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Endocrine Board Review

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Disclosures

- **Alexion Pharmaceuticals –**
  - **Site PI for Global Hypophosphatasia Registry**
  - **Site PI for Phase 3 Enzyme Replacement Study for Hypophosphatasia**

Case 1

A 68-year-old man is being treated with heparin for pulmonary embolism. Four days after admission, he has sudden onset of severe abdominal pain and flank tenderness. He is found to be hypotensive. Labs show hyponatremia and hyperkalemia, and his hematocrit is 35 percent, as compared with 40 percent at the time of admission.

The most appropriate next step is to:

A. Measure serum aldosterone
B. Measure serum cortisol
C. Measure serum cortisol before and after administration of cosyntropin (Cortrosyn, ACTH 1-24)
D. Measure urinary cortisol excretion
E. Start total fluid restriction at 1,200 cc / 24 hours

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Case 1: Explanation

This patient has acute primary adrenal insufficiency. ACTH stimulation test (C) is the best way to make this diagnosis.

A random cortisol measurement without ACTH stimulation (B) can be difficult to interpret.

Decreased production of aldosterone (A) does not necessarily indicate decreased production of cortisol, which is potentially life-threatening.

Urinary cortisol excretion (D) is not a reliable test for diagnosis of adrenal insufficiency.

Fluid restriction (E) is not indicated in treatment of hyponatremia caused by adrenal insufficiency and can, in fact, exacerbate the patient's condition.

Case 2

A 52-year-old woman is brought to the office after falling and striking her abdomen on the edge of a chair. She had abdominal pain soon thereafter, but it has subsided. She is normotensive. Physical examination is unremarkable except for mild abdominal tenderness. CT of the abdomen reveals a 3-cm hypodense left adrenal mass with smooth borders. Serum electrolytes are normal.

The most appropriate next step is to:

A. Measure plasma metanephrines
B. Fine needle aspiration of the mass
C. Measure 8 AM serum cortisol following 1 mg dexamethasone at midnight
D. Both A and C
E. Repeat abdominal CT in six months

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Case 2: Explanation

Subclinical Cushing syndrome and pheochromocytoma are relatively common in patients with adrenal incidentalomas and must be ruled out (D).

Fine needle aspiration of an adrenal mass (B) can only detect a metastatic lesion and is not indicated in a patient without a known primary malignancy.

A repeat CT (E) to ensure that the nodule is not growing will be helpful but is not the first priority – ruling out hormonal overproduction is more urgent.

Case 3

A 24-year-old veterinary student has had symptoms of hypoglycemia before breakfast for several months. Laboratory studies early one morning reveal the following:

Serum glucose 28 mg/dl
Serum insulin 65 μU/ml (normal, 5-15)
Serum C-peptide 0.1 ng/ml (normal, 0.5-3.0)
Serum cortisol 27 μg/dl (normal, 8-25)

The most likely cause of these results is

A. Adrenal insufficiency
B. Non-islet-cell tumor
C. Insulinoma
D. Surreptitious administration of insulin
E. Surreptitious ingestion of glyburide

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Case 3: Explanation

Elevated insulin and low C-peptide levels are consistent with exogenous insulin administration (D).

Adrenal insufficiency (A) is ruled out by a high-normal cortisol level.

Hypoglycemia caused by a non-islet cell tumor (B) is characterized by low insulin and elevated IGF-2 levels.

Both an insulinoma (C) and sulfonylurea overdose (E) would result in elevated insulin as well as C-peptide levels.

Case 4

A 32-year-old man comes to see you for work-up of infertility after he was found to have a low sperm count and low testosterone. He is significantly taller than both of his parents. His testicles are small and firm.

What is the best next step in the diagnostic workup:

A. Measure serum follicle stimulating hormone (FSH)
B. Measure serum luteinizing hormone (LH)
C. Order a pituitary MRI
D. Measure serum prolactin level
E. Examine his karyotype

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E. Examine his karyotype

Case 4: Explanation

Based on the physical examination, the index of suspicion is high that the patient has Klinefelter syndrome (XXY). While this syndrome is characterized by primary hypogonadism leading to elevation of FSH (A) and LH (B), neither test is diagnostic.

Karyotype analysis (E) is the best way to make the diagnosis.

