A Pregnant Mother Infected With Severe Acute Respiratory Syndrome Coronavirus 2 With Substance Dependence

A Case Report

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Abstract

Background: In December 2019, the novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in China, and now, it has spread all over the world. Pregnant women are a susceptible population, but there is scant information about COVID-19 in this population. Here, we report a case of a mother with substance use disorders who was infected with COVID-19 in her pregnancy.

Stories from the Field

Case: The patient was a 29-year-old, primigravida mother at the 37th gestational week who was referred to our center because of vaginal bleeding and severe uterine contractions. The patient was abusing opioids. With the suspicion of placental abruption, she was admitted for cesarean section. One day after delivery, she developed dyspnea, rhinorrhea, and vomiting. These were thought of as withdrawal signs. Despite methadone administration, these signs persisted. After ruling out deprivation syndrome and possible obstetric causes, a SARS-CoV-2 Polymerase chain reaction (PCR) test was ordered; the result was positive.

Conclusion: In this case, because of the flu-like symptoms of substance withdrawal and postpartum causes of shortness of breath, the medical team's attention was drawn to these causes. SARS-CoV-2 infection should be considered as a differential diagnosis for these patients.

Keywords: Case Report, COVID-19, Opioid Withdrawal, Pregnancy

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INTRODUCTION

Opioid dependence in pregnancy is an important issue that has many personal and societal consequences. Unfortunately, the consumption of opioids during pregnancy increased around the world (Fältmarch et al., 2019). It is estimated that 5%-22% of women use opioids in their pregnancies (Favre et al., 2020; Latuskie et al., 2019). To minimize the unwanted effects of addiction on the mother and her baby, mothers with substance use disorders need special attention in their pregnancies. An appropriate alternative for opiate maintenance therapy with close monitoring of the side effects should be considered (Desai et al., 2014).

The use of these drugs has many potential side effects that can affect the mother and her fetus. The risk of other medical complications of pregnancies also increased in mothers with substance use disorders (Prasad & Jones, 2019). Pregnancy itself makes a person more susceptible to infectious diseases, and mothers with substance use disorders are more vulnerable to infection (Desai et al., 2014).

The ongoing global pandemic of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is the defining global health crisis of our time (Harapan et al., 2020). The manifestations of COVID-19 are similar to the common cold. Common symptoms are fever, cough, dyspnea, shortness of breath, and lymphopenia. In some cases, the disease is associated with gastrointestinal problems such as diarrhea. It can also cause coagulation disorders and kidney failure (Rothan & Byrareddy, 2020).

Regarding opioid use in pregnancy, few studies can be found in the literature (Fältmarch et al., 2019; Shainker et al., 2012). Data about COVID-19 in addicted individuals are even scarcer (Qiao, 2020; Rothan & Byrareddy, 2020). The purpose of this article was to report a case of a mother with substance use disorders infected with SARS-CoV-2. It is hoped that this experience might help other researchers and practitioners.

CASE DISCRIPTION

Patient Information

The client was a 29-year-old pregnant woman, primigravida, at the 37th gestational week, who presented with vaginal

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bleeding and abdominal pain and had been referred to the emergency department of Imam Ali Hospital (Alborz, Iran). She was abusing opioids, which began a year ago in a dormitory. She also smoked half a pack of cigarettes a day. Her prenatal care physician prescribed her methadone syrup 3 times a day instead of opioids. She took her last dose of methadone a few hours before arriving at the hospital. She also used a salbutamol inhaler on an "as-required" basis for relief of symptoms of dyspnea related to her smoking. She had no specific surgical history.

Clinical Finding

Upon arrival to the emergency department, the fetal heartbeat was regular, as stated by the on-duty midwife (Fetal Heart Rate: 160/min). Maternal vital signs were oral temperature of 36.8°C, blood pressure of 100/60, pulse rate of 72 beats per minute, respiratory rate of 22 breath per minute, and O₂ saturation of 93% on room air, and the Glasgow Coma Scale/Score was 15.

