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April 2023 Imaging Case of the Month: Large Impact from a Small Lesion

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History of Present Illness: A 65-year-old woman with a history of diabetes mellitus complained of worsening fatigue with a 20 lbs. weight gain over the last year as well as shortness of breath. The patient also complained of bruising without recalling specific injury and complained her complexion had changed recently, becoming “ruddier”, accompanied by increasing growth of facial hair. Her past medical history was remarkable for hypertension, including a previous hospitalization for a hypertensive emergency. The patient’s diabetes had become more difficult to control in recent months, with labile blood glucose levels requiring escalating insulin doses. The patient denied recent changes in sleep, worsening anxiety or depression, or changes in mood.

PMH, SH, FH: The patient’s past medical history was also notable for diastolic dysfunction and hyperlipidemia, and she required oxygen use at night. Her past surgical history was significant for a previous hysterectomy and a knee arthroplasty. Her family history was unremarkable.

Medications: Her medications included insulin, pravastatin, lisinopril, metformin, aspirin, furosemide, felodipine, citalopram, and potassium supplementation.

Physical Examination: The patient’s physical examination showed her to be afebrile with pulse rate and blood pressure within the normal range at 128/75 mmHg. She was obese (113 kg) and her facial complexion was indeed ruddy with a rounded appearance. The patient’s skin appeared somewhat thin and several bruises were noted over her extremities. Her lungs were clear and her cardiovascular examination was normal.

Laboratory Evaluation: A complete blood count showed normal findings. The patient’s plasma glucose was elevated at 171 mg/dL (normal, 65-95 mg/dL). Her hemoglobin A1c was 9.4% (normal, 4-5.6%). The white blood cell count was normal with no left shift and her liver function studies were entirely normal. Serum chemistries were completely within normal limits aside from a borderline elevated blood urea nitrogen level of 20 mg/dL (normal, 6-20 mg/dL) serum creatinine was normal.

Radiologic Evaluation: Frontal chest radiography (Figure 1) was performed.

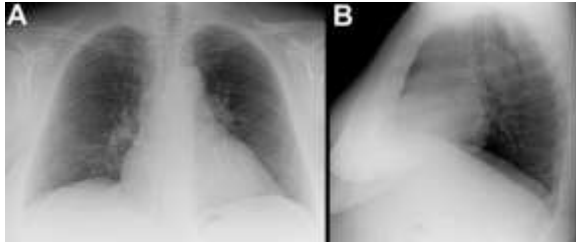


Figure 1. Frontal chest radiography. Click [here](#) to view Figure 1 in an enlarged separate window.

Which of the following statements regarding this chest radiograph is **accurate**?

1. Frontal chest radiography shows normal findings
2. Frontal chest radiography shows cardiomegaly
3. Frontal chest radiography shows mediastinal lymphadenopathy
4. Frontal chest radiography shows pleural effusion
5. Frontal chest radiography shows several nodules

Correct!

1. Frontal chest radiography shows normal findings

The patient underwent enhanced chest CT (Figure 2) given her complaint of shortness of breath.

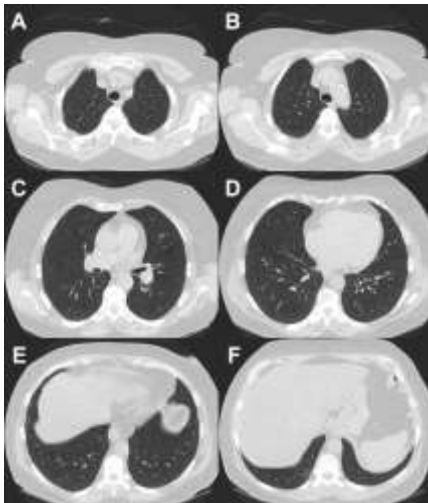


Figure 2. Representative images from axial unenhanced chest CT. Click [here](#) to view Figure 2 in an enlarged separate window. Click [here](#) for a video of the chest CT.

Which of the following represents **an appropriate interpretation** for this examination?

1. Unenhanced chest CT shows extensive mosaic perfusion
2. Unenhanced chest CT shows normal findings
3. Unenhanced chest CT shows multifocal bronchiectasis
4. Unenhanced chest CT shows multifocal lymph node enlargement
5. Unenhanced chest CT features of fibrotic lung disease

Correct!

