

CASE REPORTS OF PATIENTS WITH CHRONIC DISORDERS OF CONSCIOUSNESS IN OBSTETRIC AND GYNECOLOGICAL PRACTICE

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■ According to the modern classification system, chronic disorders of consciousness are defined as an altered state of consciousness that develops after coma and is accompanied by the restoration of wakefulness without the complete recovery of conscious activity for more than 28 days after traumatic brain injury. Clinical cases of chronic disorders of consciousness development in women after surgical interventions related to various obstetrical and gynecological pathologies, as well as after routine surgical interventions for comorbid somatic pathology, are of particular interest to obstetricians and gynecologists. In the presented chronic disorders of consciousness related clinical cases of operations for ectopic pregnancy, as well as consequences of elective surgery for gallstone disease, the development of hypo- and normogonadotropic ovarian insufficiency associated with chronic disorders of consciousness is described. The characteristics of the thyroid status, adrenocorticotrophic function, and vitamin D levels are given. Further in-depth examination and accumulation of data on patients with chronic disorders of consciousness may provide an opportunity to determine informative markers for prognostication of outcomes, as well as to develop new effective approaches to consciousness rehabilitation in this category of patients.

■ **Keywords:** chronic disorders of consciousness; gonadotropic function; ovarian insufficiency; thyroid function; adrenocorticotrophic hormone; vitamin D.

СЛУЧАИ ХРОНИЧЕСКОГО НАРУШЕНИЯ СОЗНАНИЯ В АКУШЕРСКО-ГИНЕКОЛОГИЧЕСКОЙ ПРАКТИКЕ

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■ Согласно современной классификации хронические нарушения сознания определяют как состояния, развивающиеся после комы и сопровождающиеся восстановлением бодрствования без полного восстановления осознанной деятельности более 28 дней после повреждения головного мозга. Особый интерес для акушеров-

гинекологов представляют клинические случаи развития хронического нарушения сознания у женщин после оперативных вмешательств, связанных с различной акушерской и гинекологической патологией, а также после плановых оперативных вмешательств по поводу сопутствующей соматической патологии. В представленных клинических случаях (после операций по поводу эктопической беременности, а также после планового оперативного вмешательства в связи с желчнокаменной болезнью) описано развитие гипо- и нормогонадотропной овариальной недостаточности, ассоциированной с хроническим нарушением сознания. Дана характеристика тиреоидного статуса, аденокортикотропной функции, уровня витамина D. Дальнейшее углубленное обследование и накопление данных о пациентках с хроническим нарушением сознания позволит определить информативные маркеры для прогнозирования исходов, а также разработки новых эффективных подходов к реабилитации сознания у данной категории больных.

■ **Ключевые слова:** хроническое нарушение сознания; гонадотропная функция; овариальная недостаточность; тиреотропная функция; аденокортикотропный гормон; витамин D.

Introduction

According to the modern classification, chronic disorders of consciousness (CDC) include variants emerging from coma, in which conscious activity is not restored 28 days after brain damage [1]. The main variants of CDC include the vegetative state (VS), or unresponsive wakefulness syndrome (UWS) according to the new terminology, and minimally conscious state “plus” and “minus” (MCS “plus” and “minus”). If during VS/UWS, in case of wakefulness, the patients show no signs of self-perception and environmental awareness, then with MCS, gaze fixation and tracking objects (MCS “minus”) and performing simple tasks (MCS “plus”) are possible.

The global prevalence of CDC is estimated from 2 to 5 cases per 100,000 population [2]. In the USA, the prevalence of CDC varies from 6.4 to 14 cases per 100,000 people [3]. In a study conducted in care institutions in Austria, it was revealed that the prevalence of CDC in this population is 1.5 cases per 100,000 people [4]. In Russia, no major epidemiological studies have been conducted. The largest study was a 3-year questionnaire survey in 15 hospitals in different regions of the country (2009–2012), where the total number of VS/UWS patients was 747 [5]. In 2017, a questionnaire survey was conducted in 35 hospitals in St. Petersburg, and results found that 705 people stayed in intensive care units for more than 30 days with a diagnosis of UWS in 2016, and 533 of them had CDC [1].

