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**Clinical case N. 1**

Patient X, 38 years old, addresses the AMU with complaints of continuous abdominal pain, that appeared 4 hours ago. Gradually, the pain increases in intensity and fever appears. Other complaints: tremor, sweating, palpitations, severe asthenia. In the morning when she got out of bed, she lost the consciousness.

**From the anamnesis:** The patient suffers from pulmonary TB, and 2 years ago, following a diagnostic laparoscopy (performed to determine the cause of infertility in the couple), the ovarian tuberculosis was established. She is considered ill for 2 years since she complaints of muscular weakness, border-line states between irritability and depression, periodic diarrhea (not accompanied by fever) and frequent states of lipothymia, polyuria and nocturia. She complaints of weight loss (18 kg in 2 years). 6 months ago, atrophic gastritis was determined at the FGDS. The condition worsens when the patient is submitted to a stressful situation.

**Objective data:** The patient is 172 cm, 60 kg. BP on admission 90/45, Pulse=105, RR=22. She has a tanned skin appearance.

**Paraclinical exams:**

***General blood analysis:*** Hb=85 g/l; Erythrocytes=2.1x10⁹/l, Leukocytes=14x10⁹/l; Ht=52%;

***Biochemical blood analysis:*** Na⁺-122mEq/l (135-145 mEq/l); K⁺-6 (3.5-5.5 mEq/l); pH- 7.32 (7.35-7.45); Blood osmolarity-275 (285-295 mOsmol/l); Creatinine-2.4 (<1 mg/dl).

***Endocrine markers:*** Cortisol (7:00-10:00) = 50 (172-497 nmol/l); ACTH (7:00-10:00) = 120 (7.2-63.3 pg/ml; Aldosterone = 0.5 (1.76-23.2 ng/dl).

Taking into account the acute abdomen, pain unresponsive to spasmolytics, leukocytosis with increasing dynamics, after 24 hours, a diagnostic laparoscopy is done, which proceeds to laparotomy. Intraoperatively: necrosis of the small intestine, intestinal resection and end-to-end anastomosis of the small intestine are performed.

**Diagnosis:** Primary adrenocortical insufficiency (Addison's disease). Mesenteric artery thrombosis.

**Questions:**

1. What is the pathogenetic mechanism of arterial hypotension in Addison's disease?
2. Explain the pathogenetic mechanisms of tachycardia in the patient.
3. Describe the pathogenetic chain leading to hypoglycemia in the patient.
4. What are the compensatory reactions in case of hypocortisolism induced hypoglycemia?
5. What is the pathogenetic mechanism of diarea and those of mezenterial artery thrombosis in the patient?
6. Explain from pathogenetic point of view the creatinine level is increased in this patient.
7. It is known that cortizol deficiency inhibits lipolysis, instead of this fact, the lipolysis is activated in the patient. What are the raisons?

**Clinical case N.2**

Patient x, a 42-year-old man, addresses to family doctor with skin and soft tissue lesions and fever. His medical history shows that he is a forest worker and 2 days ago, following an accident at work, he lost control of his chainsaw and cut his leg. He took ibuprofen, dexalgin and treated the wound with hydrogen peroxide solution. The wound became infected and, in the evening, appears fever. However, the family doctor was surprised by the patient's physical appearance, whom he had not seen at the clinic for 2 years: the patient had gained 18 kg in weight, with adipose tissue distributed mainly in the trunk and face, cherry-coloured striae appeared on the abdomen, and white, depigmented, itchy spots on the chest and back, with pronounced acne on the face. The patient complained of muscle weakness in his hands and legs and twice within a year, he had injured his leg when lifting weights, which is why he finds it increasingly difficult to go to work to the forest.

The patient was admitted to the traumatological hospital, where he underwent surgical intervention, requiring repeated cleaning and drainage of the postoperative wound, which had healed very slowly. Upon discharge from hospital, the family doctor contacted him to come to the medical center for **additional investigations, which are attached:**

1. Cortisol (7:00-10:00) = 900 (172-497 nmol/l)

ACTH (7:00-10:00) = 120 (7.2-63.3 pg/ml)

K⁺= 2.9 (3.5-5.5 mEq/l)

Fasting blood sugar = 145 mg/dl (70-126 mg/dl)

BP=165/100 mmHg, Ps=98 /min

2. USG-bilateral enlargement of the adrenal glands.

3. Brain MRI determined a pituitary adenoma of 1.5 cm in diameter.

With the attached results, he was referred to an endocrinologist to confirm the diagnosis and establish treatment tactics.

**Diagnosis:** Cushing's disease, secondary hypercortisolism.

**Questions:**

1. Explain the pathogenetic mechanism of the increased susceptibility to infections in the given patient:

2. Explain from a pathogenetic point of view why there is a slow healing of the postoperative wound in the given patient?

