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Reports

Therapeutic and Psychological Challenges Treating Patients in a Covid Maternity

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Abstract

On pregnant patients, the SARS COV-2 infection can present a fulminant evolution, because of a small decrease in respiratory volumes and an exacerbation of the systemic inflammatory response. In addition to these pathophysiological mechanisms that cause systemic degradation, neuropsychiatric impairments should also be considered. These are frequently encountered as a result of the modification of the birth plan, the fact that in Romania positive patients with COVID cannot give birth in the maternity hospitals where they were treated before the infection. Another important factor is the deprivation of the newborn mother during hospitalization.

A 26-year-old patient with a 30-week pregnancy and a confirmed SARS COV-2 infection two days ago is admitted to our clinic for deteriorating general condition and acute respiratory failure: dyspnea with orthopnea, tachypnea, decrease in oxygen saturation up to 69% in atmospheric air. During the hospitalization, the patient required intensive therapy with respiratory support in various non-invasive ventilation regimens. It is decided to terminate the pregnancy by emergency segmental-transverse cesarean section for acute fetal distress and severe form of SARS COV-2 infection.

The patient's evolution was slowly favorable. The patient was discharged with the newborn after 25 days. As presented at the end of this article, the patient showed signs and symptoms of postpartum depression at the time of the 6-week postpartum evaluation, most likely with a mixed component, involving both SARS-COV-2 infection and the fact that the patient did not he was allowed to see the newborn during hospitalization.

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## 1. Introduction

The impact of SARS COV-2 on patient's life has gained attention from several perspectives (Al Dhaheri et al., 2021; Epifanio et al., 2021; Keshky et al., 2020; Shek, 2021), including biological and psychological figures as in the case of stress (Cooke et al., 2020; Frisone et al., 2021; Karan & Wadhera, 2021), emotional management (Al Dhaheri et al., 2021; Jiao et al., 2020; Martino et al., 2021; Merlo et al., 2021a, 2021b; Myles & Merlo, 2021; Vita et al., 2020) and behavioral patterns (Bera et al., 2022; Conti et al., 2020).

Clearly, the number of psychopathological manifestations appears to be wide, as in the light of psychoneuroendocrinology (Dantzer et al., 2020; Levine et al., 1989; Rajcani et al., 2021). In clinical psychological terms, it is well-known how the split between body and mind can no longer be supported (Goodman, 1991; Motofei & Rowland, 2015, 2018; Negel., 1993). On the basis of the above-mentioned references, it is clear how integrated approaches can provide for scientific contributions adherent to clinical realities (Caputo et al., 2022; Hunter et al., 1991; Martino et al., 2019; Shahar, 2021). Along with this path, a clear reference is made to psychoneuroimmunology, considering its role related to interventions, pathological issues and theoretical contributions (Brietzke et al., 2020; Debnath et al., 2020; Kentner et al., 2020; Moraes et al., 2018). SARS COV-2 is a virus enveloped in an envelope that contains proteins called spike proteins (S). With their help, the virus binds to cellular receptors in the nasal epithelium, nasopharynx, oral mucosa, lung mucosa and other structures. The receptor is ACE2, angiotensin convertase two (Hoffmann et al., 2020; Mangalmurti & Hunter, 2020).

As a result of the viral infection, the body directs the T lymphocytes to the affected cells, but most cases are asymptomatic or have mild forms of the disease. In rare cases, the immune response is aberrant and exacerbated, and hyaline deposits may appear in the lungs (with destruction of the blood-lung barrier/ alveolo-capillary membrane) and brain. In case of an intensified inflammatory response, in addition to T lymphocytes, there is an extra inflammatory infiltrate composed of polymorphonuclear cells (neutrophils, eosinophils and basophils), which in severe cases can lead to acute respiratory distress syndrome (Sethuraman et al., 2020). As mentioned above, severe inflammation occurs in the brain, but the neuropsychiatric condition is not strictly related to these changes. Procoagulant status, with increased D-dimers and atrial natriuretic peptide, leads to neuropsychiatric impairment of SARS COV-2 virus infection. Pregnant women have a prothrombotic, procoagulant and inflammatory status, so that SARS COV-2 infection can have a severe evolution in such patients by amplifying the mechanisms

related to pregnancy. (Blanco-Merlo et al., 2020; Carsana et al., 2020; Xu et al., 2020; Wang et al., 2020).

