COVID-19 in a pregnant cystic fibrosis carrier with myasthenia gravis: A case report

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A R T I C L E   I N F O  

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A B S T R A C T

A 16-year-old primigravida was diagnosed with COVID-19 in her second trimester. She decompensated quickly and had to be admitted to hospital and intubated. She was diagnosed with a fetal demise after being intubated and neurology suspected myasthenia gravis due to neurologic symptoms. Due to pan-sinusitis and increased mucus secretion, cystic fibrosis screening was ordered. After she was extubated, cervical ripening and induction was performed with eventual vaginal delivery without maternal complications. Myasthenia gravis and cystic fibrosis carrier status were confirmed after the patient was discharged.

1. Introduction

COVID-19 in pregnancy increases the risk of maternal mortality and stillbirth, especially in unvaccinated women and women with comorbidities [1–3]. Cystic fibrosis (CF) and myasthenia gravis (MG) are two such comorbidities. While outside of pregnancy, most patients with CF (homozygous for the cystic fibrosis transmembrane conductance regulator (CFTR) gene) and COVID-19 are young and can have a mild course, they tend to show higher rates of severe outcomes, mostly due to low lung function and/or a history of transplantation [4]. While COVID-19 may worsen the outcome in non-pregnant patients with MG, a recent systematic review could not definitively establish causation of increased morbidity [5]. Here, a case of a pregnant patient with severe COVID-19 and subsequent diagnosis of MG and positive CF carrier (heterozygous) status is described.

2. Case Presentation

A 16-year-old primigravida Hispanic female with no relevant past medical or family history presented to her first pregnancy appointment at 7 weeks and 6 days of gestation with complaints of headache, nausea, and vomiting. She was advised to continue taking over-the-counter acetaminophen while metoclopramide was prescribed as needed for nausea and vomiting. The patient was followed up at 12 weeks and complained of “tongue swelling.” However, tongue swelling was not appreciated on exam. She was advised to discontinue the metoclopramide in exchange for ondansetron as needed for symptomatic relief of nausea and vomiting. Additionally, she was advised to take diphenhydramine for her tongue complaints and to follow-up if she did not see improvement.

Ten days later (at 13 weeks 3 days) the patient’s mother contacted the office stating that her daughter’s symptoms had not improved and added that it seemed to be exacerbated by eating. She was referred to otolaryngology and scheduled for an appointment approximately three weeks later. Two days before her otolaryngology appointment (at 16 weeks), she was seen again for a routine prenatal visit and indicated that she had been experiencing worsening depression and anxiety. Escitalopram was prescribed and she was referred to counseling. The otolaryngology notes two days later (at 16 weeks 2 days) indicated that they suspected her tongue complaints were most likely functional in etiology and they suggested that she see a speech therapist for further evaluation.

Eleven days after her otolaryngology appointment (at 17 weeks 5 days), she presented to the emergency department complaining of a 3-day history of nasal congestion, pharyngitis, cough, and inspiratory chest pain and subsequently tested positive for COVID-19 infection. Her chest x-ray was unremarkable at that time. She was given IV fluids and discharged with an albuterol prescription and advised to start low-dose aspirin (81 mg daily) based at the time on possible increased risks for preeclampsia due to COVID-19.

Three days after her discharge she returned to the emergency department (at 18 weeks 1 day), but this time she complained of hemoptysis. She was both tachypneic and tachycardic and dried blood was
noted on her lips. As she was being transferred for CTA imaging to evaluate for pulmonary embolism, she became obtunded, unresponsive to verbal and painful stimuli, and gag reflex was absent. Glasgow Coma Scale (GCS) score was 4 and she was emergently intubated. Bedside ultrasound diagnosed a fetal demise.

The next day she was extubated, but a day after being extubated, she had to be re-intubated due to hypoxic and hypercapnic respiratory failure with concurrent dysphagia and dysarthria. Bronchoscopy revealed thick mucoid secretions. She was started on piperacillin-tazobactam, remdesivir, and tocilizumab. Neurology presumed that the dysphagia and dysarthria were secondary to undiagnosed myasthenia gravis. She was treated for a myasthenic crisis with steroids, IVIG, and pyridostigmine. She eventually was extubated a second time and transferred to labor and delivery, where cervical ripening and eventual spontaneous vaginal delivery occurred. Myasthenia gravis panel results were positive for AChR binding and modulating antibodies after discharge. Cystic fibrosis mutation panel revealed one severe pathogenic mutation.

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Cystic fibrosis mutation panel revealed one severe pathogenic mutation. Pheresdel, after discharge. The COVID-19 strain was unknown at the time of her discharge.

3. Discussion

While the incidence of MG is 30/1,000,000/year [6], the incidence of CF carrier frequencies for a 69-mutation panel is 1/36 [7]. In this case, the patient’s MG and CF carrier status were unknown at the time of her COVID-19 diagnosis.