On examination of the uterus, real contractions with moderate intensity and 2-minute intervals were evident. Internal vaginal examination was performed by the midwife; fetal presentation was breech. Cervix was 50% effaced and 7 cm dilated. Because of the suspicion of placental abruption, the patient was prepared for a cesarean section. The female baby was born with a good Appearance, Pulse, Grimace, Activity, Respiration score. The mother and baby were transferred to the postpartum ward, and she started breastfeeding her baby. Both of them were in good general condition. Postoperatively, enoxaparin (40 mg, Subcutaneous daily) for thrombosis prophylaxis was prescribed for her. She also was advised to continue taking methadone at previous dose.

Diagnostic Assessment

One day after delivery, she suddenly developed shortness of breath, rhinorrhea, vomiting, hypotension, and agitation. These signs were perceived as opioid withdrawal. With the consult of the clinical pharmacist, methadone (10 mg, Intramuscular) and MgSO₄ 50% (8 ml in 500 cc of half saline, Intravenous), for maintaining the serum magnesium higher than 2 mg/dl to avoid QT prolongation related to methadone, were prescribed for her. However, her symptoms did not improve.

Doppler ultrasonography of the lower extremity was investigated for screening of venous thromboembolism, and electrocardiography for amniotic fluid embolism was performed, which was normal. Her laboratory tests were normal, expect for Erythrocyte Sedimentation Rate and C-reactive protein levels that were moderately high and a mild thrombocytopenia (white blood cell: 8000, hemoglobin: 13.3 mg/dL, platelet: $122,000 \times 10^9$ /L, Erythrocyte Sedimentation Rate: 35 mm/hour, C-reactive protein: 48 Milligram Per Litre, magnesium: 1.5 mg/dl). The patient presented with progressive dyspnea with oxygen saturation (SaO₂) of 87%. Oxygen therapy was given through a nasal cannula to maintain SaO₂ at 95%–98%.

The pulmonary computed tomography scan of the patient revealed bilateral pulmonary parenchymal ground-glass and consolidative pulmonary opacities that were in favor of COVID-19, and a COVID-19 PCR test was ordered. The PCR test result was positive for SARS-CoV-2. The mother was admitted to the intensive care unit for close monitoring. The baby showed mild symptoms of withdrawal (weakness, jitteriness, vomiting, and sleep problems). The PCR test was also ordered for the baby, which was negative.

Therapeutic Intervention

According to the COVID-19 care local protocol, the mother was admitted to an isolation ward with negative pressure. The baby was also isolated. She was advised not to breastfeed her baby. Hydroxychloroquine and Kaletra (lopinavir/ritonavir) were started for the patient. An infectious disease specialist visited the patient, prescribed acetaminophen to control the fever, and recommended adequate hydration. The patient was closely monitored. She drank fluids with the help of the medical staff. With the abovementioned measures, the patient condition was improved gradually. The patient's oxygen saturation became 98% in room air with pulse oximetry.

Follow-Up and Outcomes

After 1 week, the patient was discharged from the hospital with oral azithromycin and hydroxychloroquine. After-discharge tips and precautions were taught to the patient. The follow-up visit with the infectious disease specialist, and postnatal care was arranged within a few weeks.

DISCUSSION

Because the symptoms of COVID-19 can be similar to those of the withdrawal syndrome, the diagnosis of the infection was delayed in this patient. According to the few published studies on COVID-19, most infected pregnant mothers will experience mild symptoms. The reported symptoms were generally similar to influenza or the common cold; thus, it seems that pregnant women are not at a higher risk for COVID-19. It is probably because of the low-risk factors such as young age or absence of underlying diseases (Chen et al., 2020; Qiao, 2020). However, it is not the same for mothers with substance use disorders. These women are more vulnerable (Jiang et al., 2020). People with a low socioeconomic status, homeless people, and drug users more likely to have an infection because of their living conditions, weakened immune system, and other comorbidities. Thus, they require special attention (Satre et al., 2020).

In addition to the importance of the infected mother's health, she can spread the virus in the hospital and infect other mothers, medical staff, and other healthy people. Therefore, not paying attention to the importance of pandemic conditions in these people could lead to harm (Salisbury-Afshar et al., 2020).