In the two years since the onset of the pandemic, it has been analyzed whether vaginal or cesarean delivery is better for covid-positive patients with asymptomatic or mild forms of the disease. Most studies have shown that spontaneous birth is more beneficial because it does not increase the inflammatory process (Boelig et al., 2020; Donders et al., 2020). Another argument is the decrease in postpartum pain, because in the case of vaginal birth it decreases in about six hours postpartum, while in the case of cesarean it lasts up to 12-24 hours. Pain causes tachycardia, tachypnea, altered respiratory parameters, so it can lead to cardio-respiratory decompensation (Liu et al., 2019). In patients with moderate to severe disease, cesarean delivery was preferred. One of the reasons why this option was chosen is the altered hemodynamic condition of the mother, who generally cannot tolerate labor. Another reason for moderate-severe forms is cardio-respiratory decompensation during labor and birth (Balalau et al., 2021; Cai et al., 2021; Walker et al., 2020). A study conducted by Gurol-Urganci concluded that vaginal birth does not increase the risk of transmitting SARS VOC-2 virus infection. In COVID-positive patients, the most commonly chosen method of delivery was vaginal birth (Gurol-Urganci et al., 2021).

Postpartum depression is more common in COVID-positive patients. (Balalau et al., 2021; Iwata et al., 2016). It is a major public health problem among developing countries, especially since skin-to-skin contact in the delivery room is not allowed, nor is breastfeeding allowed for a period of 14 days from the date of the test. In positive patients, room-in service is not possible in healthcare facilities that treat COVID patients. (American Academy of Pediatrics, 2020; Bălălău et al., 2020; Salvatore et al., 2020). All this leads to an increase in cases of postpartum depression, amplifying the pathophysiological mechanisms of SARS COV-2 infection that led to neuropsychiatric impairments. (Hoertel et al., 2015).

## **2. Clinical presentation**

The 28-year-old patient with a 30-week pregnancy and SARS COV-2 infection is transferred from a county health unit for altered general condition (dyspnea with orthopnea, dry cough, headache, partial oxygen saturation = 69% - in atmospheric air  $FiO_2 = 21\%$ ). Obesity was noted in the patient's history, with BMI = 31 kg / m<sup>2</sup> before pregnancy. The patient presented to the maternity ward on the 5th day of illness.

Ultrasonographic evaluation reveals a single fetal pregnancy with live fetus, right occipitoiliac cranial presentation, ultrasound gestation age of 32 weeks. Biohumoral evaluation during

hospitalization showed a prothrombotic status (D-dimers: 2.5 micrograms / Ml), with significant biological inflammatory syndrome (fibrinogen: 607 mg / dl, C-reactive protein: 62.88 mg / l) and lymphopenia (720 / ml, mild anemia 10.10 g / dl).

