10IU, for glucose above 14 mmol/L, for glucose above 18 mmol/L. Dinner 6XU - Fiasp 10IU, for glucose above 14 mmol/L, for glucose above 18 mmol/L. Tresiba 10 p.m. 18 IU.

Control of glucose and ketones in urine at glucose above 15 mmol/l and for intercurrent diseases, increase insulin dose if necessary.

In case of hypoglycemia (blood sugar below 3.9 mmol/l), take easily digestible carbohydrates for 1 CGU (a glass of juice, 4 pieces of raffinate), then after 15 minutes measure blood glucose, if the blood glucose is low again repeat carbohydrate intake.

Change of injection sites is recommended to avoid lipodystrophy formation.

Monitor glycated hemoglobin HbA 1c, blood chemistry, morning urine for microalbuminuria every 3 months.

With hepatoprotective purpose - Ursosan 500 mg once a day - a course of 1 month.

Control of biochemical blood tests (ALT, AST, LDH, creatinine, urea, total protein, gamma-glutamyl transpeptidase, bilirubin total, free, albumin) after 1 month. In case of negative dynamics of the biochemical blood test, hospitalization in the Department of Pediatric Endocrinology and Gastroenterology of the Pediatric Center of RB №1-NCM is recommended.

Conclusion: An interesting clinical case from the Department of Pediatric Endocrinology and Gastroenterology of Pediatric Center of the Republican Hospital No.1-NCM is described in the article. Cases of toxic hepatitis in children have been described in the literature. However, there are practically no articles describing cases of toxic hepatitis in children against the background of diabetes mellitus type 1. The article will be of interest to pediatricians.

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ADRENAL AND THYROID DYSFUNCTION IN NON-TRAUMATIC SUBARACHNOID HEMORRHAGE REQUIRING THERAPEUTIC NORMOTHERMIA. CLINICAL OBSERVATION

Subarachnoid hemorrhage (SAH) is a life-threatening variant of hemorrhagic stroke. Therapeutic normothermia to reduce the risk of adverse outcomes. At the same time, the initially existing decompensation of body systems, followed by induced normothermia, gives impetus to the development of a number of pathophysiological processes in the human body. **Objective.** Timely detection and adequate correction of endocrinopathy of critical illness in patients in the most acute period of SAH against the background of therapeutic normothermia with a target temperature regime of 36 °C. **Materials and methods.** A 57-year-old patient with a diagnosis of non-traumatic subarachnoid hemorrhage, saccular aneurysm of the anterior communicating artery and anterior cerebral artery, Hunt Hess III. **Results.** The development of critically ill adrenal dysfunction considered based on the need for vasopressors. Thyroid dysfunction caused by a critical illness considered with a decrease in the level of TSH and free T3 in blood plasma against the background of therapeutic normothermia, the development of intestinal dysfunction and sinus bradycardia. **Conclusions.** Against the background of the introduction of hydrocortisone at an initial dose of 300 mg, the administration of norepinephrine discontinued on the third day. When levothyroxine sodium 300 mcg/day added to therapy, intestinal dysfunction resolved, normal resting heart rate achieved.

Keywords: critical illness, hypothyroidism, thyrotropin, thyroid hormones, thyroxine, triiodothyronine, extracorporeal membrane oxygenation, targeted temperature management, cortisol, adrenocorticotropic hormone.

Introduction. Subarachnoid hemorrhage (SAH) is a life-threatening variant of hemorrhagic stroke [1]. In the acute period of SAH, among other methods of treatment, aggressive correction of hyperthermia and maintenance of normothermia using specialized TTM body temperature control systems are justified [15]. Prophylactic normothermia is recommended for patients with a poor prognosis of SAH (Hunt-Hess 111-V) [6]. TTM, which has actively used over the

past decades in the conditions of intensive care units and intensive care units for the purpose of neuroprotection and correction of intracranial pressure, has made it possible to reduce the risk of adverse outcomes in critical illness. At the same time, the initially existing decompensation of body systems, followed by induced normo/hypothermia, gives impetus to the development of a number of pathophysiological processes in the human body. There have been no works on the diagnosis and treatment of endocrinopathies of critical illness in TTM.

