When the Usual Isn't the Cause; Rare Origins of Ectopic Cushing Syndrome and Inpatient Treatment Dilemmas

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- **Cushing syndrome** caused by **excess endogenous cortisol**[1] is rare (~8 cases per million annually)
- **Ectopic (non-pituitary) ACTH** is a rare cause[1]
- **Neuroendocrine tumors (NETs)** can drive ectopic Cushing[1]
- **Extrapulmonary NETs** have worse prognosis vs. bronchial carcinoids[2 1]
- **~40%** of ectopic cases present with **metastatic disease**[2 1]
- Associated with **severe metabolic and systemic complications**
- **Early recognition** is critical for improving outcomes
- **Case presented**: severe Cushing syndrome from **metastatic gastric NET**

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Clinical Case and Hospital Course

Clinical Case

- 62-year-old female presenting to OSUMC with **acute chest pain, shortness of breath, and respiratory distress**
- Vitals: **hypertensive**, **tachypneic**, **afebrile**
- Labs:
  - **Severe hypokalemia**: 2.4 mmol/L
  - **Hyperglycemia**: glucose 381 mg/dL
  - **Metabolic alkalosis**: CO_2 34 mmol/L
- Imaging:
  - **CTA PE negative** for pulmonary embolism
  - **Left lower lobe pneumonia** with parapneumonic effusion
  - **Spiculated left upper lobe nodule**
- Remained in respiratory distress despite escalating support → **ICU admission**
- **Past Medical History:**
  - Cerebral aneurysm repair (coil, 2014)
  - Bipolar disorder
- **Recent history:** discharged 2 days earlier after 43-day hospitalization for:
  - **Metastatic grade 3 gastric neuroendocrine tumor** (liver involvement)
  - **Severe Cushing syndrome** workup
  - **Left lower extremity cellulitis** and **esophageal candidiasis**

Hospital Course

Treated for **acute hypoxemic respiratory failure** due to **MSSA pneumonia** with parapneumonic effusion/empyema

Required **decortication**, **chest tube placement**, and **IV antibiotics**

Complications:

Atrial fibrillation with RVR → IV antiarrhythmics

Small left pneumothorax

Persistent **resistant hypertension, hyperglycemia, and recurrent hypokalemia**

Management included:

IV diuresis with loop diuretics and carbonic anhydrase inhibitors

Endocrinology consult → Ketoconazole 400 mg BID for adrenal steroid suppression

Improved hypertension, hyperglycemia, hypokalemia, and metabolic alkalosis

Final medication regimen:

Lisinopril 30 mg daily
Spironolactone 150 mg BID
Carvedilol 25 mg BID
Clonidine 0.1 mg TID PRN
Potassium chloride 120–160 mEq daily (to maintain K^+ > 3.0 mmol/L)

Notable Diagnostics

- 24-hour Urine Free Cortisol (UFC): 2005.5 µg/d (20-45 µg/d)
- Late-night salivary cortisol (LNSC): 12.230 mcg/dL[a]
- 1mg overnight dexamethasone suppression test: 111.6 mcg/dL
- CT Sella Turcica: homogenously enhancing pituitary gland with no evidence of mass[b]
- Serum Aldosterone, Renin, Aldosterone/Renin Activity: all within normal limits

[a] Contamination suspected by laboratory

- [b] MRI was not able to be obtained secondary to patient's prior aneurysm coiling

Date	Serum ACTH (pg/mL)	Serum Cortisol (mcg/dL)
9/10	6.3	50.0
9/16	12.0	97.3
10/8	19.7	141.5

- **Cushing syndrome** presents with diverse clinical features and complicates overall medical care
- **Ectopic ACTH–driven hypercortisolism** requires **prompt treatment** of the underlying malignancy
- **Diagnosis** of endogenous Cushing syndrome is **complex**, requiring time and expertise
- Severe hypercortisolism and malignancy can **delay or complicate the diagnostic process**
- **Prompt recognition and diagnosis** are **critical to improving outcomes**
- **Major causes of death**: infection, atherosclerotic disease, thromboembolism[1]
- In this case: **multiple infections, severe hypercortisolism, and malignancy** → prolonged hospitalizations and debility
- **Earlier initiation of adrenal steroidogenesis suppression** may have **improved outcomes**