2. Unenhanced chest CT shows normal findings

The unenhanced chest CT does not clearly show any abnormalities. The central airways are not dilated and lung parenchymal attenuation is within normal limits. No pleural abnormality is present and no enlarged intrathoracic lymph are seen.

Based on available information, which of the following is the **most likely** diagnosis?

1. Addison disease
2. Hyperaldosteronism
3. Grave's disease
4. Cushing disease
5. None of the above

Correct!

4. Cushing disease

The patient's presentation, including her ruddy complexion, difficult-to-control diabetes and hyperglycemia, weight gain, hypertension, and easy bruising are all consistent with excess cortisol production, or Cushing syndrome. Addison disease represents adrenal insufficiency, with typical symptoms including fatigue, hyperpigmentation, nausea / vomiting, diarrhea, abdominal pain, muscle pain, dehydration, *hypoglycemia*, and *hypotension*. Hyperaldosteronism reflects excessive

aldosterone production, often from an adrenal gland adenoma [1°] or reduced renal perfusion [2°], and may be asymptomatic but often presents with hypertension refractory to medical therapy and electrolyte imbalances [hypokalemia]; the latter may present with muscle spasms, fatigue, polydipsia, polyuria, and paresthesia. Grace's disease is autoimmune hyperthyroidism, with common presenting symptoms including unintentional weight loss, anxiety, fine motor tremor, heat sensitivity, frequent bowel movements, fatigue, and skin changes.

Which of the following represents an appropriate next step for the evaluation of this patient

1. Adrenal vein sampling
2. Inferior petrosal sinus sampling
3. Low - dose dexamethasone suppression test
4. Selective venous sampling
5. Arterial stimulation and venous sampling

Correct!

3. Low-dose dexamethasone suppression test

Adrenal vein sampling is typically employed in the setting of primary hyperaldosteronism to determine if aldosterone production is unilateral or bilateral; surgical therapy is effective for the former. Inferior petrosal sinus sampling is an invasive procedure in which adrenocorticotropic hormone (ACTH) levels are sampled from pituitary gland venous drainage and compared with blood ACTH levels to distinguish a pituitary cause from an ectopic source of ACTH-dependent Cushing syndrome. While this procedure may play a role in this patient's evaluation, it is invasive and premature at this point. The diagnosis of Cushing syndrome should first be confirmed, for which the low-dose dexamethasone suppression test is appropriate. Selective venous sampling (parathyroid venous sampling) is an invasive procedure used for detecting elevated intact

parathyroid hormone in the thyroid veins and/or internal jugular and brachiocephalic veins, typically in the context of recurrent or persistent hyperparathyroidism following surgery. Arterial stimulation and venous sampling refer to a procedure in which hepatic venous sampling is conducted after calcium is administered to assess pancreatic endocrine neoplasms.

The patient underwent low-dose dexamethasone suppression testing, which revealed a morning cortisol level of 36.5 mcg/dL (normal, 7-25 mcg/dL) following a dose of dexamethasone the previous evening, with a morning ACTH level of 37 pg/mL (normal, 10-60 pg/mL). A 24-hour urinary free cortisol measurement was abnormally elevated. Testing for coccidioidomycosis was unrevealing.

Which of the following represents the most appropriate next step for the patient's management?

1. ⁶⁸Ga-PET scan
2. ¹⁸F-FDG-PET scan
3. Brain MRI
4. Repeat thoracic CT
5. Abdominal CT

Correct!

3. Brain MRI

The dexamethasone testing is consistent with Cushing syndrome, probably ACTH-dependent. The most common etiology for Cushing syndrome is a pituitary adenoma, and thus brain MRI is indicated. ¹⁸F-FDG-PET scan is not indicated. ⁶⁸Ga-Dotatate PET, typically used for neuroendocrine tumor assessment, could eventually play a role in this patient's evaluation, but is premature at this point. Repeat chest CT is not indicated as the initial CT was of good quality and unrevealing. Abdominal CT is reasonable, but the most likely source for ACTH-dependent Cushing syndrome is the pituitary gland, and therefore brain MRI is the "best" answer.

