

MEDICAL PHYSIOLOGY

Endocrinology Conference 1 - Quiz 8B

March 1, 2001

1. Our patient suffered from hypercalcemia and elevated levels of PTH. How did these findings assist in the final diagnosis of the patient?

Elevated calcium and PTH suggest an additional endocrine organ is affected in this patient in addition to the pituitary. MEN1 frequently is associated (80% of the time) with parathyroid tumors, excess PTH secretion and hypercalcemia. Thus, this fits well with the triple P model: involvement of the pituitary, parathyroid and pancreas.

2. What would you predict the relative concentration of ACTH to be (LOW/HIGH) at 0800 and 2300 h in a patient with an adrenal tumor that secretes cortisol?

Low at both time points and no rhythm due to the negative feedback of the high levels of cortisol. Cortisol is being synthesized and secreted from the adrenal in an ACTH-independent manner.

3. A common characteristic of Cushing's syndrome is muscle wasting. Why?

Glucocorticoids oppose the effects of insulin (insulin resistance) on most tissues including skeletal muscle. As such, glucocorticoid excess inhibits protein synthesis supports muscle proteolysis. This leads to protein breakdown which supplies amino acids for hepatic gluconeogenesis and maintenance of plasma glucose levels.

4. Our patient was diagnosed as having diabetes mellitus. Can excess secretion of cortisol lead to diabetes mellitus, and if so how? If it can not, what led to this condition in our patient?

Yes, glucocorticoid excess stimulates protein and lipid breakdown and the formation of gluconeogenic substrates. Hepatic gluconeogenesis is also stimulated leading to an increase in hepatic glucose output. Cortisol has a glucose-sparing effect. Furthermore, insulin levels will rise, but the high glucocorticoid levels will reduce responsiveness to insulin leading to insulin resistance and diabetes mellitus.

5. You are presented with a patient that has all of the symptoms of Cushing's syndrome. You subject the patient to a dexamethasone suppression test and determine that dexamethasone does not suppress glucocorticoid production/excretion. What would be your diagnosis?

An ectopic ACTH-producing tumor
An adrenal tumor that secretes glucocorticoids
Excess administration of exogenous glucocorticoids

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Endocrinology Conference 1 - Quiz 8A

March 6, 2001

1. Describe two potential clinical characteristics of a patient with MEN1.

Parathyroid tumor (excess PTH, hypercalcemia)
Insulinoma (excess insulin, hyperglycemia)
Pituitary tumor (excess prolactin, GH, ACTH)
Gastrinoma
(thyroid disorders, hyperaldosteronism)

2. Briefly describe why ACTH/cortisol levels are determined by sampling a patient in the morning and late afternoon/evening.

ACTH is secreted in an episodic and diurnal pattern with peak secretion occurring shortly after awakening and reaches its nadir in the evening. Cortisol follows a similar pattern. These two points would allow one to assess whether the normal diurnal pattern of secretion is occurring.

3. Describe one way in which excess secretion of glucocorticoids can lead to hypertension.

Stimulation of mineralcorticoid receptors (Na and H₂O reabsorption, hypervolemia).

or

Increased secretion of catecholamines and sensitivity of catecholamine receptors resulting in subsequent vasoconstriction.

4. Hyperglycemia is a common symptom in Cushing's patients. Why?

Excess glucocorticoids cause protein breakdown and lipolysis (extremities). The subsequent amino acids serve as a gluconeogenic substrate and free fatty acids can be used as an energy source sparing glucose. Gluconeogenesis by the liver is stimulated resulting in increased glucose output. Furthermore, excess glucocorticoids cause insulin resistance (decreased receptor affinity).

5. What would happen to secretion of ACTH or cortisol following a high dose dexamethasone test in the following patients diagnosed with Cushing's:

A patient with an ectopic ACTH-producing tumor:

ACTH would _____ (increase, **not change**, decrease).

A patient with an ACTH-producing pituitary tumor:

Cortisol would _____ (increase, not change, **decrease**).