After a few days it was decided to transfer the patient to the Intensive Care Unit for deterioration of general condition, lower limb edema and acute respiratory failure (respiratory rate: 34-36 breaths per minute, increased respiratory accessory muscle labor, dyspnea with orthopnea and polypnea, partial oxygen saturation: 69% for  $FiO_2 = 21\%$ ). Oxygen therapy is instituted by non-invasive ventilation in CPAP regime with  $FiO_2 = 100\%$ , ventilation assistance pressure (PASB) = 15 cmH<sub>2</sub>O and end expiratory pressure (PEEP) = 10 cmH<sub>2</sub>O, with “total face mask” and later BIPAP / ASB increasing the assist pressures from day 2 TI and with P / F ratio = 116. Broad spectrum antibiotic therapy was initiated with Meropenem 3g / day, associating corticotherapy with Dexamethasone fiII / day, anticoagulation with low molecular weight heparin (Enoxaparin 1mg / day kgc / 12 hours), antiretroviral therapy with Remdesivir, with careful monitoring of creatinine and transaminase clearance. Evaluation of the patient's immune response was performed by dosing IL-6 (interleukin 6) for immunomodulatory therapy with Tocilizumab - a dose of 800 mg by slow intravenous infusion was administered. The patient was agitated psychomotor, expressing concern about the pregnancy and the fact that all family members were positive, including the other three children she has. Of all the members of the family, she is the only one with a severe form of the disease, the rest being asymptomatic or with a mild form. She was worried about a premature birth and how it would affect her newborn. Pulmonary X-ray was performed and inhomogeneous micronodular opacities with bilateral congestive appearance and diminished left lateral-basal pulmonary transparency were detected. In the second day of hospitalization in the intensive care unit, the patient's condition worsens and requires VMNI with increasing parameters and ventilation ratio <100. It is decided after the multidisciplinary consultation and the indication of the gynecologist the fetal extraction by emergency cesarean section transverse segment. Preoperatively, the central venous catheter was mounted on the subclavian. The patient still remains psychomotor agitated, having concerns about the birth of the fetus at the gestational age of 30 weeks and neonatal complications that may occur due to prematurity. On the same day, a live male fetus weighing 1980 g was extracted, with an Apgar 7 index and an anterior left occipito-iliac cranial presentation. It should be noted that the patient did not tolerate supine position and the surgery was performed with the patient positioned at an angle of 30 degrees between the patient's torso and parallel to the ground, thus increasing the difficulty of the surgery. Difficulty increased by non-invasive mechanical

ventilation that led to gastric distension and intestinal loops, which covered the lower segment. When the peritoneal cavity was opened, there was a major adhesion syndrome due to multiple adhesions between the anterior uterine wall and the ileal and jejunal intestinal loops. Careful adhesion of the dehiscence uterine tract was performed. L3-L4 level spinal anesthesia was administered with 0.5% 15 mg hyperbaric Marcaine. General anesthesia with orotracheal intubation was avoided in order to perform the surgery, the patient being subsequently transferred to the Intensive Care Unit, where it was mechanically ventilated non-invasively (receiving Tocilizumab 8 mg / kg body weight as dose two and three). Following administration of the third dose of immunomodulatory therapy, interleukin 6 decreased from 2562 pg / ml to 117 pg / ml, hepatic cytolysis syndrome occurred (with an increase in liver enzymes by 7 times until day 14 from the admission in the intensive care unit, and with a gradual decrease thereafter until normalization). Peritoneal drainage on day one postoperatively (day three of intensive care) was 100 ml serohematic fluid. The patient was intensely meteoric in the upper abdominal floor and a nasogastric tube was required.

Biohumoral evaluation on day 4 of intensive care showed a reduction in lymphopenia and a decreased biological inflammatory syndrome (C-reactive protein decreasing up to 4.63 mg / L), but an increased prothrombotic status. Chest CT scans revealed interstitial changes with the appearance of confluent "matte glass" that occupy almost the entire lung parenchyma indicating lung damage of 97%, bilateral inferior subcutaneous laterocervical emphysema and 30 mm thick pneumomediastinum, without images suggestive of PET. Clinical evaluation revealed an abdomen with discomfort, preserved diuresis, stable hemodynamics, peritoneal drainage being 800 ml serosanguineous fluid with white flakes (bacterial cultures were harvested from the drain tube, being negative for bacterial or fungal infection, and the dose of amylase from the drained liquid and serum amylase were within normal limits). A nasogastric tube was fitted to remove 250 ml of bile fluid and an evacuation enema was indicated. The patient continued to be anxious, asking about the baby and wanting to stay with him to breastfeed. Because the patient was hospitalized in the Intensive Care Unit, she did not benefit from room-in service, and she did not see her child either at birth or after that so that she could breastfeed. Another reason for not being able to access the child is the positive COVID status, while the child was negative COVID. In our maternity hospital, only COVID-positive newborns can stay with their mothers in the salon.

