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NEW CORONAVIRUS INFECTION COVID-19 IN A PREGNANT WOMAN COMPLICATED WITH ACUTE TRANSVERSE MYELITIS

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The incidence of various neurological complications among hospitalized patients with novel coronavirus infection (NCI) COVID-19 ranges from 13% to 40% according to the literature. To date, the variants and nature of clinical manifestations, the impact of neurological complications of NCI COVID-19 on pregnancy are poorly understood due to the insufficient number of stud-ies on this issue. The article presents a clinical case of the development of acute transverse myeli-tis in a pregnant woman against the background of NCI.

Keywords: COVID-19, new coronavirus infection, pregnancy, neurological complications, acute transverse myelitis.

Introduction. After two years of new coronavirus infection (NCI) COVID-19 pandemic it became evident that it is a multisystem disorder. SARS-CoV-2 binds to the cell receptor of angiotensin transforming enzyme-2 (ACE2), activating its S-protein necessary for the SARS-CoV-2 intrusion into a cell. ACE2 is located in cytoplasmic membrane of numerous cell types of a human, including II-type alveolar cells in the lungs and entherocytes of the small intestine, endothelial cells of the arteries and veins, cells of the smooth musculature of the heart arteries, adrenal glands, bladder, brain and others [1], which predetermines the polyorganic nature of the disorder.

According to the data of various scientists, neurological complications of the NCI, are observed in 13-40% of hospital patients [2, 3]. A number of researchers revealed a correlation between the NCI and frequency of occurrence of this or that neurological pathology due to hypoxia associated with respiratory deficiency [5, 6]. However, at the current stage numerous pathogenic factors of the SARS-CoV-2 damage to the central (CNS) and peripheral (PNS) nervous systems are being discussed. Both the virus invasion, and its mediating effect are being studied taking into account the presence of ACE2 in neurons and glial cells of the brain and spinal cord [7, 8]. Apparently, SARS-CoV-2 has a very high neuro-invasive potential relative to the previous coronaviruses.

Acute transverse myelitis (ATM) is one of the neurological complications of the NCI. It is an acute focal inflammatory autoimmune disease of the spinal cord that leads to motor, sensory and autonomic dysfunction [12, 13]. Frequency of ATM occurrence is 1-8 cases per million people per year [14]. There exist two types of the latent period before the onset of clinical manifestations. The first type is a short latent period (from 2 hours to 5 days). It is caused by direct neurotropic effect of the virus. The second type is a long latent period (from 10 days to 6 weeks). It is indicative of the post-infectious neurological complication [2]. Currently 43 cases of ATM, that have developed against the background of NCI, have been described [15, 16]. Notably, only single cases of the first type ATM development together with the signs of NCI such as fever, cough and general weakness, were depicted [17, 18, 20]. We have not come across the information of the NCI complicated by ATM in pregnant women in the available published papers.

We present our own clinical case report of the favorable outcome of the NCI COVID-19 complicated by community-acquired bilateral polysegmental pneumonia and ATM with short latent period.

A pregnant woman M., 24 years old, resident of Magnitogorsk. It was the patient's first wanted pregnancy. The patient was under regular medical check-up from the 7-8th week. The pregnancy course was complicated by threatened miscarriage at the 11th, 19th and 22nd gestation week (the patient received treatment in the day-stay hospital). At the 24th gestation week an increase in the level of transaminase (ALT up to 45 IU/L) and mild hypochromic anemia were registered. The patient started to receive iron therapy. At the 25th week she fell down on the buttocks (the patient "slipped"), did not seek treatment, did not suffer from pain in the back, locomotor functions were not impaired. Specifics of the somatic anamnesis: infrequent cold-related diseases; in 2015 she had combined trauma due to road accident (by patient's own account – she had pelvic fracture, complete recovery). She did not have NCI COVID-19 prior to maternity hospital admission, and had negative epidemiological anamnesis for NCI.