CDC is mainly caused by traumatic brain injury (42.12%), ischemic stroke (20.53%), cerebrosubarachnoid hemorrhage (17.36%), hypoxia (10.09%), brain tumors (4.46%), meningoencephalitis (4.25%), toxic lesions (1.06%), and hydrocephaly decompensation (0.13%) [5].

The clinical cases are of particular interest for obstetricians-gynecologists, which are associated with the development of CDC after surgical interventions for various emergency conditions (in particular, after surgeries for ectopic pregnancy and planned surgical interventions due to concomitant somatic pathology) and possible prognostic markers of recovery from the CDC. Several clinical examples of CDC patients are presented. All patients underwent examination and treatment in the department of anesthesiology and resuscitation of the Professor A.L. Polenov Russian Research Neurosurgical Institute, a branch of the V.A. Almazov National Medical Research Center (hereinafter, department).

Clinical case 1

The anamnesis revealed that patient A., 30 years old, was admitted in an urgent order to the gynecological department in connection with a right-sided tubal pregnancy terminated by tubal abortion type. Surgical intervention was performed through laparoscopic right-sided tubectomy, adhesiolysis, and small pelvis sanitation and drainage. During the surgery, circulatory arrest occurred. After a period of coma, arousal reactions (opening of the eyes) without signs of consciousness appeared, that is, there was a transition to VS/UWS. The expansion of consciousness to the level of MCS “plus” was registered within 1 month. For further treatment, the patient was transferred to the department.

Upon physical examination, the patient has a weight of 55 kg, height of 162 cm, and body mass index of 21 kg/m².

The skin was of a physiological color, and the mucous membranes were pale pink. Breathing was spontaneous through a tracheostomy cannula, and

hemodynamics was stable. Enteral feeding with mixtures was implemented through a nasogastric collapsing tube. The abdomen was not enlarged, and it was soft and painless in all parts upon superficial palpation. The peritoneal symptoms were negative, and swelling was not detected. Postoperative scars were in a satisfactory condition. Urination was through the urethral catheter, and the urine in the urine-collecting bag was light, and diapers were used for defecation.

Results of a neurological examination. The consciousness level corresponded to the MCS “plus,” as the patient fixed her gaze on her reflection in the mirror, followed some objects, and periodically bent her leg upon request. There were frequent stereotypical compulsive movements involving the muscles of the neck, arms, and trunk (permanent generalized hyperkinesia). The assessment score using the Coma Recovery Scale-Revised (CRS-R) [6, 7] was 16 points (assessment range was 0–23 points; auditory, visual, motor, and verbal functions were assessed, including communication and wakefulness). Assessment on the scale of paroxysmal sympathicotonia [8] was 6 points (1–6 points indicated mild degree; score from 0 indicated no signs of sympathicotonia to 13 severe sympathicotonia). Magnetic resonance imaging (MRI) of the brain revealed signs of previous hypoxic brain damage, as there were changes in the MR signal from the cerebral cortex and subcortical nuclei. On MRI of the chiasmo-sellar region, the size of the pituitary gland was 11×6×12 mm, with no displacement of structures, chiasm, and hypoplasia of the neurohypophysis and adenohypophysis. Fluorine-18-fluorodeoxyglucose positron emission tomography revealed signs of a decrease in metabolism in the cerebral cortex. The brain areas with the most intact metabolism were the anterior cingulate gyri of both hemispheres and medial parts of the temporal lobe cortex. An increase in metabolism in the subcortical nuclei was also noted, and metabolism in the cerebellar cortex and optic thalami was preserved. Thus, neuroimaging data indicated diffuse atrophic changes in the cerebral cortex with impaired glucose metabolism in the cerebral cortex.