Prolactin (D) is not affected in Klinefelter syndrome and there is no anatomic pituitary pathology that could be visible on the MRI (C).

Case 5

A 61-year-old man comes to see you for the first time after recently moving to this area. He has type 2 diabetes and HbA1c is measured at 8.5%. He takes metformin 1,500 mg/day and insulin glargine 20 units at bedtime. His fasting glucose is in 140-160 mg/dL range. He was hospitalized 3 months ago for a myocardial infarction. He has no h/o heart failure, pancreatitis, chronic kidney disease or medullary thyroid cancer.

The best next step to treat his hyperglycemia is:

A. Start glipizide
B. Titrate glargine dose up aiming for fasting glucose 80-130 mg/dL
C. Start sitagliptin (Januvia)
D. Start semaglutide (Ozempic)
E. Increase metformin dose to 2,000 mg/day

Case 5

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Case 5: Explanation

This patient is in his early 60s with few complications of diabetes. Therefore, intensive glycemic control aiming for HbA1c < 7.0% is warranted. All of the options listed will decrease his blood glucose levels. However, several (e.g. increasing metformin (E) or starting sitagliptin (C)) are unlikely to decrease it sufficiently to reach HbA1c < 7.0%.

Even more importantly, he has established ASCVD. Therefore GLP-1 agonists, like semaglutide (D), or SGLT2 inhibitors that have been shown to reduce the risk of CV events are a better choice than other options (e.g. increasing glargine dose (B) or starting glipizide (A)) that could have adequately improved his blood glucose levels.

Case 6

A 44-year-old woman has had weakness and nervousness for several months. She also has noted occasional palpitations and has lost 5 lbs. Her pulse rate is 96 beats/minute. She has mild eyelid retraction and a slight tremor of her hands, but no thyroid enlargement or nodules.

Her serum TSH is 0.01 µU/ml (normal, 0.4-4.0) and serum free thyroxine concentration is 2.0 ng/dl (normal, 0.8-1.6). Her thyroid radioiodine uptake at 24 hours is 52 percent (normal, 15-35) with diffuse pattern. Pregnancy test is negative.

The best next step is to:

A. Measure serum C-reactive protein
B. Begin a beta-blocker
C. Administer I-131 radioiodine isotope
D. Start propylthiouracil
E. Start methimazole

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Case 6: Explanation

This patient has mild Graves disease. First line treatment for Graves disease are thionamides, and specifically methimazole (E).

Beta-blockers (B) can alleviate palpitations, tachycardia, and tremulousness but do not lower thyroid hormone levels. In patients with more severe symptoms, beta-blockers can be useful.

Propylthiouracil (D) is associated with an increased risk of liver failure.

Measurement of C-reactive protein level (A) does not assist in management of Graves disease.

Treatment with I-131 isotope (C) usually leads to permanent hypothyroidism and is therefore not recommended as first line choice in most cases.

Case 7

A 32-year-old woman has had erratic menstrual periods since adolescence and amenorrhea for about 4 months. She has had mild facial hirsutism for more than 10 years. She recently gained about 5 pounds, and has had less energy than in the past. She takes no medications. She has mild facial hirsutism, but no striae, central adiposity, hot flashes, or galactorrhea. Her prolactin is measured to be 52 ng/mL (nl 4-30), and the pregnancy test is negative.

The most appropriate next step is to order:

A. Ovarian ultrasonography
B. Serum follicle stimulating hormone (FSH)
C. Pituitary MRI
D. Serum testosterone
E. Serum TSH

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Case 7: Explanation

Mild hyperprolactinemia associated with secondary amenorrhea can be due to primary hypothyroidism (E) as low free T4 stimulates increased TRH production from the hypothalamus which stimulates secretion of both TSH and prolactin from the pituitary.

Ovarian ultrasonography (A) and measurement of testosterone levels (D) are not helpful in diagnosing the etiology of hyperprolactinemia.

FSH (B) will be suppressed in patients with hypothalamic amenorrhea. She does not have hot flashes so premature ovarian insufficiency is unlikely and it would not be associated with hyperprolactinemia.

Hypothyroidism is more common than pituitary masses and should be ruled out before a pituitary MRI (C) is considered.