The patient had an acute onset of a disease on 23 February 2022 when there appeared pain in the back, ostalgia, the temperature increased to 38.6°C. In 40-60 minutes after the disease onset the patient noted sharp pains in the lumbar region with irradiation to the thoracic spine; then tensive lower abdominal pain, weakness in the lower extremities that increased within the next 20-30 minutes. The patient could not stand up unassisted, felt sensory loss and numbness in her lower extremities. She was transported to the maternity hospital of Magnitogorsk city by an ambulance team. No pregnancy pathology was detected. In accordance with the intra-hospital patients' routing she was hospitalized to the

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department of infectious diseases where she got a positive SARS-CoV-2 ICT (immunochromatographic test for quantitative detection of a virus antigen).

Multispiral computed tomography (MSCT) of the chest organs has been performed: CT-signs of the interstitial changes of both lungs, medium probability of COVID-19, degree of severity CT-1 (5%). MSCT of the lower thoracic and lumber regions of the spine has been performed: no signs of haematomyelia have been registered; manifestations of the advanced degenerative disc disease, spondylarthrosis, L_4-S_1 disc protrusion, degenerative joint disease of sacroiliac joints were registered. Objective status: the status of the pregnant woman is that of medium severity due to lung damage, intoxication syndrome, plegia. Respiratory rate is 18 breaths per minute, SpO_2 98% without respiratory support.

Neurological status: the face is symmetrical, midline tongue protrusion, no bulbar disorders. The upper extremities have full range of motion. There is no motion in the lower extremities. Foot clonus. Decrease in sensation due to impaired conduction function: on the right side D_{10}, on the left side D_{11}-D_{12}; pain on palpation at D10, bitter pain on palpation at L_3-L_4. Pelvic organ dysfunction is present: no urge to defecate and urinate.

Laboratory evaluation revealed: leukocytosis ($12.3x10^9$/L), mild anemia (Hb 94 g/L); C reactive protein (32.7mg/L), procalcitonin <0.1 ng/mL, positive SARS-CoV-2 (PCR) dated 23 February 2022.

Diagnosis at admission: pregnancy 27 weeks. NCI COVID 19, virus identified, moderate severity. Community-acquired bilateral viral pneumonia, CT-1, respiratory deficiency 0. Unspecified acute transverse myelitis at the thoracic spine. Lower paraplegia with decrease in sensation due to impaired conduction function. A differential diagnosis between spinal stroke and myelitis has been performed.

Magnetic resonance imaging (MRI) of the cervical, thoracic and lumber section of the spinal cord reveals the following: MRI signs of initial dystrophic changes of the cervical part of the spinal cord, focal changes of the Th_{11} vertebral body (probably a small hemangioma), MRI signs of synovitis of sacro-iliac joint, initial MRI signs of dystrophic changes of the lumber section of the spinal cord. Lumbar puncture has been performed, 1.5 ml of colorless clear fluid has been taken, protein 0.099 g/L, cytosis 1.2 x 10^6/L, glucose 4.9 mmol/L. SARS-CoV-2 (PCR) from cerebrospinal fluid was negative. The treatment was started. The patient received: antiviral therapy (interferon alfa-2b, 10000 IU/mL, endonasal, 3 drops per each nasal passage 5 times/day (t/d), antibacterial therapy (intravenous ceftriaxone 2 ml x 1 (t/d), subcutaneous unfractionated heparin 5000 unit/day, metabolic therapy (cytoflavin, intravenous bolus injections), nootropic agents (citicoline, 1000 mg x 1(t/d), intravenous fluid drip). Under advice of the regional multidisciplinary case management team, the pregnant woman was routed to maternity hospital of the Chelyabinsk Regional Clinical Hospital № 2 (RCH №2). On 3 April, 2020 the hospital was repurposed to an infectious diseases hospital to provide medical assistance to pregnant, parturient women, and puerperants with NCI as well as their newborns in the territory of the Chelyabinsk city and Chelyabinsk Region. In accordance with the recommendations of the case management team the patient was also given the following drugs: methylprednisolone 1000 mg intravenous fluid drip, 1 t/d for 5 days; omeprazole 20 mg capsules x 2 t/d per os; subcutaneous nadroparin 0.4 ml x 2 t/d; IV infusion of monoclonal antibodies etesevimab 1400 mg + bamlanivimab 700 mg, antiviral therapy remdesivir 200 mg, IV fluid drip.