Results of the gynecological examination. The mammary glands were symmetrical and developed. The skin over the mammary glands

had no abnormalities. There was no lactorrhoea. The external genitals were developed regularly.

Per speculum: The vaginal mucosa was hyperemic. The cervix was covered with intact mucosa, and the discharge was abundant and mucus-whitish.

Per vaginam: Uterus was in anteflexion, of normal size, dense, and mobile. The appendages on the left and ovary on the right could not be clearly palpated; there were no infiltrates.

The history revealed that the patient had a regular menstrual cycle before the disorder of consciousness, one tubal right-sided pregnancy, which was terminated by the tubal abortion type, and laparoscopic tubectomy on the right. After the impairment of consciousness, there was no menstrual reaction; and at the time of examination, the opsomenorrhoea duration was 1 month.

The results of hormonal examination (during opsomenorrhoea) are presented in Table 1.

Ultrasound examination of the pelvic organs. The body of the uterus was in avf, 44.7×33.1×37.1 mm in size, and the echo structure of the myometrium was of normal anatomy. The endometrium was 1.8 mm, with the echo structure of normal anatomy. The cervix was 30×20 mm, and endocervical cysts with a diameter of 4–6 mm were determined. The right ovary was 31.7×16.8×17.3 mm, with a volume of 4.9 cm³, and contained 9–10 follicles with a diameter of 2–3 mm, and the stroma was of normal volume. The left ovary was 34.5×25.8×21.4 mm, with a volume of 11.6 cm³, and contained 9–10 follicles with a diameter of 2–3 mm, and the stroma was of normal volume. Free fluid in the small pelvis was not detected. Imaging conditions were satisfactory. After repeated examination in 1 month, the body of the uterus was in avf, 46.8×55.6×37.4 mm in size, and the myometrium echo structure was of normal anatomy. The endometrium was 2.3 mm, and the echo structure was of normal anatomy. The uterine cervix was 30×20 mm, and endocervical cysts with a diameter of 4–6 mm were determined. The structure and volume of the ovaries had no changes compared with the results of primary ultrasound of the pelvic organs.

Ultrasound of the mammary glands. The skin of the mammary glands was normal on both sides, and the premammary fiber had no abnormalities. The thickness of the fibroglandular zone

Table 1 / Таблица 1

Dynamic endocrine testing data (the first study was performed 35 days after an episode of cardiac arrest in the presence of opsomenorrhoea)

Результаты гормонального обследования в динамике (первое исследование выполнено через 35 дней после эпизода остановки сердечной деятельности на фоне опсоменореи)

Indicators	Week 1	Week 2	Week 3	Reference values
Follicle-stimulating hormone, IU/L	0.53	1.58	1.86	2.5–14.4
Luteinizing hormone, IU/L	0.15	0.18	1.28	1.1–11.6
Progesterone, ng/mL	0.64	<0.64	<0.64	0–3.59
Estradiol, pmol/L	<73.4	102.03	155.24	73.4–587.2
Total testosterone, nmol/L	0.7	<0.69	<0.69	0.7–2.78
Prolactin, mIU/L	139.28	–	–	95.4–699.6
Thyroid-stimulating hormone, mIU/L	0.86	–	–	0.40–4.0
Free thyroxine, pmol/L	13.38	–	–	10.3–24.45
Free triiodothyronine, pmol/L	2.96	–	–	2.31–6.31
Adrenocorticotrophic hormone (morning), pmol/L	–	–	–	0–10.13
Adrenocorticotrophic hormone (evening), pmol/L	6.03	–	–	0–10.13
Cortisol (morning), nmol/L	13.4	–	–	13–69
Cortisol (evening), nmol/L	15.1	–	–	6.9–34.5
Vitamin D-25(OH), ng/mL	14.66	–	–	30–100

was 8 mm on the right and 7.8 mm on the left. The echogenicity of the fibroglandular zone was within normal limits on both sides, and the structure was of normal anatomy. The diameter of the ducts was 1.0–1.1 mm on both sides. Focal lesions were not revealed. The lymph nodes were not enlarged, according to the Breast Imaging-Reporting and Data System (BI-RADS) 1.