Case 8

A 68-year-old woman was found unresponsive at home by her daughter. In the Emergency Department, her temperature was 103.2, oxygen saturation 70% on room air, blood pressure 90/40 and heart rate 115. When given oxygen she was sleepy, but arousable. Her thyroid exam was normal. She was hospitalized and treated with intravenous fluids and antibiotics.

On day 2, TFTs were drawn because of persistent sinus tachycardia. TSH was 0.15 μU/ml (nl 0.5-5.0) and free thyroxine was 0.6 ng/dL (nl 0.8-1.6). The best next step is:

A. Pituitary MRI

B. Thyroid ultrasound

C. Thyroid I-123 scan and uptake

D. Levothyroxine 100 mcg daily

E. Re-evaluate in 4-6 weeks

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Case 8: Explanation

This patient's thyroid function tests are consistent with both sick euthyroid syndrome and secondary hypothyroidism. However, in a setting of critical illness in a patient without a known pituitary lesion, sick euthyroid syndrome is much more likely, and expectant management (E) is recommended.

Pituitary MRI (A) would only be indicated if the patient's thyroid hormone levels do not normalize as she recovers from her illness.

Thyroid ultrasound (B) and radioiodine scan and uptake (C) are not helpful in diagnosing the etiology of hypothyroidism.

Levothyroxine supplementation (D) has not been shown to be of benefit in patients with sick euthyroid syndrome.

Case 9

A 67-year-old woman comes for a follow-up visit two years after initiating alendronate (Fosamax) for treatment of osteoporosis. She takes calcium 500 mg twice daily and vitamin D 800 units daily. She takes alendronate on Sunday mornings together with the rest of her medications. She walks a mile 5 days a week. Her 25-OH-vitamin D level is 32 ng/mL (normal). Two years ago, her T-score in the left hip was -2.6. A week ago, follow-up bone densitometry showed a 6% decrease in the left hip (significant). The best next step is:

A. Review proper administration of alendronate
B. Double her calcium dose
C. Double her vitamin D dose
D. Switch to raloxifene (Evista)
E. Switch to ibandronate (Boniva)

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Case 9: Explanation

This patient has a failure of treatment with an oral bisphosphonate. She takes alendronate together with calcium which can decrease bisphosphonate absorption. Therefore, the first step is to make sure calcium and alendronate are taken separately (A).

She already takes adequate calcium (B) and vitamin D (C) doses. Increasing these is unlikely to be of clinical benefit and could have adverse effects.

Neither raloxifene (D) nor ibandronate (E) have been shown to reduce the risk of hip fractures or non-vertebral fractures and thus, are not ideal osteoporosis therapies for this patient.

Case 10

A 62-year-old man comes for follow-up of diabetes. He used to be treated with metformin 1000 mg bid and glipizide 10 mg bid but two years ago glipizide was stopped and glargine (Lantus) insulin started. He now takes 30 units of glargine at night. He wakes up during the night from hypoglycemia 2-3 times a week but his daytime glucose ranges between 150-220 mg/dL. His A1C is 7.5%. The best next step is:

A. Stop glargine and restart glipizide

B. Take glargine in the morning instead of at night

C. Decrease glargine and add a rapid acting insulin before every meal

D. Stop glargine and start detemir (Levemir) insulin at night

E. Ask him to eat a snack before going to bed

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Case 10: Explanation

This patient has excessive basal insulin dose as evidenced by nocturnal hypoglycemia; his hyperglycemia is likely post-prandial. Therefore, basal insulin dose should be decreased and prandial insulin added (C).

Replacing glargine with glipizide (A) will further increase his daytime glucose levels.

Administering glargine in the morning instead of at night (B) is unlikely to make a difference.

Replacing glargine with evening detemir (D) will not reduce nocturnal hypoglycemia.

Bedtime snack (E) will reduce nocturnal hypoglycemia but will not improve his overall glycemic control.

Case 11

A 63-year-old woman is evaluated for severe hypertension resistant to treatment with three anti-hypertensive medications (ACE inhibitor, calcium channel blocker, and HCTZ) and hypokalemia. She is found to have serum aldosterone 24 ng/dL (nl 4 – 21) and plasma renin activity 0.2 ng/mL/hr (nl 0.6 – 3.0). Plasma metanephrine and normetanephrine levels are normal. A 24 hour urine aldosterone level is 20 mcg with urine sodium of 220 mEq. Abdominal CT shows a 2-cm benign appearing nodule in the right adrenal gland. The best next step is:

A. Abdominal MRI
B. Repeat the CT in 6 months
C. Refer to an experienced surgeon for right adrenalectomy
D. Adrenal vein sampling
E. Stop all anti-hypertensives and repeat biochemical tests

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Case 11: Explanation

This patient has primary hyperaldosteronism. However, adrenal nodules are common in this age group, while excess aldosterone production could have a different source (e.g. bilateral adrenal hyperplasia). Therefore, confirmation of laterality of aldosterone production (D) is the first step and adrenalectomy (C) is premature.