Brain MRI (Figure 3) was performed and reported as normal. A corticotropin releasing hormone test suggested an ectopic source of ACTH production.

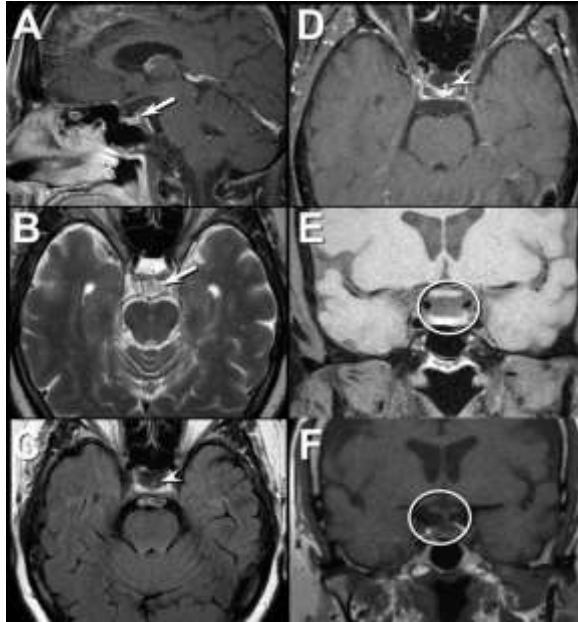


Figure 3. Brain MRI in the sagittal (A), axial (B-D) and coronal (E and F) planes shows a normal pituitary gland (arrows), sellar region (circle), and infundibulum (arrowhead). Click [here](#) to view Figure 3 in an enlarged separate window.

Which of the following represents *the most appropriate next step* for the patient's management?

1. ^{68}Ga -PSMA-11 PET/CT
2. ^{18}F FDG-PET scan
3. Somatostatin scintigraphy
4. Lutetium Lu177 vipivotide tetraxetan
5. ^{68}Ga -DOTA-FAPI-04 PET/CT

Correct!

3. Somatostatin scintigraphy

Somatostatin scintigraphy is an appropriate test to assess for a site of ectopic cortisol production. ^{68}Ga -PSMA-11 PET/CT is an agent used for the detection and staging of prostate carcinoma. ^{18}F FDG-PET scan could disclose a metabolically active lesion producing cortisol, a cortisol-producing

neoplasm may not be metabolically active, and frequently carcinoid tumors, which could be the source of Cushing syndrome, not infrequently show little glucose utilization at ^{18}F FDG-PET. Lutetium Lu 177 vipivotide tetraxetan is an agent recently approved for use for adult patients with prostate-specific membrane antigen-positive metastatic castration-resistant prostate cancer previously treated with androgen receptor inhibition and taxane-based chemotherapy. ^{68}Ga -DOTA-FAPI-04 PET/CT is a technique for malignancies expressing fibroblast activation protein (FAP), particularly lung malignancies, breast cancer, prostate cancer, various sarcomas, and head and neck cancers. Abdominal CT assessing for a pancreatic source of ACTH production was performed (Figure 4) and showed fatty liver but bilaterally normal adrenal glands. Brain MRI was normal.



Figure 4. Axial enhanced coronal abdominal CT shows normal adrenal glands (arrows) and a somewhat hypointense liver (Liv) compared with the spleen (Spl), suggesting fatty infiltration. Click [here](#) to view Figure 4 in an enlarged separate window.

A 2-day low-dose dexamethasone suppression test was performed and was abnormal, again indicating hypercortisolism and Cushing syndrome. Somatostatin (octreotide) SPECT-CT was performed (Figure 5).