Results of the smear study for *oncocytopology* showed an inflammatory type of smear from the cervical surface and stratified squamous epithelium without atypia and an inflammatory type of smear from the cervical canal and epithelium without atypia.

According to the gynecological examination, hyperemia of the vaginal mucosa and abundant discharges were revealed. Cytological examination of the discharge revealed an inflammatory smear. Vaginitis was diagnosed, and the vagina was sanitized.

Based on the levels of follicle-stimulating and luteinizing hormones and prolactin (Table 1), hypogonadotropic normoprolactinemic ovarian insufficiency and opsomenorrhoea were diagnosed.

The vitamin 25(OH)D level was 14.66 ng/mL. According to the recommendations of the Russian Association of Endocrinologists [9], vitamin D deficiency was diagnosed, and substitution therapy was prescribed.

Thus, in the presence of neurological disorders and depression of consciousness to the MCS “plus” level — which resulted in hypoxia — hypogonadotropic normoprolactinemic ovarian insufficiency, anovulation, opsomenorrhoea, and vitamin D deficiency were revealed.

The patient received complex intensive treatment and underwent an early rehabilitation program. After a 1-year follow-up, it was possible to achieve relief of hyperkinesia during therapy, but no significant expansion of consciousness was noted, and the consciousness level corresponded to MCS “plus.” The patient’s menstrual cycle did not resume.

Clinical case 2

In female patient R., 37 years old, circulatory arrest occurred when performing right-sided tubectomy (tubal pregnancy). Repeated arrest of

blood circulation occurred in the intensive care unit 1 day later. Because of the cardiac arrhythmias identified, a cardioverter defibrillator was installed. Emerging from coma occurred with VS/UWS. Later, the patient was transferred to the department.

Upon physical examination, the patient has a weight of 50 kg, height of 155 cm, and BMI of 20.8 kg/m².

The skin was clean and pale. Visible mucous membranes were pale pink. There was a spontaneous breathing through a tracheostomy cannula, and hemodynamics were stable. Nutrition was performed through a gastrostomy tube. The abdomen was not enlarged and was soft and painless in all parts upon superficial palpation. Peritoneal symptoms were negative, and swelling was not detected. Postoperative scars were in a satisfactory condition. Urination was through the urethral catheter. The urine in the urine-collecting bag was light, and diapers were used for defecation.

Results of a neurological examination. The consciousness level corresponded to the UWS/Vs. The score on the CRS-R scale was 3 points. Assessment on the scale of paroxysmal

sympathicotonia showed 2 points. Tetraparesis with increased muscle tone was noted.

Results of the gynecological examination. The mammary glands were symmetrical and developed. The skin over the mammary glands had no abnormalities. There was no lactorrhoea.

The external genitals were developed.

Per speculum: The vaginal mucosa was hyperemic. The uterine cervix was covered with intact mucous membrane, and the discharge was abundant and mucus-whitish.

Per vaginam: Uterus was in a flexed position, of normal size, dense, and mobile. The appendages on the left and ovary on the right could not be clearly palpated; there were no infiltrates.

History revealed that the patient had a regular menstrual cycle before the disorder of consciousness, and there were three pregnancies in the anamnesis that ended with two uncomplicated cesarean sections and one right-sided tubal pregnancy terminated by tubal abortion type; surgical treatment through laparoscopic right-sided tubectomy was conducted on June 06, 2018. After disorder of consciousness, there was no menstrual reaction, and the duration of secondary

Table 2 / Таблица 2

Dynamic endocrine testing data (the first study was performed 9 months after an episode of cardiac arrest in the presence of amenorrhoea)