On the fifth day of intensive care, the postoperative evolution was favorable (physiologically retracted uterus, supple breasts, serous blood vessels, peritoneal drainage approximately 100 ml / 24 hours serous), being decided to suppress the drain tube because the meteorism has

decreased. The case was re-evaluated together with the infectious disease doctor who decided to administer Fluconazole for 7-10 days (depending on the clinical-biological evolution) and human Albumin. A vial. 50 ml of bile fluid and gastric stasis were externalized on the nasogastric tube.

It is decided to supplement the antibiotic therapy with Vancomycin 1gx2 / day and to continue with VMNI BIPAP / ASB, then CPAP / ASB, with ventilation periods in "prone-position". On day 4 postoperatively it is decided to establish ventilation with Pulmodyne type device with  $FiO_2 = 60\%$  and  $PEEP = 10\text{ cmH}_2\text{O}$  with nebulization on the special port of the device at 8 hours with betamimetic, fluidifier of bronchial secretions and hypertonic serum. Metabolic correction was performed with human albumin fl I, rebalancing the volume with Furosemide fl I / 2 per day. On the seventh day after admission to intensive care, the patient asked to have her baby breastfed, but this was impossible at the time. Due to the psychomotor agitation, the oxygen demand increased to 60L / min which was maintained for 48 hours. Carbamazepine 200 mg x3 / day was administered to prevent generalized tonic-clonic seizures in the probable context of prolonged hypoxia.

The patient developed decubitus ulcers located at the pressure sites, on the bilateral buttocks and at the sacral level. Active patient mobilization was recommended, initially mobilization for approximately 15 minutes at 6 hours, then on the thirteenth day physical effort was recommended for thirty minutes every three hours.

On the 10th day after admission to the intensive care unit, it was decided to progressively decrease the parameters for mechanical ventilation weaning (the patient resuming her intestinal transit). Related to "incentive spirometry" and the application of mechanical and pharmacological prevention methods of PET, the oxygen requirements decreased to 30 L / min. Biological evaluation revealed a decrease in D-dimers (2.18 micrograms / ml) and a return to normal levels of inflammatory markers, an improvement in anemia ( $Hb = 11.4\text{ g / dl}$ ) and a decrease in markers of hepatic cytolysis. On the 12th day after being admitted to the intensive care unit, the oxygen requirement decreased to 15L / min, with the decrease in the following days to 7L / min.

On the fifteenth day after admission to intensive care, the patient was re-evaluated by the infectious disease doctor who decided to complete the antibiotic therapy with Meropenem 1g x2 / day and Linezolid 600mg twice a day. On the seventeenth day of admission the patient was transferred to the gynecology obstetrics department with good general condition, afebrile, supple abdomen, mobile with respiration, without spontaneous pain, intestinal transit present,

normochromic physiological urination, retracted uterus, serous lochia, SpO<sub>2</sub> = 97% below 2L oxygen / minute. At the time of the transfer, the biohumoral parameters were normalized. The patient has tolerated lying on his back and no longer shows signs and symptoms of acute respiratory failure. The radiological evaluation showed a favorable evolution, with the reduction of pseudonodular opacities.

On the eighteenth day after admission, an attempt was made to stop the oxygen therapy (the partial oxygen saturation being 94% at FiO<sub>2</sub> = 94%), but the patient complained of difficulty breathing. It was decided to continue the oxygen therapy with 2L / min, under which the partial oxygen saturation was 98%. On the twenty-first day of hospitalization, the oxygen saturation without oxygen therapy was 97% and the oxygen therapy was completely suppressed.

It was decided to discharge her in good general condition seven days after transferring the patient to the obstetrics-gynecology department, without signs of respiratory failure, without the need for oxygen therapy, lactation present and retracted uterus. On the day of discharge, the patient first contacts the newborn, 27 days after birth. The patient became emotional, began to cry, being bewildered if she could take care of the newborn and the other three children she has at home. With the help of the neonatologist and the maternity psychologist, the patient regained her composure and went home with the newborn.