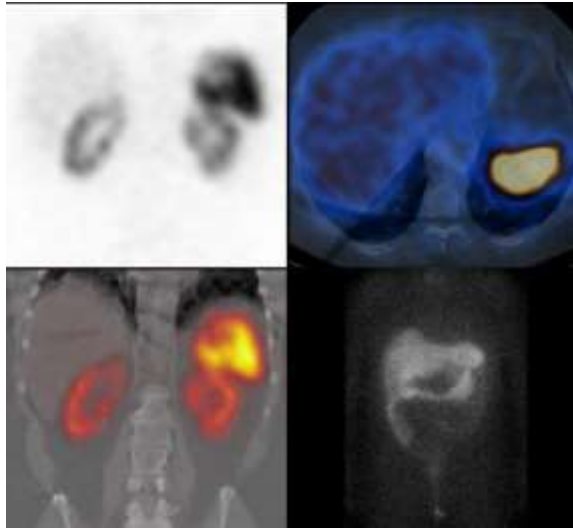


Figure 5. Octreotide In¹¹¹ SPECT-CT scintigraphy. Click [here](#) to view Figure 5 in an enlarged separate window.

Which of the following represents *an appropriate interpretation* for this examination?

1. Octreotide In¹¹¹ SPECT-CT scintigraphy is technically limited and is non-diagnostic
2. Octreotide In¹¹¹ SPECT-CT scintigraphy shows normal findings
3. Octreotide In¹¹¹ SPECT-CT scintigraphy shows abnormal biodistribution of tracer, suggesting possible misadministration
4. Octreotide In¹¹¹ SPECT-CT scintigraphy shows localized abnormal tracer accumulation suggesting an ectopic source of ACTH-production
5. Octreotide In¹¹¹ SPECT-CT scintigraphy shows multiple foci of abnormal tracer accumulation

Correct!

2. Octreotide In¹¹¹ SPECT-CT scintigraphy shows normal findings

Octreotide In¹¹¹ SPECT-CT scintigraphy shows normal tracer biodistribution and no abnormal findings. A repeat low-dose

dexamethasone suppression test again showed failure to suppress cortisol production. A repeat chest CT (Figure 6) was performed.

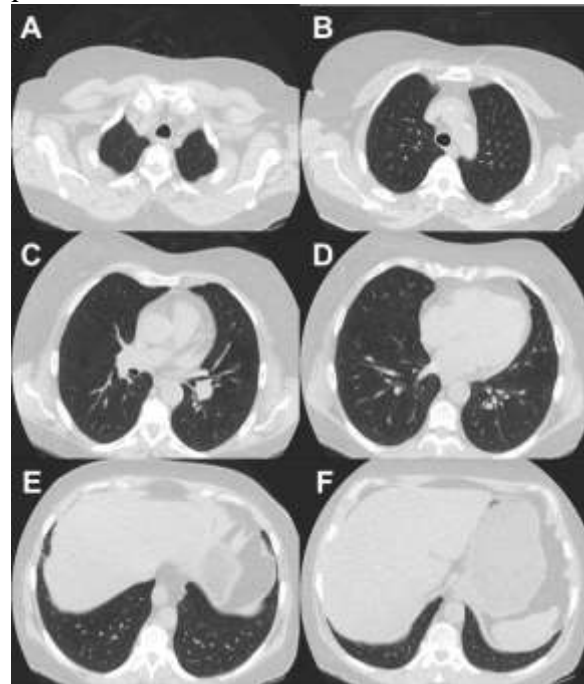


Figure 6. Representative images from repeat axial unenhanced chest CT. Click [here](#) to view Figure 6 in an enlarged separate window. Click [here](#) to view a video of the chest CT.

Which of the following represents *an appropriate interpretation* for this examination?

1. Unenhanced chest CT shows extensive mosaic perfusion
2. Unenhanced chest CT shows features of fibrotic lung disease
3. Unenhanced chest CT shows multifocal bronchiectasis
4. Unenhanced chest CT shows multifocal lymph node enlargement
5. Unenhanced chest CT shows normal findings

Correct!

5. Unenhanced chest shows normal findings

The unenhanced chest CT was interpreted as not clearly show any abnormalities. The central airways are not dilated and lung parenchymal attenuation is within normal limits. No pleural abnormality is present and no enlarged intrathoracic lymph are seen. Given all the information presented thus far, which of the following represents ***the most appropriate next step*** for the patient's management?

1. Expectant management
2. Percutaneous adrenal gland radiofrequency ablation
3. Brain surgery to remove the pituitary gland
4. Consider bilateral adrenalectomy
5. Percutaneous embolization of adrenal vascular supply

Correct!

