If you’re preparing for the United States Medical Licensing Examination® (USMLE®) Step 2 exam, you might want to know which questions are most often missed by test-prep takers. Check out this example from Kaplan Medical, and read an expert explanation of the answer. Also check out all posts in this series.

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This month’s stumper

A 72-year-old man comes to the physician because of a worsening cough productive of blood-tinged sputum and progressively darkening skin. He has a history of type 2 diabetes mellitus, hypertension, and obesity. Current medications include metformin, glyburide, lisinopril, hydrochlorothiazide and metoprolol. He has smoked two packs of cigarettes daily for 50 years. His blood pressure is 164/94 mm Hg. Examination shows truncal obesity with thin extremities. There are violaceous striae on the abdomen.

Laboratory studies show:

- Serum glucose: 265 mg/dL.
- Adrenocorticotropic hormone (ACTH) level: 260 pg/mL (n, 20-80 pg/mL).

Which of the following is the most likely cause of this patient’s condition?

A. Anterior pituitary acidophil adenoma.
B. Congenital adrenal hyperplasia.

C. Pancreatic adenoma.

D. Small-cell carcinoma.

E. Squamous cell carcinoma of the lung.

The correct answer is D.

Kaplan Medical explains why

The patient described is suffering from Cushing syndrome resulting from ectopic production of ACTH. Patients who have ectopic ACTH syndrome present with signs and symptoms consistent with classic Cushing disease, such as weight gain, central obesity, buffalo hump, supraclavicular fat pads, violaceous striae, diabetes, hypertension and depression, among other findings.

It is notable that cutaneous hyperpigmentation tends to be more pronounced in cases of ectopic ACTH production than in cases of excessive adrenal cortisol production and classic Cushing disease.
caused by a pituitary adenoma. This is because tumors producing ectopic ACTH tend to do so in large quantities, and alpha-melanocyte stimulating hormone (MSH) is also released in the production of ACTH. Patients who have ectopic ACTH production tend to be older, and ACTH levels tend to be very high. In contrast, patients who have pituitary-based ACTH excess caused by a pituitary adenoma tend to be younger, and ACTH levels are slightly elevated or inappropriately normal.

Furthermore, patients who have a pituitary adenoma may complain of visual changes (bitemporal hemianopsia) and headaches. Tumors known to produce ectopic ACTH include small cell carcinoma of the lung, carcinoid tumor, and pancreatic adenomas, among others. Given the patient's complaints of cough and hemoptysis, and the fact that small-cell lung carcinoma is the most common cause of ectopic ACTH production, this is the most likely diagnosis.

**Why the other answers are wrong**

**Choice A:** Acidophils in the anterior pituitary include somatotrophs and lactotrophs, which secrete human growth hormone and prolactin, respectively. Growth hormone excess causes acromegaly, whereas prolactin excess causes amenorrhea and galactorrhea.

**Choice B:** Congenital adrenal hyperplasia presents early in life with classic symptoms related to the defective enzyme, including ambiguity or virilization of the genitalia, hypertension, and electrolyte abnormalities.

**Choice C:** Pancreatic adenomas are very uncommon causes of ectopic ACTH production.

**Choice E:** Squamous cell carcinoma of the lung more commonly causes hypercalcemia caused by production of parathyroid hormone-related peptide.

**Tips to remember**

- Small-cell lung cancer is the most common malignancy associated with ectopic ACTH production.
- Cutaneous hyperpigmentation tends to be more pronounced in cases of ectopic ACTH production than in cases of excessive adrenal cortisol production and classic Cushing disease.
- Ectopic ACTH production causes Cushing disease with signs and symptoms of central obesity, hypertension, hyperglycemia, striae, and depression.

For more prep questions on USMLE Steps 1, 2 and 3, view other posts in this series.