Recommendations for the treatment of MG in pregnancies complicated by COVID-19 have been summarized [8] and include acetylcholinesterase inhibitors, corticosteroids and low-dose aspirin. Care should be taken to try to find alternatives to magnesium sulfate, calcium-channel blockers, and β-adrenoceptor blockers, especially in light of the increased risk of preeclampsia in pregnancies associated with COVID-19 [9,10].

No studies on pregnant CF carrier (heterozygous) patients with COVID-19 have been reported. Yet the recent GEN-COVID multicenter trial showed that non-pregnant CF carriers (heterozygous) are predisposed to severe COVID-19 and a higher risk of death. The authors also noted previous studies suggesting that active CF patients (homozygous) appeared to undergo a mild form of COVID-19 and postulate this discrepancy could be due to their treatment with CFTR modulators while the CF carriers (heterozygous) are not treated [11].

Since around 2001, in the United States, health care providers have been encouraged or required to screen for active CF in newborns using a two-tier algorithm [12,13]. While the American College of Obstetricians and Gynecologists (ACOG) has recommended that carrier screening should be offered to all women who are pregnant or considering getting pregnant, the stated goal of CF carrier screening is to identify individuals at risk of having a child with active cystic fibrosis [14]. CF screening currently is dependent upon a patient’s desire to make an informed choice, utilizing their autonomy, rather than improving the patient’s health [15]. If it can be shown that a positive CF carrier status in pregnancy would be harmful to the patient’s health, and that harm could be mitigated, then physicians should recommend CF screening on two fronts. While larger randomized controlled trials may be needed to definitively show the health benefits to CF carrier screening, the risk/benefit ratio discussion should not eliminate this current observation.

Based on good and consistent scientific evidence, ACOG recommends starting low-dose (81 mg) aspirin for preeclampsia prophylaxis in women with any of the high-risk factors for preeclampsia [16]. A recent meta-analysis suggests that COVID-19 is associated with an increased risk of preeclampsia in pregnancy, yet concludes that the role of low-dose aspirin to prevent preeclampsia and COVID-19 infection remains unclear [10]. The risk of recurrence of preeclampsia can range between 7.5% and 65% and depends upon the severity of the initial episode [17]. Women with COVID-19 during pregnancy have a significantly higher odds (62%) of preeclampsia compared with those who do not have the infection [10].

In this case, the use of acetylcholinesterase inhibitors, while standard treatment in women with MG and COVID-19 in pregnancy, may have exacerbated mucus production, delaying the ability to extubate this patient, especially in the context of her CF carrier status. While over 65% of all pregnant women have been vaccinated for COVID-19 prior to or during pregnancy [18], this patient was not vaccinated at the time of her diagnosis. While knowing her diagnosis of CF carrier status may not have changed the outcome, vaccination and a low-dose aspirin regimen, due to preeclampsia risk, could have been offered or at least encouraged more strongly if she was thought to be higher risk.

4. Conclusion

Previous research has suggested that genetic testing could help prevent, diagnose, and treat conditions related to CF carrier status [19]. Independent of MG, providers have a unique opportunity to protect all pregnant women by recommending CF carrier genetic testing for not just family planning but just as importantly to identify a silent risk factor for severe COVID-19 and subsequent mortality.

Contributors

John Coté cared for the patient, and contributed to the analysis of data, writing, and revising the manuscript.

Peter Granger contributed to the analysis of data, writing, and revising the manuscript.

Anjali Mishra contributed to the analysis of data, writing, and revising the manuscript.

Giavanna Sorini contributed to the analysis of data, writing, and revising the manuscript.

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Patient consent

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Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

References

[1] C.L. DeSisto, B. Wallace, R.M. Simeone, K. Polen, J.Y. Ko, D. Meaney-Delman, S. Ellington, Risk for stillbirth among women with and without COVID-19 at delivery hospitalization—United States, March 2020–September 2021, Morb. Mortal. Wkly Rep. 70 (47) (2021) 1640, https://doi.org/10.15585/mmwr.mm7047e1.
[2] J. Villar, S. Arif, R.B. Gunier, R. Thiruvengadam, S. Rauch, A. Kholin, P. Roggero, F. Prefumo, M.S. Do Vale, J.A. Cardona-Perez, Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study, JAMA Pediatr. (2021), https://doi.org/10.1001/jamapediatrics.2021.1050.
[3] Z.S. Lassi, A. Ana, J.K. Das, R.A. Salam, Z.A. Padhani, O. Irfan, Z.A. Bhutta, A systematic review and meta-analysis of data on pregnant women with confirmed COVID-19: clinical presentation, and pregnancy and perinatal outcomes based on COVID-19 severity, J. Glob. Health 11 (2021), https://doi.org/10.7189/jogh.11.05018.
[4] P.-R. Burgel, C. Goss, COVID-19 outcomes in people with cystic fibrosis, Curr. Opin. Pulm. Med. 27 (6) (2021) S38–S43, https://doi.org/10.1097/MCP.0000000000001025.