Abdominal MRI (A) will not provide any additional information.

Deferral of definitive treatment (B) of primary hyperaldosteronism is not appropriate.

The diagnosis of primary hyperaldosteronism is definitive and no further biochemical workup (E) is needed.

Case 12

A 41-year-old man comes to your office complaining of progressive erectile dysfunction over the last several years. Evaluation shows testosterone 1,200 pg/ml (nl 1,800 – 6,900) and prolactin of 68 ng/ml (nl 4-23), confirmed by dilution. TSH is normal. Pituitary MRI shows a 2.5-cm intrasellar mass consistent with pituitary adenoma. He denies headaches; his neurological examination is normal and visual fields are intact. Morning cortisol is 12 mcg/dl, IGF-1 is normal, and LH and FSH are low. The best next step is:

A. Refer to a neurosurgeon

B. Start bromocriptine (Parlodel)

C. Start cabergoline (Dostinex)

D. Start testosterone patch

E. Repeat pituitary MRI in 6 months

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Case 12: Explanation

This patient has a non-secretory pituitary macroadenoma and should be referred to a neurosurgeon for resection (A) to prevent further complications, such as optic chiasm compression.

Deferral of treatment (E) is not appropriate.

Prolactin elevation is mild and thus due to pituitary stalk compression rather than production by the tumor. Consequently, treatment with bromocriptine (B) or cabergoline (C) is not the appropriate therapy.

Gonadotropin production may recover after resection of the tumor, and therefore testosterone supplementation (D) is premature.

Case 13

A 56-year-old previously healthy woman reports intense flushing (her face turns purple) that's been going on for 6 months. She underwent menopause 4 years ago and was asymptomatic at the time. She also complains of frequent watery bowel movements. She takes no medications. She has one of the episodes during her visit and her blood pressure falls to 102/61 down from 127/74. The best next step is:

A. Magnetic resonance imaging of the brain

B. 24-hour urine collection for catecholamines and metanephrines

C. 24-hour urine collection for 5-hydroxyindoleacetic acid (5-HIAA)

D. 24-hour urine collection for tryptase

E. Start estrogen supplementation

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D. 24-hour urine collection for tryptase

E. Start estrogen supplementation

Case 13: Explanation

This woman's symptoms are most consistent with carcinoid syndrome; therefore, 24-urine collection for 5-HIAA (C) is the best way to confirm the diagnosis.

Pituitary tumors do not typically cause flushing and thus pituitary MRI (A) will not be helpful.

Pheochromocytomas (B) rarely cause flushing and are not usually associated with diarrhea.

Serum (rather than urine) tryptase (D) measurement can be used to diagnose systemic mastocytosis.

New onset of flushing several years after the menopause is unlikely be due to estrogen deficiency (E).

Case 14

A 25-year-old man comes in for routine physical. He had craniopharyngioma resection at the age of 12 and has been taking levothyroxine ever since. His current dose is 112 mcg daily. Blood tests show TSH of 0.05 μU/ml (nl 0.5-5.0) and free thyroxine 0.7 ng/dL (nl 0.8-1.6). The best next step is:

A. Decrease levothyroxine to 88 mcg daily
B. Increase levothyroxine to 125 mcg daily
C. Radioactive iodine uptake
D. Pituitary MRI
E. Re-evaluate in 6 months

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D. Pituitary MRI

E. Re-evaluate in 6 months

Case 14: Explanation

This patient with a known pituitary lesion that has been surgically resected has secondary hypothyroidism. In these circumstances, TSH is not a useful indicator of thyroid hormone adequacy. His free thyroxine levels are low and his levothyroxine dose should be increased (B) rather than decreased (A). Deferral of treatment (E) is not appropriate.