The presented clinical observation is to demonstrate the importance of timely detection and adequate correction of endocrinopathy of critical illness in patients in the most acute period of SAH against the background of therapeutic normothermia with a target temperature regime of 36°C. The observation period for the patient was three days.

Materials and methods. This article describes a clinical observation of a 57-year-old patient with a diagnosis of non-traumatic subarachnoid hemorrhage, saccular aneurysm of the anterior communicating artery and anterior cerebral artery (AComm-ACA). Hunt Hess III, requiring therapeutic normothermia. When prescribing hydrocortisone and levothyroxine sodium, the patient was in a serious condition with drug-induced depressed consciousness. Based on p. 9.1 art. 20 of the Federal law № 323-FZ from 21.11.2011 as medical intervention was necessary for emergency indications to eliminate the threat to the life of the patient, and the patient's condition did not allow the patient to express his will, the decision to prescribe drugs was made by the council without the consent of the patient. **Results.** *Patient Z., 57 years old*, transferred from the primary hospital on the second day of illness with a diagnosis of non-traumatic subarachnoid hemorrhage, saccular aneurysm of the anterior communicating artery and anterior cerebral artery (AComm-ACA). Hunt Hess III" to A.I. Burnasyan Federal Medical Biophysical Center FMBA. *Associated pathology.* Hypertonic disease. Obesity 1 degree according to WHO (BMI 33,2 kg/m2). *At the time of admission to the clinic,* the patient's condition was of moderate severity, the level of consciousness on the Glasgow coma scale was 14 points (stunning): disoriented in space and time, mild dysarthria. Body mass index 31,9 kg/m2. Temperature 36,9 °C. Breathing spontaneously. O2 saturation 98%. Heart sounds are muffled, rhythmic, heart rate (HR) 75 beats / min, blood pressure (BP) 170/80 mm Hg. art. The result of the electrocardiogram (ECG): sinus rhythm. There was no stool for three days. *Surgery on the day of admission* - microsurgical clipping of the AComm-ACA aneurysm using neurophysiological monitoring. *In the early postoperative period.* Consciousness is drug-depressed, - 5 points on the Richmond Agitation Sedation Scale (RASS), sedation (propofol). Body temperature 36,7 °C. Continued artificial ventilation of the lungs. Hemodynamics is unstable, supported by the introduction of norepinephrine at a dose of 1-1,5 mg/kg/min. For the purpose of invasive blood pressure monitoring, a radial artery catheterization performed. Invasive BP was 110/73 mmHg. Despite hemodynamically significant hypotension, heart rate of 67-71 beats per minute, a nasogastric tube placed. There was no reset on the probe. On auscultation, peristalsis is sluggish. There was no stool for three days. Urinary function preserved, a urethral catheter installed. *Instrumental studies:* CT scan of the brain with the introduction of a contrast agent. Signs of subarachnoid hemorrhage. *Laboratory data:* potassium 3,1 mmol/l, sodium -137 mmol/l. Due to the development of cerebral vasospasm and secondary ischemia, coma 1 (GCS 9 points), fever up to 40 °C, *external cooling* was performed for three days in the automatic control mode of the BLANKETROL II system (CSZ, USA). Central body temperature monitored by inserting a 400 series esophageal probe. The target core temperature was 36°C. Sedation with morphine, sodium thiopental/propofol, and rocuronium performed for episodes of muscle tremors. Once, with a decongestant purpose, an