In a pandemic situation, mothers with substance use disorders may not attend regular visits, not express all their symptoms, or refrain from taking prescribed medications regularly that can cause withdrawal symptoms (Satre et al., 2020). The symptoms of withdrawal, such as fatigue, muscle pain, rhinorrhea, and decreased level of consciousness, are very similar to COVID-19 symptoms. On the other hand, the symptoms of intoxication, such as increased heart rate and respiratory suppression, could also be misleading. These

similarities make the diagnosis difficult. Our case had no fever, cough, or gastrointestinal symptoms that are more common in COVID-19, which made the diagnosis harder. Smoking exacerbated the complications of shortness of breath and the susceptibility for pneumonia. The medical staff should pay close attention to these similarities to correctly diagnose and isolate the infected mother in a timely manner. In these cases, it is recommended to focus on more definite symptoms of withdrawal, such as yawning, itching, and lacrimation. The pharmacological properties of the drug are important aspects of the certainty of the withdrawal diagnosis. Methadone is a long-acting opioid, and withdrawal symptoms usually appear at least 12-24 hours after the last dose. By misdiagnosing the infection as toxicity caused by opioid overdose, drug discontinuation can lead to the symptoms of iatrogenic withdrawal (Berghella et al., 2003; Tobon et al., 2019).

Drug interaction between COVID-19 treatment and methadone is another important aspect of the management. Hydroxychloroquine, azithromycin, and lopinavir/ritonavir could potentially increase the risk of cardiac arrhythmia and death. The risk is increased when they are used with other drugs that prolong the QT interval, like methadone. Baseline QTc status should be obtained either by a 12-lead Electrocardiogram or with the use of a smartphone-enabled mobile QTc meter. Patients with a baseline QTc interval of more than 500 ms (with a QRS duration \leq 120 ms) are at a higher risk for significant QT prolongation and subsequent polymorphic ventricular tachycardia. In these patients, contributing factors like electrolyte abnormalities (hypocalcemia, hypokalemia, hypomagnesemia) should be corrected. If 2-3 hours after a dose of hydroxychloroquine or other QT-prolonging agents, the QTc increases to more than 500 ms, or if the change in QT interval is more than 60 ms, the risk of torsades de pointes versus benefit of the medication should be reassessed (Giudicessi et al., 2020).

Supportive measures in pregnant mothers include adequate rest, adequate fluid intake, nutritional support, correcting water and electrolyte disturbances, and oxygen supplementation or ventilation (Yang et al., 2020).

CONCLUSION

On the basis of what has been discussed about this case, it is very important to distinguish infection signs in mothers with substance use disorders with possible withdrawal symptoms. In particular, as COVID-19 continues to devastate lives around the world and affect the most vulnerable the hardest, mothers with substance use disorders should be carefully assessed for this infection.

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REFERENCES

Berghella, V., Lim, P. J., Hill, M. K., Cherpes, J., Chennat, J., Kaltenbach, K. (2003). Maternal methadone dose and neonatal