As hyperthyroidism is not suspected, radioactive iodine uptake (C) will not be helpful.

His pituitary disease is well established and there is no reason to suspect any changes that could be revealed by a pituitary MRI (D).

Case 15

A 71-year-old man returns to see you for follow-up of type 2 diabetes. He also has hypercholesterolemia, stage IV chronic kidney disease, heart failure, hypertension, osteoarthritis, remote history of pancreatitis and bladder cancer and family history of medullary thyroid cancer. His current medications include glipizide 10 mg bid and simvastatin 20 mg qhs. His hemoglobin A1c is 8.2% and fasting blood glucose 130-150 mg/dL. The best next step is to add the following medication to glipizide:

A. Metformin 1000 mg daily
B. Liraglutide (Victoza) 0.6 mg SQ daily
C. Sitagliptin (Januvia) 100 mg daily
D. Pioglitazone (Actos) 15 mg daily
E. Glargine (Lantus) insulin 15 units SQ qhs

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D. Pioglitazone (Actos) 15 mg daily
E. ***Glargine (Lantus) insulin 15 units SQ qhs***

Case 15: Explanation

In this patient metformin (A) and pioglitazone (D) are contraindicated because of history of advanced kidney disease and heart failure, respectively.

Liraglutide (B) and sitagliptin (C) are contraindicated because of history of pancreatitis, and pioglitazone (D) is also contraindicated because of history of bladder cancer. Liraglutide (B) is additionally contraindicated because of family history of medullary thyroid cancer.

Therefore, glargine insulin (E) is the only remaining treatment option. SGLT2 inhibitors could be beneficial for his heart failure but are not indicated in Stage IV CKD.

Case 16

A 65-year-old woman comes to see you as a new patient. She has type 2 diabetes, hypertension and hypothyroidism. She takes metformin XR 2000 mg daily, glimepiride 4 mg daily, lisinopril 20 mg daily, and diltiazem XR 240 mg daily. Her fasting lipid profile shows LDL cholesterol of 120 mg/dL, HDL cholesterol 51 mg/dL, and triglycerides 167 mg/dL. The best next step is:

A. Start ezetimibe (Zetia) 10 mg daily
B. Start niacin extended release 500 mg daily
C. Start fenofibrate (Tricor) 145 mg daily
D. Start simvastatin (Zocor) 40 mg daily
E. Start atorvastatin (Lipitor) 20 mg daily

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E. Start atorvastatin (Lipitor) 20 mg daily

Case 16: Explanation

This woman needs to lower her LDL (guidelines recommend at least moderate intensity statin therapy for most patients with diabetes).

Niacin (B) and fenofibrate (C) have not been unequivocally shown to decrease the incidence of cardiovascular events in patients with elevated cholesterol, while ezetimibe (A) benefits are relatively weak; they are therefore not recommended as first line treatment.

Simvastatin (D) has significant drug-drug interactions with many calcium channel blockers and is contraindicated in doses greater than 10 mg daily in patients who take diltiazem.

Consequently atorvastatin (E) is the best treatment choice.

Case 17

A 53-year-old woman comes to see you for follow-up of type 2 diabetes. She also has hypertension and obstructive sleep apnea. She has struggled with obesity for many years and her current BMI is 37.5 kg/m^2. She takes metformin 2,000 mg/day and subcutaneous semaglutide 2.4 mg/wk. Her A1c is 9.2%. Her blood pressure is well controlled on lisinopril 20 mg daily, amlodipine 10 mg daily and hydrochlorothiazide 25 mg daily. She has tried multiple weight loss diets over the years but has been unable to lose additional weight. The best next step is:

A. Start glipizide 10 mg daily
B. Start glargine (Lantus) insulin 15 units at bedtime
C. Recommend that she consider a bariatric procedure
D. Start phentermine 30 mg daily
E. Start empagliflozin (Jardiance) 10 mg daily

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Case 17: Explanation

This woman needs to improve her glycemic control. It would also be ideal for her to lose weight as she has several reversible complications of obesity.

As she is already on a glucagon-like peptide-1 (GLP-1) receptor agonist, a bariatric procedure (C), such as a Roux-en-Y gastric bypass or a sleeve gastrectomy, will achieve both of these goals.