infusion of 3% hypertonic solution carried out. Thus, (day 4 from the moment of critical illness development) in a patient after surgery (aneurysm clipping), the severity of the condition is due to multiple organ dysfunction with a predominance of cerebral dysfunction (cerebral vasospasm, secondary ischemia), respiratory and cardiovascular dysfunctions. *On* second day (D2) *and D3 days of observation*, according to laboratory data c-reactive protein - 284 - 212 mg/l, potassium 4,3 - 3,9 mmol/l, sodium 140 - 149 mmol/l, glucose 11,4 - 9,8 - 7,3 mmol/l In connection with the appearance of signs of infection - an increase in markers of inflammation, fever at D2, antibiotic therapy (cefoperazone-sulbactam and amikacin) was added to therapy. *Diagnosis and correction of adrenal and thyroid dysfunctions. Reference ACTH values are (4.7-48.8 pg/ml). The reference value of total cortisol in plasma (*171–536 *nmol/l). Reference values of the level of TSH in plasma (0.4 - 4.0 mU / l). Reference values of the level of free T4 (12–22 pmol/l) and free T3 (3.1 - 6.8 pmol / l).* On the day of admission (D0), plasma levels of cortisol and adrenocorticotropic hormone (ACTH) were: cortisol (1435 nmol/l) and ACTH (3 pg/dl). The level of TSH in blood plasma was 0,2 mU/l, St. T4 17 pmol/l, St. T3 2,1 pmol/l. On the first and third days against the background of therapeutic normothermia: the level of cortisol on C1 (1655 nmol/l), C3 (1514 nmol/l); ACTH level at C1 (3 pg/dl), C3 (6.7 pg/dl). TSH level at D1 (0.01 mU/l), D3 (0,01 mU/l); the level of free T4 on D1 (18.8 pmol / l), on D3 (20 pmol / l), the level of FT3 on D1 (2,1 pmol/l), on D3 (1,9). Due to the need for noradrenaline more than 0,25 mcg/kg/min in the early postoperative period (D0), hydrocortisone was added to therapy at an initial dose of 300 mg (100 mg IV bolus, then 50 mg every 6 hours). On D1 of therapeutic normothermia, intestinal dysfunction persisted (on the 4th day of illness). Against the background of trial enteral nutrition, there was no discharge through the nasogastric tube; there was no stool for 4 days. Prokinetics prescribed: erythromycin at a dose of 200 mg 3 times a day, i.v., and metoclopramide at a dose of 10 mg, 4 times a day, i.v. [9, 11]. A cholinesterase inhibitor, neostigmine methyl sulfate, prozerin, 1.5 mg 3 times a day, also used. Against the background of hydrocortisone, the dose of norepinephrine at D1 decreased to 1–0,7 μg/kg/min, and sinus bradycardia developed (heart rate 48–52 beats/min). According to the results of the electrocardiogram: sinus bradycardia, left ventricular hypertrophy with insufficiency of coronary blood supply in the anterolateral and apical region (systolic load). The level of lactate is 1,3 mmol / l (the norm is up to 1,6 mmol / l). Troponin level up to 0,11 (norm up to 0,023). Echocardiogram result: ejection fraction 62%, violation of local and global myocardial contractility not detected. Considering: the duration of the critical illness caused by non-traumatic SAH; development of the adrenal dysfunction caused by a critical illness (CIRCI); persisting intestinal dysfunction, low levels of TSH and FT3, the development of sinus bradycardia, it was decided to consider this clinical and laboratory picture as thyroid dysfunction caused by a critical illness (TDCCI). Levothyroxine sodium (L-T4) added to therapy. Replacement therapy of L-T4 was carried out at the rate of 3 mcg/kg/day (150 mcg. 2 times a day) - the starting dose, the next day - 100 mcg. 2 times a day. The drug administered through a nasogastric tube into an empty stomach in crushed