Результаты гормонального обследования в динамике (первое исследование выполнено через 9 мес. после эпизода остановки сердечной деятельности на фоне аменореи)

Indicators	Week 1	Week 2	Week 3	Reference values
Follicle-stimulating hormone, IU/L	14.4	4.41	7.01	2.5–14.4
Luteinizing hormone, IU/L	1.95	0.43	2.78	1.1–11.6
Progesterone, ng/mL	<0.64	<0.64	<0.64	0–3.59
Estradiol, pmol/L	<73.4	<73.4	<73.4	73.4–587.2
Total testosterone, nmol/L	<0.7	<0.7	<0.7	0.7–2.78
Prolactin, mIU/L	174.26	–	–	95.4–699.6
Thyroid-stimulating hormone, mIU/L	1.69	–	–	0.40–4.0
Free thyroxine, pmol/L	19.7	–	–	10.3–24.45
Free triiodothyronine, pmol/L	5.8	–	–	2.31–6.31
Adrenocorticotrophic hormone (morning), pmol/L	7.55	–	–	0–10.13
Adrenocorticotrophic hormone (evening), pmol/L	7.39	–	–	0–10.13
Cortisol (morning), nmol/L	8.22	–	–	13–69
Cortisol (evening), nmol/L	12.3	–	–	6.9–34.5
Vitamin D-25(OH), ng/mL	22.05	–	–	30–100

amenorrhea at the time of examination was 9 months.

Ultrasound examination of the pelvic organs. The body of the uterus was in afv, measuring 23.8×22.8×19.7 mm, and the echo structure of the myometrium was of normal anatomy. The endometrium was 1.3 mm, and the echo structure was of normal anatomy. The cervix was 30×16 mm. The right ovary could not be visualized because of enlarged intestinal loops. The left ovary was 11.8×5.5×9.7 mm, with a volume of 0.3 cm³, and the follicular apparatus was not expressed. Free fluid in the small pelvis was not detected. Visualization was difficult.

Ultrasound of the mammary glands. The skin of the mammary glands was normal on both sides, and the premammary fiber had no abnormalities. The thickness of the fibroglandular zone was 7.1 mm on the right and 6.6 mm on the left. The echogenicity of the fibroglandular zone was within normal limits on both sides, and the structure was of normal anatomy. The diameter of the ducts was 1.0–1.2 mm on both sides. Focal lesions were not revealed. The lymph nodes were not enlarged based on the BI-RADS 1.

Results of examination for *oncocytopology* showed an inflammatory type of smear from the cervical surface and stratified squamous epithelium without atypia and an inflammatory type of smear from the cervical canal and cervical epithelium without atypia.

The gynecological examination of the patient revealed hyperemia of the vaginal mucosa and abundant discharges. Vaginitis was diagnosed, and the vagina was sanitized.

Based on the hormonal examination data presented in Table 2, the diagnosis of normogonadotropic normoprolactinemic ovarian insufficiency with secondary amenorrhea was made.

The vitamin 25(OH)D level was 22.05 ng/mL. Vitamin D deficiency was diagnosed, and substitution therapy was prescribed.

Thus, in patient R., in presence of complete inhibition of mental functions to the level of VS/UWS, normogonadotropic normoprolactinemic ovarian insufficiency, amenorrhea, and signs of vitamin D deficiency were registered. Considering the episode of deep vein thrombosis of the lower leg and thigh, hormonal therapy was contraindicated. After a 1-year follow-up, no

signs of recovery of consciousness were detected, and the patient remained in a state of chronic VS/UWS. The patient also had amenorrhea.

Clinical case 3

The anamnesis revealed that patient G., 41 years old, in the postoperative period after laparoscopic surgery for cholecystectomy, had pulmonary artery thromboembolism (PATE). After a period of coma, there was a transition to the VS/UWS. After 3 months, she was transferred to the department for further treatment.

The objective examination revealed a weight of 60 kg, height of 162 cm, and BMI of 22.4 kg/m².

