
  - **81.3 ng/mL (ref range: <36.4 ng/mL)**
- **24 hour urinary 5-HIAA:**
  - **5.9mg (ref range: < 6 mg/24hr)**
- **Bronchoscopy**
- **EGD**
- **Colonoscopy**
- **Somatostatin-receptor scintigraphy (Octreotide) scan**
- **MRI**
- **CT**



INVESTIGATION FOR PRIMARY LESION

- **Image-guided percutaneous liver biopsy.**
- **Pathology revealed…**
  - **Hepatic parenchyma with preserved architecture and moderate steatohepatitis (BENIGN).**
- **In 2010, her cough was worse, and lung lesions progressively increased to 2-3cm.**
- **She underwent a video-assisted thorascopic wedge biopsy for further pathologic diagnosis.**



Neuroendocrine cell hyperplasia, multiple carcinoid tumorlets, in the background of normal lung.

WHAT IS DIFFUSE IDIOPATHIC PULMONARY NEUROENDOCRINE CELL HYPERPLASIA (DIPNECH)?

- **Less that 150 cases reported; largest series is 30 patients.**
- **Chronic cough, often given an alternate diagnosis for many years.**
- **More common in women (>89%).**
- **CT reveals multiple nodules and air-trapping.**
- **Pathology displays intraepithelial pulmonary neuroendocrine cell hyperplasia often with adjacent carcinoid clusters (tumorlets) <1cm and typical carcinoid tumors all adjacent to normal lung.**

TREATMENT

- **In 2011, she was started on Somatostatin-receptor therapy (Octreotide) with little improvement in the cough.**
- **In 2013, she began chemotherapy with carboplatin, etoposide, and sunitinib.**
- **No regression of tumors' sizes and developed intolerance to the chemotherapy.**

But the story doesn't end…..

- **In 2014, she developed worsening hypertension, glucose-intolerance, weight gain, edema, and muscle wasting and was admitted for diuresis and hypokalemia.**
- **She underwent a work-up for hypercortisolism….**

INVESTIGATION

- Serum AM cortisol: **34.6** (ref range: 3.4 – 26.9 mcg/dL).
- Late-night salivary cortisol: **1.31** (ref range: <0.09mcg/dL).
- 24-hour urinary cortisol: **7980** (ref range: <100 mcg/24hrs).
- Serum ACTH: **157** (ref range: 8-42 pg/mL).
- Overnight 1mg Dexamethasone-suppression test: **35.3** (ref range: <1.8 mcg/dL).
- Pituitary MRI – **negative**.
- Abdominal CT – **no adrenal lesions**.

CUSHING'S SYNDROME

- **Hypercortisolism.**
- **Elevated ACTH.**
- **Failed dexamethasone suppression.**
- **No pituitary lesion or adrenal mass.**
- **ACTH-dependent Cushing's syndrome.**
- **Ectopic source:**
  - **DIPNECH.**

CLINICAL COURSE

- **In late 2014, she began Ketoconazole, but she did not tolerate.**
- **She was offered (pasireotide, mifepristone) but also she was referred to Endocrine Surgery to consider bilateral adrenalectomy.**
- **In early 2015, she underwent laparoscopic posterior bilateral adrenalectomy.**
- **Discharged home POD#1.**
- **Three months later, her weakness, edema, blood pressure, and glucose have all markedly improved.**

Discussion

KEY TEACHING POINTS

HORMONALLY-ACTIVE DIPNECH:

- **Less than 10 reports in the literature.**
- **One case of acromegaly from GHRH, ACTH staining is heterogeneous.**
- **Initial theory was clinical Cushing's disease occurred either from new secretion of ACTH or after DIPNECH or tumorlet reached cumulative cellular mass.**
- **ACTH staining: NEGATIVE.**

KEY TEACHING POINTS

- DIPNECH is an uncommon cause of respiratory pathology, but should be suspected in women with chronic cough and multiple pulmonary nodules.
- Extremely rarely hormonally active, but clinicians should be vigilant for the development of clinical syndromes.
- This represents a case of Cushing's syndrome from ACTH-secreting DIPNECH cured by laparoscopic bilateral posterior adrenalectomy.

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