4. Consider bilateral adrenalectomy

Given the evidence of ectopic ACTH production with the inability to locate the source of ACTH production and clear evidence of Cushing syndrome, the only available approach to alleviate the patient's hypercortisolism is by removing the target of ACTH-induced cortisol production- the adrenal glands.

The patient underwent laparoscopic bilateral adrenalectomy, with removal of large, hyperplastic adrenal glands, without complication. Over the subsequent 4 years, the patient's Cushing syndrome improved, her shortness of breath resolved, her skin bruising regressed, her weight decreased, her hypertension resolved, and her diabetes was more readily controlled. Her overall cushingoid appearance resolved.

Approximately 6 years following her adrenalectomy, the patient's shortness of breath returned, she gained weight, and her diabetes again became difficult to control. A repeat chest CT (Figure 7) was performed.

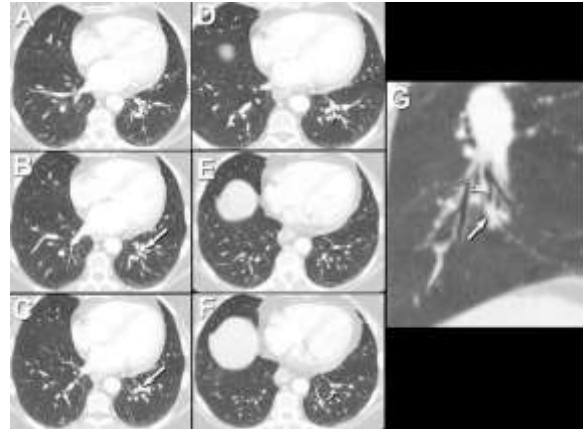


Figure 7. Representative images from the axial enhanced chest CT obtained 6 years following initial presentation and subsequent bilateral adrenalectomy, following recurrence of symptoms suggesting Cushing syndrome.

Click [here](#) to view Figure 7 in an enlarged separate window.

Which of the following represents ***an appropriate interpretation*** for this examination?

1. Unenhanced chest CT shows a small nodule
2. Unenhanced chest CT shows development of fibrosis
3. Unenhanced chest CT shows new bronchiectasis
4. Unenhanced chest CT shows multifocal lymph node enlargement
5. Unenhanced chest CT normal findings

Correct!

1. Unenhanced chest CT shows a small nodule

A small nodule is barely detectable in the medial left lower lobe. Some tubular opacity extending distally from this nodule suggests an association with a subsegmental airway. The nodule is retrospectively visible on the two previous chest CTs (Figure 8). The remainder of the enhanced chest appears normal.

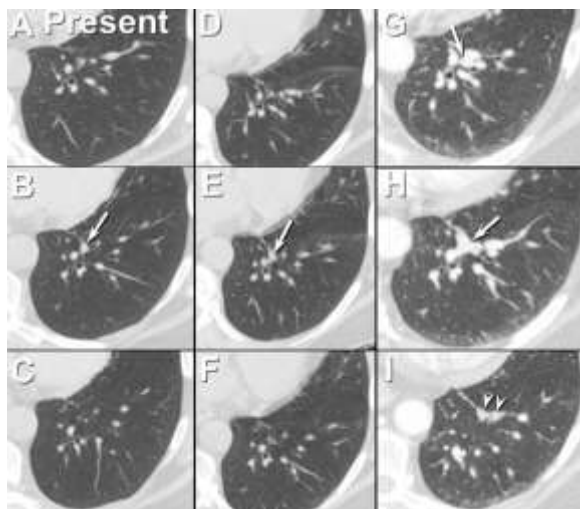


Figure 8. Axial focused unenhanced CT images performed at presentation (Present) show a small nodule in the medial left basal initially overlooked. Images immediately cranial (A) and caudal (C) to the lesion (arrow, B) do not show an abnormality; the nodule (arrow) is visible on one image only. D-F: Axial focused unenhanced images less than one year following presentation again show the lesion visible on one image only (arrow, E) the nodule merges indistinctly with adjacent vessels. G-I: Axial focused enhanced CT 6 years following presentation and bilateral adrenalectomy, and following recurrence of symptoms suggesting Cushing syndrome, shows an enlarging medial left lower lobe nodule (arrows) at the site of the previously overlooked lesion on the two previous CTs. The nodule has a branching configuration (arrow in H), with tubular opacities distal to the lesion (arrowheads in I), suggesting an airway association. Click [here](#) to view Figure 8 in an enlarged separate window.