form, diluted in saline in a volume of 20 ml, at 6 am and 6 pm. The probe clamped for 2 hours. During the period of therapeutic normothermia, heart rate, assimilation of enteral nutrition were assessed daily, levels of TSH, free T4, free T3, glucose control (with insulin correction for hyperglycemia over 14,5 mmol / l) and electrolyte control. Criteria for reducing the dose of levothyroxine sodium: with the development of fever (body temperature above 38,3, outside therapeutic normothermia), the dose of levothyroxine sodium was reduced by 50% of the initial dose; with an increase in heart rate above 60 beats per minute, the dose of levothyroxine sodium was reduced by 25-50 mcg once a day. At D5, the patient had large stools. At D9, the dose of L-T4 was reduced to 100 mcg/day; on D11 up to 75 mcg / day, on D13 the abolition of L-T4. In the period after the completion of therapeutic normothermia, the administration of norepinephrine discontinued at D3, after which the dose of hydrocortisone reduced by 50 mg per day. With the introduction of hydrocortisone at a dose of 50 mg per day, the patient transferred to the tablet form of hydrocortisone. At D13, hydrocortisone was completed. The patient transferred to the specialized department on day D13. According to the FOUR scale (Full Outline of UnResponsiveness) at the time of discharge: E4, M3, B4, R4 - 15, which corresponded to moderate stunning. The patient's quality of life on the Glasgow Outcome Scale was 4 points.

Discussion. Multiple protective neuroimmunoendocrine reactions that develop when critical illness occurs, lead to the formation of a systemic inflammatory response syndrome. At the first stage of critical illness development, the hypothalamic-pituitary-adrenal system is activated by pro-inflammatory cytokines and afferent pathways of the vagus nerve [5, 9, 12]. If the vital functions of the body not restored within a few days, the critical illness passes from the acute to the subacute phase. The development and formation of the subacute phase of critical illness is based on the increasing systemic level of pro-inflammatory cytokines, hypoxic-ischemic brain damage, pathological permeability of capillary endothelial cells that form the blood-brain barrier and, as a result, the penetration of pro-inflammatory mediators and other neurotoxic molecules into the brain [4]. *The high level of cortisol in the blood plasma that we observed on the second, third and fourth days and the increasing level of inflammatory markers from the third day of critical illness development reflected just the transition of the acute to the subacute phase. It is during this period that adrenal dysfunction develops, caused by a critical illness* [16]. The high concentration of cortisol in the blood plasma can explained by several factors. A decrease in the level of thyroid hormones against the background of a low or low-normal TSH level in the subacute and chronic phases of critical illness may be a consequence of depletion of the hypothalamic centers that regulate pituitary activity [13]. *In the results obtained by us, we also observed a sharp decrease in the level of TSH and free T3 in blood plasma, but against the background of therapeutic normothermia.* Before considering adrenal/thyroid dysfunction in terms of critical illness, it is necessary to state why endocrinopathy considered in terms of dysfunction and not insufficiency. “Dysfunction” is a dysfunction of a system, organ or tissue of the body, expressed as an inadequacy of the response to stimuli [7], and it is the term “dysfunction” of the adrenal glands/thyroid gland that most fully characterizes the ambiguity of both laboratory and clinical results in the diagnosis of CICRI/TDCCI. When the term “adrenal insufficiency” is used, a violation in the HPA system itself implied, without affecting cortico-resistance in critical illness. *To date, there are no unambiguous criteria for diagnosing adrenal dysfunction in critical illness* [14]. The syndrome of euthyroid pathology in the acute phase of critical illness considered as an adaptive response of the hypothalamus-pituitary-thyroid gland-target tissue system and does not require correction by substitution therapy [3]. However, this recommendation should not considered as the only correct solution. A similar denial of hydrocortisone use observed in patients with septic shock until 2016 year, when the issue of "critically ill adrenal dysfunction" went from "does not need to be treated" to "needed to be treated." In conditions of damage to the diencephalic zone, the drug of choice is T4 at a dose of 2–3 μg/kg/day. The feasibility of combining T4 with T3 as initial therapy is controversial [10, 17]. We used in our clinical observation, due to the lack of an intravenous form of levothyroxine sodium, the oral form of L-T4. In addition, we did not use triiodothyronine due to its absence on the territory of the Russian Federation. Before starting treatment for critically ill thyroid dysfunction (TDCCI), the presence/absence of clinical evidence of critically ill adrenal dysfunction (CIRCI) should assessed. If CIRCI detected, hydrocortisone prescribed, and L-T4 prescribed on the second day after the start of hydrocortisone treatment.