25 February 2022, on the 3rd day from the disease onset the patient was transported to the maternity hospital of the RCH №2 by helicopter, was presented to the emergency department with complaints of acute highly intensive pain in the low back, without irradiation that increased with movement, lower limb weakness up to the impossibility to produce motion in them. By the woman's own account against the background of the received therapy she noted some improvement – she noted single spontaneous movement in left limb. The patient's status on hospital admission is that of moderate severity.

The patient was awake, Glasgow coma scale (GCS) score of 15, oriented to place, time and space. NEWS score of 0. Body mass index – 29.7. Symmetric face, midline tongue protrusion, no bulbar disorders. The upper extremities have full range of motion, decrease in sensation of the due to impaired conduction function on the right side D_{10}, on the left side - D_{11-12}. Pain on palpation at D_{10}, acute painfulness at L_3-L_4. No motion in the lower extremities. Unlabored nasal breathing. SpO_2 - 98% without respiratory support. Blood pressure of 110/70 (110) mm Hg, heart rate of 98 beats per minute. The abdomen is enlarged due to pregnant uterus in accordance with gestational age, non-tender in all the sections. The uterus is normally toned. Active fetal movements. Fetal heart rate is clear and even, of 135-144 beats per minute.

Neurological status of the pregnant woman: lower paraparesis with decrease in muscular strength in the left limb up to 1 score, plegia in the right limb. The muscle strength score in hands is 5. The tendon reflexes in the legs are brisk to clonus, symmetrical, no pathological reflexes. Coordinating tests: the patient performs finger - nasal test accurately, without intention, D=S, impaired conduction function from the level T12 on the left, L1 on the right. Autonomic functions are not violated. Meningeal syndrome is negative. Pronounced pelvic disorders with no urge to urinate or defecate. Laboratory evaluation revealed the following: mild anemia (Hb 104 g/L, hematocrit 29%), stab shift up to 24%, C reactive protein – 18 mg/L, activated partial thromboplastin time 40.1%, Lactate 3.2 mmol/L, Aspartate aminotransferase - 45 (unit/L), Alanine aminotransferase 34 (unit/L). The levels of leukocytes, thrombocytes, glucose, bilirubin, creatinine, ferritin, D-dimer, lactate dehydrogenase, procalcitonin, hemostatic profile were within the normal range.

Ultrasound screening of the fetus, Doppler examination of the uteroplacental and fetal blood flow did not reveal any pathology. On 25 February 2022 a regional multidisciplinary case management team (obstetrician-gynecologist, neurologist, anesthesiologist-intensivist, infectious disease specialist, neurological surgeon) meeting was held. It was recommended to continue the NCI treatment with the change in antibacterial drug (meropenem 1 g x 3 t/d, IV), methylprednisolone pulse therapy, metabolic therapy (cytoflavin 10 mg/day), nootropic agents (citicoline, 1000 mg x 1(t/d) IV), thromboembolic complication prophylaxis (nadroparin 0.6 s/c, daily), anti-anemic therapy (Iron(II) sulfate / ferrous sulfate 100 mg + ascorbic acid 60 mg tablet x 2 t/d per os).

Positive dynamics was observed in the course of the treatment: motions appeared in the right foot toes, the strength in the proximal part of the left limb increased (the patient started to bend the leg in the knee joint, to hold it in this position on the bed). Partial regress of the sensory impairment was also registered. The border of the hypostesia lowered from both sides: 1segment on the right side, 2 segments on the left side. Position sense was still impaired. However, this impairment could be evaluated as the one of moderate degree of manifestation (it was difficult for the patient to name the toes of her left foot and movement

direction in them, she could tell the toes of the right foot, sometimes mixed up the movement direction). The patient already could sit in the bed unassisted for a long time with her legs down, started to feel the urge for urination.