Given all the information presented thus far, which of the following represents ***the most appropriate next step*** for the patient's management?

1. Follow up unenhanced CT in 6 months
2. ¹⁸F-DG-PET scan
3. Somatostatin scintigraphy

4. ¹⁸F-DG-PET MRI
5. Flexible fiberoptic bronchoscopy

Correct!

5. Flexible fiberoptic bronchoscopy

Performing follow up CT is a common management approach for indeterminate lung nodules, but in the context of recurrent Cushing syndrome, a lung nodule, particularly one apparently associated with an airway, merits immediate assessment. ¹⁸F-DG-PET scanning would not be contributory in this circumstance- active tracer uptake would prompt a tissue diagnosis (which is needed anyway), and negative results would not be useful. Furthermore, the nodule is rather small for ¹⁸F-DG-PET assessment. Repeat somatostatin scintigraphy could be of benefit, strongly indicating the presence of an ACTH-secreting tumor given the patient's Cushing syndrome if positive, but negative results would be non-contributory. Furthermore, somatostatin scintigraphy is most useful for localizing a site of ectopic ACTH production, and now that an airway-associated nodule has been identified at CT, further management should be directed at obtaining a tissue diagnosis. ¹⁸F-DG-PET MR plays little role in the evaluation of lung nodules and would not be appropriate in this circumstance. The patient underwent flexible fiberoptic bronchoscopy (Figure 9).

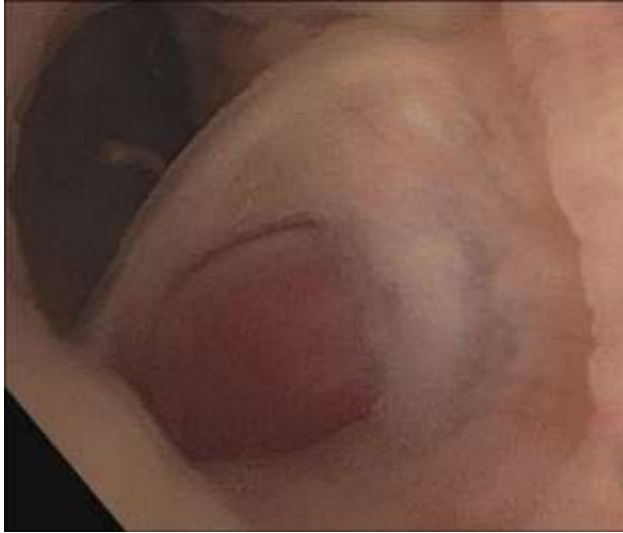


Figure 9. Bronchoscopy of the left lower lobe anterior basal segmental airway lesion. Click [here](#) to view Figure 9 in an enlarged separate window.

Which of the following findings at biopsy would be ***least consistent*** with the clinical behavior and bronchoscopic appearance?

1. Carcinoid tumor
2. Hamartoma
3. Glomus tumor
4. Dieulafoy's lesion
5. Mucoepidermoid carcinoma

Correct!

4. Dieulafoy's lesion

Dieulafoy's lesion is a developmental vascular malformation usually seen in the gastrointestinal tract but occasionally the lungs. It is an enlarged submucosal blood vessel that bleeds in the absence of any abnormality, such as ulcers or erosions. Dieulafoy's lesion may cause a nodular endobronchial appearance, but often a white "cap" may be seen, the mucosal may be congested, and tortuous dilated submucosal blood vessels may be evident. The latter contribute to hemoptysis when present, and this patient never complained of such. The other lesions listed may result in an endobronchial nodular appearance as seen in

this patient, and the visual appearance of these lesions may be similar.

The bronchoscopic biopsy revealed histologic feature consistent with carcinoid tumor. The patient underwent video-assisted left lower lobe resection with pathologic confirmation of carcinoid tumor. Her Cushing syndrome subsequently resolved. **Diagnosis:** Endobronchial carcinoid tumor causing recurrent Cushing syndrome

References

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