3. List the criteria for differentiating Cushing's Disease from Cushing's Syndrome:

4. What is the pathogenetic mechanism of hyperglycemia in the patient?

5. What are the pathogenetic mechanisms of chronic arterial hypertension in the given patient?

6. Specify the pathogenetic mechanisms of bone fractures in the given patient?

7. How do we pathogenetically explain the appearance of depigmented and pruritic spots in the patient.

**Clinical case N.3**

Patient X, 60 years old age, addresses to the family doctor with the following ***complaints:***

-Using the maximum dose of metformin and sulfonylurea derivatives, the patient cannot maintain adequate glycemic control

-The patient, being on antihypertensive treatment, has had frequent hypertensive crises for the last 3 months

-Weight gain +4 kg within 2 months

-Burning sensation starting with the fingers and toes and spreading throughout the limbs.

**From the anamnesis:** he is a mayor in the village, a stressful job. He frequently copes with stress, according to the patient, with "wine", does not follow the diet, prefers meals with fatty grilled meat. He has been diagnosed with diabetes mellitus for 8 years, and 2 years ago he suffered a myocardial infarction, and 1 year ago he underwent laser ophthalmological intervention. Frequent urinary infections on the background of erectile dysfunction. The patient's mother also died from complications of diabetes mellitus.

**Objective data:** BP: 170/100 mmHg, Ps: 68 -/min, Weight: 115 kg, Waist 182 cm,

**Paraclinical exams:** fasting blood sugar 182 mg/dl, total cholesterol= 52 (<200 mg/dl), HDL=25 (>40 mg/dl), LDL= 210 (<100mg/dl), TG 290 (<150mg/dl), glycosylated Hb=11% (N=4.8-5.6 %), Serum sodium-160 mEq/l, potassium =3.1 mEq/l.

Diagnosis: Type 2 diabetes complicated with diabetic macroangiopathy (coronary artery atherosclerosis) and microangiopathy (proliferative diabetic retinopathy/peripheral diabetic neuropathy). HTN gr. II additional very high risk. Obesity gr. II. Dyslipidemia.

**Questions:**

1. Explain the pathogenesis of insulin resistance in the case of genetic defects occurring at the insulin receptor level and intracellular signaling pathways.

2. List 3 pathogenetic mechanisms by which obesity induces insulin resistance.

3. Describe the pathogenetic mechanisms of insulin resistance in the case of increased non-esterified fatty acids in the specific patient with type 2 diabetes.

4. Explain the role of adipokines in the occurrence of insulin resistance.

5.What are the pathogenetic mechanisms of hyperlipidemia in the patient? (High LDL and TG).

5. The given patient has a history of myocardial infarction caused by coronary artery atherosclerosis. What is the mechanism of atherosclerosis in the patient with type 2 diabetes?

6. One of the mechanisms of diabetic neuropathy is the activation of the polyol pathway. Explain, using a pathogenetic chain, how neuronal damage occurs upon activation of this pathway.

7. Microvascular complications in the patient can also be explained by activation of the protein kinase C pathway. List the resulting effects on the vascular endothelium.

**Clinical case N.4**

Patient A., 34 years old, addresses the gynaecologist with complaints of primary infertility in a couple for 8 years, amenorrhea and watery discharge from the nipples of both mammary glands. Other complaints: feeling of chronic fatigue, weight gain (12 kg over 5 years), decreased work capacity, intolerance to cold, feeling of suffocation if the coat, scarf touches the neck area, chronic constipation.

**Objective data:** Weight 98 kg, Waist=1.65 m, BP=100/60, Ps=54 b/min, pastiness of the face, abdominal striae. Palpation - thyroid gland enlarged in volume.

**Paraclinical exams:** Hb=100g/l, RBC=2.7x10⁹/l; TSH=6.2 μIU/ml (0.27-4.2 μIU/ml), T₃=0.5 nmol/l (1.3-3.1 nmol/l), T₄= 40 nmol/l (66-181 nmol/l); PRL=920 (127-637μIU/ml), Na⁺= 125 mEq/l (135-145 mEq/l), blood sugar=3.9 mmol/l, cortisol= 600 nmol/l(172-497 nmol/l), total cholesterol=380 mg/dl (< 240 mg/dl), LDL=200 mg/dl (100-129 mg/dl), TG= 450 mg/dl (<150 mg/dl).

**Diagnosis:** Primary hypothyroidism. Endemic goitre. Myxedema. Hyperprolactinemia. Primary infertility. Dyslipidemia.

**Questions:**

1. Describe the pathogenetic chain of hypercholesterolemia in the patient.

2. What is the pathogenetic mechanism of goitre in the patient with hypothyroidism?

3. Explain the pathogenetic mechanism of hypoglycemia in the patient.

4. Specify the pathogenetic factors of the pathological weight gain in the patient.

5. Explain why despite the low glomerular filtration in the patient with hypothyroidism, BP has low values.

6. Describe the pathogenetic link of infertility in the patient with primary hypothyroidism.

7. Explain, in pathogenetic raison, why the patient has anemia.