At the time of the consultation (six weeks postpartum), the obstetrical/ surgical evolution was good. She reported that the adaptation with the newborn was difficult, the emotional connection being quite difficult and delayed. The newborn was deprived of contact with the mother throughout the hospitalization period, breastfeeding being also impossible. All of this has led to a late consolidation of the mother-child emotional bond. Therefore, a form of postpartum depression associated with post-COVID depression can be considered, especially in the case of severe forms of SARS COV-2 infection (the procoagulant status from the beginning of the disease and the biological inflammatory syndrome). The release of proinflammatory cytokines, in addition to damaging the lungs, can also cause damage to brain structures (Oliver et al., 2021; Janssen Covid-19 Vaccine, see references). Most cases of postpartum depression generally occur in the first month of breastfeeding (Cox et al., 1987; Putman et al., 2015). In the case presented, the patient was hospitalized in a COVID health unit throughout the month, so that the access of the newborn to the mother was forbidden and the mother-child connection could not be strengthened (Gilner et al., 2021; Martenot et al., 2021). The patient repeatedly asked to see her child, to breastfeed, but all this could not be achieved due to virological mismatch between mother and child and the risk of neonatal infection (Chambers et al., 2020; Keskin & Karslioglu,

2021; Shlomai et al., 2021; Wieser et al., 2021; Zhu et al., 2021; Care for Breastfeeding Women, see references). In our case, the patient felt guilty about the premature birth and the lack of interaction with the newborn in the first month of his life, reporting that during the hospitalization she felt unable to help her baby. When she got home, she reported a change in sleep-wake rhythm, extreme fatigue, and loss of appetite. It is difficult to say to what extent these symptoms occurred as a result of SARS COV-2 infection and its recovery period, as a result of the patient having three more children at home, or if they were symptoms of postpartum depression (ACOG Opinion no.630; Merlo et al., 2020; Paulson et al., 2006; Yonkers et al., 2012).

In this particular situation, both mechanisms by which SARS-COV-2 infection can lead to postpartum depression were presented. The direct mechanism is the biologically inflammatory syndrome marked by the release of proinflammatory cytokines that lead to an inflammatory response in the brain at the level of prefrontal lobe and cingulate gyrus. The second is an indirect mechanism by affecting the mother-child relationship. Patients positive for SARS-COV-2 infection do not have access to the newborn in our maternity hospital, they cannot breastfeed and do not benefit from room-in service, so the mother-child emotional connection is delayed (Bohilea et al., 2020; Cojocaru et al., 2020; Gale et al., 2021; McDevitt et al., 2020; Ronchi et al., 2021).

### **3. Conclusions**

The case presented is particularly consisting of a young patient who presented with a severe form of SARS-VOC-2 infection, with 97% lung damage. The patient was admitted to Intensive Care from the beginning, with an altered general condition, with a high oxygen requirement and a severe form of SARS-COV-2 infection, all these contributing to the decision to extract the fetus by cesarean section.

During hospitalization, the patient received several antibacterial and antifungal agents, anticoagulant therapy, immunomodulatory therapy to reduce the procoagulant and inflammatory condition and to prevent systemic inflammatory syndrome. The patient was ventilated was ventilated non-invasively with BiPAP and CPAP (involving the placement of a central catheter), and a nasogastric tube was fitted to evacuate gastric contents in order to reduce postoperative flatulence.

The surgery was difficult due to several factors, such as the decision to remove a premature fetus by cesarean section, severe adhesion syndrome due to the other two previous cesarean operations, dehiscence wound at the hysterotomy trance and the patient's position. From an

obstetric/ surgical point of view, the patient's recovery was favorable, while the respiratory evolution was slowly favorable, requiring 17 days of hospitalization in the intensive care unit.

During hospitalization, the patient has multiple episodes of psychomotor agitation, anxiety related to premature birth, inability to breastfeed the newborn, the fact that she cannot see her baby, the fear that she may never see him. At the time of discharge, the patient becomes agitated again, being worried that she will not be able to cope with all four children, and at the same time she is excited at the sight of the child for the first time. At a six-week reassessment, some symptoms of postpartum depression were identified, and it is unclear whether they are related to COVID-induced neuropsychiatric impairment after childbirth and the late mother-child relationship, or whether they are the result of convalescence due to major lung damage.

### **Conflict of Interest Statement**

The authors declare that the research was conducted in the absence of any potential conflict of interest.

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