On 27 February 2022 paraesthesiae appeared in the lower limbs, sensory impairment decreased, she could raise her pelvis a little bit above the bed, leaning on her legs. Weakness in the lower limbs, tingling in the heels persisted. General status is of moderate severity due to focal neurological pathology. GCS score of 15. NEWS score of 0. SpO_2/FiO_2 – 466. A positive dynamics was observed in the neurological status: gradual recovery of the sensation and increase in the motion volume in the lower extremities. The patient was verticalized with the assistance of the healthcare workers. The defication and urination were under full control. Upon the end of methylprednisolone pulse therapy, the patient was given prednisolone per os at an initial daily dose (based on her body mass) 70 mg in the morning with a 5 mg decrease every three days until complete cessation.

On 3 March 2022 taking into account the positive dynamics in the patient's status, absence of the damage to the bronchopulmonary system, normal body temperature along the whole course of treatment, absence of changes in the laboratory parameters, negative SARS-CoV-2 (PCR) from nasopharyngeal swab dated 1 March 2022, she was dismissed from the maternity hospital of the RCH №2 with subsequent admission to the inpatient neurological department of the Clinics of the South Ural State Medical University of the Chelyabinsk city. The patient was transported by medical ambulance. By 11 March 2022 a regress in the clinical symptoms of the ATM and patient's complaints was observed. She was dismissed from the hospital in a satisfactory condition and recommended to continue taking prednisolone 10 mg/day per os every other day. Further on, she was under ambulatory observation of neurologist, obstetrician-gynecologist, including the use of telemedicine consultations. Stable positive dynamics was noted in terms of ATM. The pregnancy proceeded without obstetric complications.

On 18 May 2022 the patient was examined by a neurologist. Diagnosis: residual symptoms of the previous acute transverse myelitis at the level of thoracic spine, cone of the spinal cord (as of 22 February 2022). Syndrome of central lower spastic paraparesis (decrease in the algesthesia along the anteroexternal surface of the femur and shin till the lower third of the left leg shin, femur and knee to the shin – on the right leg, pelvic organ function was not disturbed. Delivery without active pushing phase is recommended. On 23 May 2022 the patient performed delivery at the gestation age 38-39 weeks on a scheduled basis via cesarean section without complications. A girl was born weighing 3,000 g, 50 cm in height, Apgar score 8/9. They were discharged from the hospital on the 4th day after the delivery in a satisfactory condition. Morphological characteristics of placenta: involutional-distrophic and compensatory reactions in placenta corresponded to the gestation age.

Discussion. In view of the NCI pandemic, researchers pay special attention to the infectious myelitis, enteroviruses, herpes-zoster virus, herpes simplex virus of type 1, and zika virus being considered its etiological agents in the pre-covid era [17]. Specialists assume a pathogenetic link between the NCI complicated by ATM and cytokine storm mechanism, explaining the clinical picture of the disease by inflammatory reaction with the release of various inflammation mediators. Moreover, if activated immune cells enter the CNS, then immune mediated inflammation of the brain or spinal cord develops [17, 20, 21]. Direct entry of the virus into the spinal cord is possible especially if the permeability of the blood-brain barrier is increased. We assume that in this particular clinical case, NCI-associated ATM was caused by systemic inflammatory response despite negative SARS-CoV-2 PCR in the CSF. This is evidenced by an obvious curative effect of methylprednisolone pulse therapy together with complex NCI COVID-19 therapy. We have studied the majority of the described cases of NCI-associated ATM in the non-pregnant state. What calls attention to itself is the fact that the disease manifestations develop after a patient's discharge from the hospital or days/weeks after the viral infection symptoms relief [2, 14, 20, 21, 27]. In this particular case symptoms of ATM (clinical picture of sensory and motor disorders together with pelvic organ dysfunction) developed together with the acute onset of NCI COVID-19. Such disease development variant is rather rare. Much more often, lower paraparesis and urine retention gradually increase within several days [27, 29].

According to the published research data, the diagnosis of ATM is based on clinical presentations, spinal cord MRI report and CSF analysis. A number of researchers described patients with NCI and clear clinical manifestations of ATM whose spinal cord MRI did not reveal any pathological foci just as in the given clinical case report [17, 29]. In the CSF analysis in patients with NCI and ATM different mild shifts in protein content and cytosis were observed. In all the available case descriptions the CSF glucose level was within the normal range [17, 18, 23, 30]. In the reported clinical case the patient's CSF demonstrated normal cytosis and protein content against the elevated glucose level. Different outcomes of NCI-associated myelitis in non-pregnant state were reported: from complete recovery of the lost functions to persistent neurological deficit and even deaths [20, 31].