- withdrawal. American Journal of Obstetrics and Gynecology, 189(2), 312–317. https://doi.org/10.1067/S0002-9378(03)00520-9
- Chen, H., Guo, J., Wang, C., Luo, F., Yu, X., Zhang, W., Li, J., Zhao, D., Xu, D., Gong, Q., Liao, J., Yang, H., Hou, W., Zhang, Y. (2020). Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *The Lancet*, 395, 809–815 https://doi.org/10.1016/S0140-6736(20)30360-3
- Desai, R. J., Hernandez-Diaz, S., Bateman, B. T., Huybrechts, K. F. (2014). Increase in prescription opioid use during pregnancy among Medicaid-enrolled women. *Obstetrics and Gynecology*, 123(5), 997–1002. https://doi.org/10.1097/AOG.000000000000000208
- Fältmarch, S., Perttilä, I., Tuomi, U., Kautiainen, H., Gissler, M., Pennanen, P., Eriksson, J. G., Laine, M. K. (2019). Use of opioids during pregnancy and effects of pregnancy outcomes. *Pharmacoepidemiology and Drug Safety*, 28(9), 1239–1245. https://doi.org/10.1002/pds.4848
- Favre, G., Pomar, L., Qi, X., Nielsen-Saines, K., Musso, D., Baud, D. (2020). Guidelines for pregnant women with suspected SARS-CoV-2 infection. *The Lancet Infectious Diseases*, 20, 652–653. https://doi.org/10.1016/S1473-3099(20)30157-2
- Giudicessi, J. R., Noseworthy, P. A., Friedman, P. A., Ackerman, M. J. (2020). Urgent guidance for navigating and circumventing the QTc-prolonging and torsadogenic potential of possible pharmacotherapies for coronavirus disease 19 (COVID-19). Paper presented at the Mayo Clinic Proceedings (Vol. 95, pp. 1213-1221). https://doi.org/10.1016/j.mayocp.2020.03.024
- Harapan, H., Itoh, N., Yufika, A., Winardi, W., Keam, S., Te, H., Megawati, D., Hayati, Z., Wagner, A. L., Mudatsir, M. (2020). Coronavirus disease 2019 (COVID-19): A literature review. *Journal of Infection and Public Health*, 13, 667–673. https://doi.org/10.1016/j.jiph.2020.03.019
- Jiang, H., Su, H., Zhang, C., Liu, X., Li, R., Zhong, N., Zhao, M. (202 0). Challenges of methadone maintenance treatment during the COVID-19 epidemic in China: policy and service recommendations. *European Neuropsychopharmacology*, 35, 136–137. https://doi.org/10. 1016/j.euroneuro.2020.03.018
- Latuskie, K. A., Leibson, T., Andrews, N. C., Motz, M., Pepler, D. J., Ito, S. (2019). Substance use in pregnancy among vulnerable women seeking addiction and parenting support. *International Journal of Mental Health and Addiction*, 17(1), 137–150. https://doi.org/10.1007/s11469-018-0005-7
- Prasad, M., Jones, M. (2019). Medical complications of opioid use disorder in pregnancy. Paper presented at the Seminars in Perinatology (Vol. 43, pp. 162-167). https://doi.org/10.1053/j.semperi.2019.01.005
- Qiao, J. (2020). What are the risks of COVID-19 infection in pregnant women? *The Lancet*, 395(10226), 760–762. https://doi.org/10.1016/S0140-6736(20)30365-2
- Rothan, H. A., Byrareddy, S. N. (2020). The epidemiology and pathogenesis of coronavirus disease (COVID-19) outbreak. *Journal of Autoimmunity*, 109, 102433. https://doi.org/10.1016/j.jaut.2020.102433
- Salisbury-Afshar, E. M., Rich, J. D., Adashi, E. Y. (2020). Vulnerable populations: Weathering the pandemic storm. American Journal of Preventive Medicine, 58, 892–894. https://doi.org/10.1016/j.amepre.2020.04.002
- Satre, D. D., Hirschtritt, M. E., Silverberg, M. J., Sterling, S. A. (2020). Addressing problems with alcohol and other substances among older adults during the COVID-19 pandemic. *The American Journal of Geriatric Psychiatry*, 28, 780–783 https://doi.org/10.1016/j.jagp.2020.04.012
- Shainker, S. A., Saia, K., Lee-Parritz, A. (2012). Opioid addiction in pregnancy. *Obstetrical & Gynecological Survey*, 67(12), 817–825. https://doi.org/10.1097/OGX.0b013e3182788e8c
- Tobon, A. L., Habecker, E., Forray, A. (2019). Opioid use in pregnancy. *Current Psychiatry Reports*, 21(12), 118. https://doi.org/10.1007/s11920-019-1110-4 Yang, H., Wang, C., Poon, L. (2020). Novel coronavirus infection and pregnancy. *Ultrasound in Obstetrics & Gynecology*, 55, 435–437. https://doi.org/10.1002/uog.22006

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