Glipizide (A) and glargine (B) will lead to weight gain. Phentermine (D) will achieve modest weight loss, but is only recommended for short-term use and will not improve her glucose control. Empagliflozin (E) will only result in modest weight loss and is unlikely to bring her A1c below 7.0%.

Once-weekly tirzepatide, a dual agonist for glucose-dependent insulinotropic polypeptide (GIP) and GLP-1 receptors given subcutaneously, received FDA approval in 2022 for the treatment of Type 2 diabetes and helped patients achieve significant weight loss.

Case 18

A 68-year-old woman was found to have primary hyperparathyroidism with mild hypercalcemia of 10.9 mg/dl (nl 8.5-10.5) and normal renal function. She is asymptomatic with no prior history of fractures or kidney stones. She has normal mineralization on DEXA with no evidence of vertebral fractures on spine imaging.

What is the most appropriate next step?

A. Measure 24h urine calcium excretion
B. Refer for parathyroidectomy
C. Start cinacalcet
D. Obtain a neck ultrasound
E. Obtain a parathyroid scan

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Case 18: Explanation

The initial evaluation of patients with asymptomatic primary hyperparathyroidism is focused on identifying patients who would benefit from parathyroidectomy (B).

Indications for parathyroidectomy include age < 50 yrs, serum calcium levels 1 mg/dL or more above the upper limits of normal, abnormal renal function, osteoporosis or the presence of asymptomatic vertebral fractures on imaging, and the presence of asymptomatic kidney stones or hypercalciuria with increased risk of nephrolithiasis based on 24hr urine collection (A).

Neck ultrasound (D) and parathyroid scan (E) are not required to identify candidates for surgical intervention.

Although cinacalcet (C) can correct serum calcium levels, it does not typically normalize PTH values or protect against bone loss.

Case 19

A 76-year-old woman who is taking biotin supplements is evaluated for depression, fatigue, and weight loss. Her serum TSH is undetectable (normal 0.5-5.0 μU/ml) with free thyroxine concentration of 2.1 ng/dl (normal 0.8-1.6). She does not have tremors, heat intolerance, or increased sweating. Her pulse is normal at 92 bpm and she has a palpable 2 cm thyroid nodule. A thyroid scan shows a focal increase in radioiodine uptake from the isolated nodule with suppression of uptake in the rest of the gland.

The most appropriate next step is to:

A. Start a beta-blocker
B. Administer I-131 radioiodine isotope
C. Start levothyroxine
D. Stop biotin and repeat labs in 1 week
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Case 19: Explanation

This patient has apathetic hyperthyroidism due to a toxic thyroid adenoma which can be treated with radioiodine ablation (B).

Compared to typical hyperthyroidism, patients with apathetic hyperthyroidism have fewer features of sympathetic overactivity. Beta-blockers (A) would provide little benefit in the absence of tachycardia and levothyroxine (C) would worsen the hyperthyroidism.

Triiodothyronine (T3) measurements (E) are not indicated for the diagnosis or treatment of apathetic hyperthyroidism.

Although biotin can interfere with the assays used in thyroid function tests (D), the thyroid scan indicates that there is autonomous thyroid function.

Case 20

A 62-year-old man with osteopenia develops low libido, sexual dysfunction, and weakness after resection of a large pituitary macroadenoma. He is found to have central hypogonadism with suppressed gonadotropins and low testosterone levels. He is started on testosterone injections.

The best next step is to monitor:

A. Serum testosterone level
B. Serum LH level
C. Hematocrit
D. Both A and C
E. Lower extremity ultrasound

Case 20

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The best next step is to monitor:

A. Serum testosterone level
B. Serum LH level
C. Hematocrit
D. **Both A and C**
E. Lower extremity ultrasound

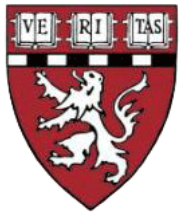
Case 20: Explanation

Patients on testosterone replacement therapy should be monitored to ensure normalization of serum testosterone levels and avoidance of complications.

Erythrocytosis is a common adverse effect of testosterone injections. Thus, measurement of both testosterone levels and hematocrit (D) should be done several months after initiation of testosterone therapy.

Monitoring of gonadotropin levels (B) is not necessary in central hypogonadism.

Although testosterone therapy increases the risk of venous thromboembolism, routine screening for thromboembolism (E) is not recommended.



GOOD LUCK!

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