Conclusion. In the presented case report what attracts the attention is the peracute onset of ATM against the background of NCI COVID-19 in a pregnant woman with the developed clinical manifestations of sensory and motor impairment combined with pelvic organs dysfunction, quick persistent positive dynamics, symptoms regression and recovery of the impaired functions of the spinal cord against the background of the timely adequate comprehensive therapy of NCI and ATM which was approved by specialists of the multidisciplinary telemedicine case management team.

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ORGAN-SPARING TREATMENT FOR ENDOMETRIAL CANCER (CLINICAL CASE)

Endometrial cancer ranks among the leading malignant diseases of the female reproduc-tive system and remains a pressing issue in oncogynecology. Although endometrial cancer is pre-dominantly a disease of the menopausal period, 10-14% of cases are diagnosed in patients of re-productive age. Most of these women do not yet have children, making fertility-preserving treatment a priority. As such, if a patient wishes to maintain her reproductive function, standalone hormone therapy may be conducted. Hormonal treatment induces atrophy of the tu-mor-altered endometrium, after which estrogen-progestin medications restore its function. The article presents a clinical case of successful realization of generative function following a favora-ble outcome of endometrial cancer treatment. A 41-year-old patient with low ovarian reserve and unrealized reproductive potential was offered fertility-preserving treatment, involving hyster-oscopic resection followed by hormone therapy. In deciding on fertility-preserving treatment, the presence of favorable prognostic factors was considered: positive receptor status of the tumor and tumor differentiation degree. After treatment, follow-up examinations revealed no recur-rence or disease progression, and the patient was advised to plan for pregnancy using assisted reproductive technologies. However, this was not carried out because of the patient's spontane-ous pregnancy. During gestation, the patient underwent regular oncogynecological examinations according to the established schedule, and no recurrence or disease progression was detected. At 35 weeks of gestation, a surgical delivery was performed, resulting in the birth of a girl weighing 2820 g, with a height of 48 cm and an Apgar score of 8/8 points. This clinical case demonstrated that fertility-preserving treatment for early-stage endometrial cancer not only cured the malignant process but also subsequently fulfilled the generative function, without reducing the effective-ness of the treatment.

Keywords: endometrial cancer, organ-preserving treatment, hormone therapy, clinical case.

Introduction. In contemporary society, a significant proportion of women of childbearing age are susceptible to gynecological cancer, many of whom wish to preserve their fertility for the future [25]. Uterine body cancer (UBC) is one of the leading malignancies affecting the female reproductive system. According to statistics, in 2019, 62,000 new cases of endometrial cancer (EC) were diagnosed worldwide, and alarmingly, both the incidence and mortality rates are projected to increase by 1-2% annually [2, 16, 17, 23]. For comparison, American healthcare statistics indicate the annual identification of approximately 40,000 new cases, and an increase in the frequency of UBC by about 50% over the past 20 years [9]. The lowest mortality rates due to EC are recorded in Central and South Asia, while the highest rates are observed in African countries [15]. UBC survivors may experience treatment-related issues, including infertility, early menopause, sexual dysfunction, and lymphatic edema of the lower extremities [26]. In Russia, EC remains the most common oncogynecological disease, ranking first in the structure of gynecological cancer. In 2021, there were 22,951 patients registered [3]. Among them, 84.4% were diagnosed at stages I-II with a 5-year survival rate of up to 73.1%. Women aged 45 to 74 are more frequently affected, with an average age of diagnosis at 62 years [18]. However, in rare cases, EC can be diagnosed in patients of reproductive age. In such situations, the oncogynecologist faces not only the challenge of treating the young patient but also the possibility of preserving fertility [13, 21, 22]. In 5.2% of cases, the diagnosis was made in patients of reproductive age (18 to 45 years), amounting to an absolute number of 1,317 individuals. Over the past 10 years (2006-2016), there has been not only a steady increase in the incidence of EC,

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