According to the results of our study, the development of CIRCI and TDCCI during the use of therapeutic normothermia observed in a patient due to several reasons. First, the development of critical illness caused by CNS damage is an independent factor in the impairment of the hypothalamic-pituitary-adrenal system. At the same time, the duration of the critical illness leads to the depletion of the hypothalamic-pituitary-thyroid system and can no longer considered as a "syndrome of euthyroid pathology". Secondly, the purpose of using TTM is to suppress the activity of metabolic processes in the brain, which in turn also inhibits the activity of the hypothalamic region [2]. Thirdly, long-term use of sedative, narcotic and narcotic drugs to control body temperature, as well as to overcome muscle tremors, especially at target values of 36^0 C, also suppress the hypothalamic-pituitary system. The use of propofol, benzodiazepines and barbiturates increases the sensitivity of gamma-aminobutyric acid receptors (GABA receptors) to the GABA mediator and leads to inhibition of the activity of the cerebral cortex [11], which in turn can cause inhibition of the activity of the hypothalamus-pituitary-thyroid gland/adrenals system [9]. The use of selective α2-adrenergic receptor agonists (dexmedetomdine) suppresses the activity of the locus coeruleus of the brainstem [11]. In addition to the level of consciousness, the noradrenergic system also regulates the functional activity of the hypothalamus during a stress response [8]. Since opiate receptors are located not only in the pathways of pain, but also in the hypothalamus, hippocampus and amygdala, these areas are also subject to the inhibitory effects of drugs. Thus, drugs for general anesthesia, sedation and analgesia, routinely used during TTM and during ECMO, lead to inhibition of the function of the diencephalon.

Conclusion. Thus, the high level of cortisol observed on the day of admission against the background of vascular insufficiency was caused by corticoresistance and is not a criterion for making a decision on the appointment of hydrocortisone. The need for norepinephrine is a key factor in the decision to prescribe hydrocortisone. The development of the clinical picture of hypothyroidism (bradycardia, intestinal dysfunction) against the background of low TSH and free T3 during therapeutic normothermia was considered as TDCCI. L-T4 therapy made it possible to achieve normocardia, and combination with prokinetics and antiparetic therapy, resolution of intestinal dysfunction.

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CLINICAL CASE OF MEGALOBLASTIC ANEMIA IN A TEENAGER WITH NEW CORONAVIRUS INFECTION

This article presents a clinical case of newly diagnosed megaloblastic anemia in a 15-year-old teenager girl from the Republic of Sakha (Yakutia), in combination with intercurrent disease COVID-19. The new coronavirus infection occurs rapidly on the background of of suppressed hematopoiesis, with the development of complications in the form of community-acquired bilateral severe polysegmental pneumonia and bilateral exudative pleurisy, which required observation and treatment in a hospital. The performed standard complex therapy for megaloblastic anemia and pneumonia caused by SARS-CoV-2 made it possible to achieve clinical and laboratory improvement in the patient and restore the function of the red bone marrow.

Keywords: megaloblastic anemia, cobalamin deficiency, folic acid deficiency, COVID-19, new coronavirus infection, pneumonia.

Introduction. Megaloblastic anemia (MA) encompasses a heterogeneous group of macrocytic anemias characterized by the presence of large red blood cell precursors called megaloblasts in the bone marrow [2]. Megaloblastic anemia is ubiquitous, regardless of gender and age.

This condition is due to impaired DNA synthesis, which inhibits nuclear division. Cytoplasmic maturation, mainly dependent on RNA and protein synthesis, is less impaired. This leads to an asynchronous maturation between the nucleus and cytoplasm of erythroblasts, explaining the large size of the megaloblasts [2].