[5] A.S. Abbas, N. Hardy, S. Ghosy, M. Dibas, G. Paranjape, K.W. Evanson, N. L. Reiersen, K. Cowie, S. Kamrowski, S. Schmidt, Characteristics, treatment, and outcomes of Myasthenia Gravis in COVID-19 patients: a systematic review, Clin. Neurol. Neurosurg. (2022), 107146, https://doi.org/10.1016/j.clineuro.2022.107146.

[6] A. McGrogan, S. Sneddon, C.S. De Vries, The incidence of myasthenia gravis: a systematic literature review, Neuroepidemiology 34 (3) (2010) 171–183, https://doi.org/10.1159/000279334.

[7] V.V. Zvereff, H. Faruki, M. Edwards, K.J. Friedman, Cystic fibrosis carrier screening in a North American population, Genet. Med. 16 (7) (2014) 539–546, https://doi.org/10.1038/gim.2013.189.

[8] K.K. Neykova, M. Milanova, P.N. Ignatov, Myasthenia gravis and covid-19 in pregnancy: a review of the literature and case series report, J. Matern. Fetal Neonatal Med. (2021) 1–9, https://doi.org/10.1080/14767058.2021.1973418.

[9] J. Occan, I.F. Balson, A.T. Dennis, New diagnosis myasthenia gravis and preeclampsia in late pregnancy, Case Rep. 2015 (2015), https://doi.org/10.1136/bcr-2014-208323.

[10] A. Conde-Agudelo, R. Romero, SARS-COV-2 infection during pregnancy and risk of preeclampsia: a systematic review and meta-analysis, Am. J. Obstet. Gynecol. (2021), https://doi.org/10.1016/j.ajog.2021.07.009.

[11] M. Baldassarri, F. Fava, C. Fallerini, S. Daga, E. Benetti, K. Zguro, S. Amitrano, F. Valentino, G. Doddato, A. Giliberti, Severe COVID-19 in hospitalized carriers of single CFTR pathogenic variants, J. Personal. Med. 11 (6) (2021) 558, https://doi.org/10.3390/jpm11060558.

[12] P.M. Farrell, E. Langfelder-Schwind, M.H. Farrell, Challenging the dogma of the healthy heterozygote: implications for newborn screening policies and practices, Mol. Genet. Metab. 134 (1–2) (2021) 8–19, https://doi.org/10.1016/j.ymgme.2021.08.008.

[13] P.M. Farrell, M.R. Kosorok, M.J. Rock, A. Laxova, L. Zeng, H.-C. Lai, G. Hoffman, R. H. Laesig, M.L. Splaingard, W.C.F.N.S.S. Group, Early diagnosis of cystic fibrosis through neonatal screening prevents severe malnutrition and improves long-term growth, Pediatrics 107 (1) (2001) 1–13, https://doi.org/10.1542/peds.107.1.1.

[14] B. Rink, S. Romero, J. Biggio, D. Saller, R. Giardine, Carrier screening for genetic conditions. Committee Opinion No. 691, Obstet. Gynecol. 129 (2017) e41–e55, https://doi.org/10.1097/AOG.0000000000001952.

[15] S.J. Kessels, D. Carter, B. Ellery, S. Newton, T.L. Merlin, Prenatal genetic testing for cystic fibrosis: a systematic review of clinical effectiveness and an ethics review, Genet. Med. 22 (2) (2020) 258–267, https://doi.org/10.1038/s41436-019-0641-8.

[16] American College of Obstetricians and Gynecologists, Gestational hypertension and preeclampsia: ACOG Practice Bulletin, number 222, Obstet. Gynecol. 135 (6) (2020) e237–e260, https://doi.org/10.1097/AOG.0000000000003891.

[17] G.A. Dildy III, M.A. Belfort, J.C. Smulian, Preeclampsia recurrence and prevention, Semin. Perinatol. (2007) 135–141, https://doi.org/10.1053/j.semperi.2007.03.005. Elsevier.

[18] Centers for Disease Control and Prevention, COVID Data Tracker, US Department of Health and Human Services, CDC, Atlanta, GA, 2022. February 20, https://covid.cdc.gov/covid-data-tracker.

[19] A.C. Miller, A.P. Comellas, D.B. Hornick, D.A. Stoltz, J.E. Cavanaugh, A.K. Gerke, M.J. Welsh, J. Zabner, P.M. Polgreen, Cystic fibrosis carriers are at increased risk for a wide range of cystic fibrosis-related conditions, Proc. Natl. Acad. Sci. 117 (3) (2020) 1621–1627, https://doi.org/10.1073/pnas.1914912117.