The skin was clean and pale. Visible mucous membranes were pale pink. Respiration was spontaneous through a tracheostomy cannula, and hemodynamics was stable. Nutrition was through a gastrostomy tube. The abdomen was not enlarged and was soft, painless in all parts upon superficial palpation, and the peritoneal symptoms were negative. Swelling was not detected. Urination was through the urethral catheter. The urine in the urine-collecting bag was light, and diapers were used for defecation.

Results of a neurological examination. Assessment on the CRS-R scale revealed 7 points (MCS “minus”); the score on the scale of paroxysmal sympathetic hyperactivity was 6 points (mild). Spastic tetraparesis with constant hyperkinesia (eye squeeze and compulsive mouth movements) was noted.

MRI of the brain revealed diffuse atrophic changes with signs of secondary normotensive hydrocephalus and bilateral lesions of the basal nuclei, which was a manifestation of hypoxic-ischemic brain damage.

Results of the gynecological examination. The mammary glands were symmetrical and developed. The skin over the mammary glands had no abnormalities. There was no lactorrhoea. The external genitals were developed.

Per speculum: The vaginal mucosa was hyperemic, and the uterine cervix was covered with intact mucous membrane. The discharge was moderate and mucus-whitish.

Per vaginum: Uterus was in afv, of normal size, dense, and mobile. The appendages on both sides could not be clearly palpated; there were no infiltrates.

Table 3 / Таблица 3

Dynamic endocrine testing data (the first study was performed 4 months after an episode of pulmonary embolism in the presence of opsomenorrhea)

Результаты гормонального обследования в динамике (первое исследование выполнено через 4 мес. после эпизода тромбоза легочной артерии на фоне опсоменореи)

Indicator	Week 1	Week 2	Week 3	Reference values
Follicle-stimulating hormone, IU/L	5.73	2.98	4.67	2.5–14.4
Luteinizing hormone, IU/L	8.67	0.69	5.51	1.1–11.6
Progesterone, ng/mL	<0.64	0.95	0.79	0–3.59
Estradiol, pmol/L	198.9	107.53	291.03	73.4–587.2
Total testosterone, nmol/L	<0.7	<0.7	<0.7	0.7–2.78
Prolactin, mIU/L	142.5	–	–	95.4–699.6
Thyroid-stimulating hormone, mIU/L	3.9	–	–	0.40–4.0
Free thyroxine, pmol/L	15.4	–	–	10.296–24.45
Free triiodothyronine, pmol/L	5.25	–	–	2.31–6.31
Adrenocorticotrophic hormone (morning), pmol/L	7.4	–	–	0–10.13
Adrenocorticotrophic hormone (evening), pmol/L	8.17	–	–	0–10.13
Cortisol (morning), nmol/L	23.8	–	–	13–69
Cortisol (evening), nmol/L	18.9	–	–	6.9–34.5
Vitamin D-25(OH), ng/mL	16.4	–	–	30–100

History revealed that the patient had a regular menstrual cycle before the disorder of consciousness, and there was one delivery at term through the vaginal birth canal. After disorder of consciousness, there was no menstrual reaction, and the duration of opsomenorrhea was 4 months.

Ultrasound of the pelvic organs. The dimensions of the uterus were 57.5×49.9×53.4 mm, and the echo structure of the myometrium had no abnormalities. The endometrium was 1.6 mm. The uterine cervix was 36×22 mm. The right ovary was 29.2×14.6×17.2 mm, with a volume of 3.9 cm³, and contained two to three follicles up to 3 mm in diameter, and the stroma was in the usual volume. The left ovary was 21.8×11.9×18.3 mm, with a volume of 2.5 cm³, and it contained two to three follicles with a diameter of 3 mm, and the stroma was of the usual volume. Free liquid was not detected. Imaging conditions were satisfactory.

Ultrasound of the mammary glands. The skin of the mammary glands was normal on both sides, and the premammary fiber had no abnormalities. The thickness of the fibroglandular zone was 8.2 mm on the right and 7.1 mm on the left. The echogenicity of the fibroglandular zone was

within normal limits on both sides, and the structure was of normal anatomy. The diameter of the ducts was 1.0–1.2 mm on both sides. In the upper outer quadrant of the right mammary gland, a hypoechoic formation of 6.1×2.7 mm in size was revealed. The lymph nodes were not enlarged based on BI-RADS 2 MD and BI-RADS 1 MS.

According to the results of a study from the cervical surface and canal for *oncocytology*, stratified squamous epithelium and cervical epithelium without atypia were obtained.

The vitamin 25(OH)D level was 16.4 ng/mL. Vitamin D deficiency was diagnosed, and substitution therapy was prescribed.

Thus, according to the results of hormonal examination data presented in Table 3, in the presence of depression of consciousness up to MCS “minus,” normogonadotropic normoprolactinemic ovarian insufficiency was revealed, as well as anovulation, opsomenorrhea, and right mammary gland cyst.

Hormone therapy was contraindicated because of a history of massive PATE. The menstrual reaction was noted once after 14 months of CDC. The patient was repeatedly admitted to the department after 4 months. Neurologically,

Table 4 / Таблица 4

Endocrine testing data (the study was performed 16 months after an episode of cardiac arrest (pulmonary embolism) in the presence of opsomenorrhea)

Результаты гормонального обследования (исследование выполнено через 16 мес. после эпизода остановки сердечной деятельности (тромбоэмболия легочной артерии) на фоне опсоменореи)

Indicator	Chronic disorder of consciousness for 16 months	Reference values
Follicle-stimulating hormone, IU/L	3.96	2.5–14.4
Luteinizing hormone, IU/L	5.52	1.1–11.6
Progesterone, ng/mL	<0.636	0–3.59
Estradiol, pmol/L	–	73.4–587.2
Total testosterone, nmol/L	<0.7	0.7–2.78
Prolactin, mIU/L	337	95.4–699.6
Thyroid-stimulating hormone, mIU/L	4.01	0.40–4.0
Free thyroxine, pmol/L	11.3	10.3–24.45
Free triiodothyronine, pmol/L	4.6	2.31–6.31
Adrenocorticotrophic hormone (morning), pmol/L	7.01	0–10.13
Adrenocorticotrophic hormone (evening), pmol/L	4.82	0–10.13
Cortisol (morning), nmol/L	444.1	13–69
Cortisol (evening), nmol/L	141.5	6.9–34.5

the expansion of consciousness to MCS “plus” was noted, as the patient fixed and turned her gaze on the speech addressed and finished a sentence from well-known poems.

Ultrasound examination of the pelvic organs upon repeated hospitalization. The dimension of the uterus was 48.4×49.4×53.2 mm, and the echo structure of the myometrium had no abnormalities. The endometrium was 7.8 mm, homogeneous. The uterine cervix was 35×20 mm in size. The right ovary was 23.2×17.4×18.5 mm, with a volume of 3.8 cm³, and contained four to five follicles up to 4–5 mm in diameter. The left ovary was 25.1×18.4×19.7 mm, with a volume of 4.7 cm³, and contained three follicles up to 4–5 mm in diameter. There was no free fluid in the pelvic cavity. Imaging conditions were satisfactory.

Ultrasound of the mammary glands during repeated hospitalization. The skin of the mammary glands was normal on both sides, and the pre-mammary fiber had no abnormalities. The thickness of the fibroglandular zone was 8.15 mm on the right and 7.1 mm on the left. The echogenicity of the fibroglandular zone was normal on both

sides, and the structure was of normal anatomy. The diameter of the ducts was 1.2 mm on both sides. The lymph nodes were not enlarged. In the upper outer quadrant, a hypoechoic formation of 9×5 mm in size and a formation of 4.6×2.6 mm in size on the right were revealed based on BI-RADS 2 MD and BI-RADS 1 MS.

According to the results of smear study for *oncocytopology*, stratified squamous epithelium and cervical epithelium without atypia were obtained.

Thus, in the presence of MCS “minus,” according to the hormonal examination presented in Table 4, normogonadotropic normoprolactinemic ovarian insufficiency, opsomenorrhea, and anovulation were diagnosed. Given a history of massive PATE, hormone therapy was contraindicated.

Discussion

It should be noted that the hormonal state in CDC patients is almost not studied. The literature describes cases of prolonged coma in pregnant women after severe traumatic brain injury, which resulted in VS/UWS. With therapy aimed at maintaining pregnancy, it was possible to achieve the

fetal gestational age sufficient for delivery [10–12]. A scandalous case in a hospice is known when a CDC patient was subjected to violence by medical staff, and the resulting pregnancy ended with delivery at term [13]. However, no fundamental studies summarizing the data on neurohumoral and endocrine disorders in CDC patients have been conducted.

In the above clinical examples, in the case of amenorrhea/opsomenorrhea, hypogonadotropic normoprolactinemic ovarian insufficiency was diagnosed in patient A. and normogonadotropic normoprolactinemic ovarian insufficiency in patients R. and G. It should be noted that the gonadotropin levels of healthy women during the menstrual cycle fluctuate widely; therefore, the division of amenorrhea into normogonadotropic and hypogonadotropic is largely provisory since regulatory disorders similar in pathogenesis can lead to different degrees of decrease in the secretion of gonadotropin-releasing hormone and, therefore, to different degrees of reduction of gonadotropins in the blood.

The hypothalamus plays a unique role in neuroendocrine regulation. In addition to the secretion of releasing hormones and statins, hypothalamic neurons are involved in the regulation of appetite, sleep and wakefulness rhythms, and body temperature maintenance. The disturbance of the frequency and impulse secretion of gonadotropins is a common link in the pathogenesis of all forms of ovarian insufficiency. Hormone replacement therapy with estrogen and progesterone is prescribed to patients with ovarian insufficiency. There is overwhelming evidence to support the protective effect of estrogen in various diseases. Estrogens induce a cascade of cellular and molecular effects that include both genomic and nongenomic mechanisms in brain injury. They can also restore the integrity of the blood–brain barrier [14] and subsequently reduce cerebral edema [15], improve cerebral circulation [16–18], provide an antioxidant effect [19–21], reduce inflammation [14, 22, 23], and activate cell survival mediators [24–26]. Progesterone also has neurostimulating and neurosteroidal effects on the central nervous system, and its neuroprotective effect has been demonstrated in numerous preclinical and clinical studies. Progesterone reduces cerebral edema [27, 28], restores the blood–brain barrier

integrity [29, 30], reduces the inflammatory response [31], and prevents brain cell necrosis and apoptosis [32].

It can be assumed that therapy with estrogen and progesterone in CDC patients, by altering the synthesis and metabolism of neurotransmitters and neuropeptides, will create a positive feedback by acting on the adenohypophysis through a long regulation loop. The adenohypophysis through gonadotropic hormones influences the hypothalamus through an ultrashort feedback loop, which activates the cerebral cortex using neurotransmitters.

That is why the prescription of hormonal replacement estrogen–progesterone therapy in a cyclic mode in CDC patients seems to be promising in terms of improvement of the results of treatment of this category of patients, considering the concomitant complications caused by both the critical condition itself and prolonged immobilization. In several patients, there are serious restrictions on the use of this therapy. Several associated complications (PATE and deep vein thrombosis) are contraindications, and prolonged immobilization can be considered a risk factor.

Further accumulation of the database on the results of hormonal examination will help identify markers for predicting outcomes in CDC patients.

Conclusion

The study of the mechanisms of regulation of the pituitary-hypothalamic system in CDC patients will contribute to the search for new effective approaches to the treatment and rehabilitation of this category of patients.

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