



COVID-19 infection presenting as pancreatitis in a pregnant woman: A case report

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ABSTRACT

Background: The coronavirus 2019 (COVID-19) pandemic has posed unique challenges in healthcare. In obstetrics, there is little information available to guide practice. As new data emerge, the spectrum of initial presenting symptoms has expanded from fever, cough, and dyspnea to gastrointestinal and other symptoms in both pregnant and non-pregnant patients.

Case: A 36-year-old woman, G4P2, at 33 weeks of gestation presented very early in the COVID-19 course with four days of cough and fever, without recent travel or known exposure. She appeared well, with stable vital signs, and was sent home to self-quarantine after a specimen for COVID-19 testing was collected. Two days later, she presented with nausea, vomiting, and abdominal pain, and was diagnosed with acute pancreatitis.

Conclusion: To date, no cases of human pancreatitis have been identified as related to a COVID-19 infection, although multiple other gastrointestinal symptoms have been described. Given the lack of other etiology, we consider the possibility that patient's acute pancreatitis could be secondary to COVID-19 infection.

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1. Introduction

The coronavirus 2019 (COVID-19) pandemic has had a vast and lasting impact on global health care. In obstetrics, there is limited information to guide practice. As new data emerge, the spectrum of initial presenting symptoms has expanded. Initial presentation can include fever, fatigue, dry cough, anorexia, myalgias, dyspnea, and sputum production [1]. Less common symptoms include anosmia and dysgeusia along with nausea or diarrhea [2]. Up to 40–50% of COVID-19 infections in pregnant and non-pregnant patients present initially with gastrointestinal symptoms [3]. Patients with chronic medical conditions such as diabetes mellitus, obesity, hypertension, cardiovascular disease, chronic lung or kidney disease, and cancer have an increased risk of severe illness and mortality from COVID-19 [4].

Pancreatitis has a multitude of potential causes, including gallstones, alcohol, hypertriglyceridemia, trauma, post-endoscopic retrograde cholangiopancreatography (ERCP), hypercalcemia, medications, anatomic anomalies, and infections or toxins. Known viral causes of pancreatitis include mumps, coxsackievirus, hepatitis B, cytomegalovirus, varicella-zoster, herpes simplex, and human immunodeficiency virus

[5]. With the appearance of new viruses such as COVID-19, the number of viral etiologies for pancreatitis has the potential to expand. While COVID-19 has not yet been described in cases of human pancreatitis, other coronaviruses have been associated with clinical pancreatitis in animals [6,7]. In addition, coronaviruses have been identified in pancreatic cells at time of animal autopsy [8,9]. In human autopsies, coronavirus associated with severe acute respiratory syndrome (SARS) has been identified in multiple body organs, including the pancreatic acinar cells [10,11].

According to the Centers for Disease Control and Prevention, at the time this article was written the number of cases from COVID-19 in the United States surpassed one million, compared to 7038 at the time of our patient's initial presentation just two weeks earlier [12]. This pandemic is predicted to continue to grow, and the impact on pregnancy, the postpartum period, and neonates is still largely unknown. This case study expands the breadth of knowledge in pregnancy along with a novel presentation of COVID-19 in a pregnant patient.

2. Case Report

2.1. First Hospital Admission

A 36-year-old woman, G4P2, at 33 weeks of gestation presented with fever, dry cough, and myalgia of four days' duration. She denied

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dyspnea or use of her rescue inhaler in the previous two months. Her maximum temperature at home via tympanic thermometer was 38.3 °C (101 °F). She had no recent travel history. She reported her son's elementary school teacher had been ill two weeks but did not know the details of this illness. She denied known COVID-19 exposure.

Her medical history was complicated by type 1 diabetes mellitus (T1DM), mild intermittent asthma, maternal obesity with a pre-pregnancy body mass index (BMI) of 44 kg/m², and preeclampsia with severe features in two previous pregnancies. Her T1DM was well controlled with an insulin pump, with a recent HbA1C of 5.4%. She had had one preterm delivery due to preeclampsia with severe features. Her surgical history was remarkable for two cesarean sections and a cholecystectomy.

On presentation, the patient appeared overall comfortable without respiratory distress. Her temperature was 38 °C (100.9 °F), heart rate 121 beats per minute, blood pressure 115/68 mmHg, respiratory rate 16 breaths per minute, and oxygen saturation 94%. The patient was treated with acetaminophen and was subsequently afebrile, but remained tachycardic for the first 12 h of her admission. Her lung exam was notable for faint expiratory wheezes in the bilateral lower lung fields, without rhonchi or rales. Her abdomen was gravid, soft, and non-tender.

The viral respiratory panel was negative, and COVID-19 (SARS-CoV-2) polymerase chain reaction (PCR) testing was done on a specimen collected via nasopharyngeal swab. At the time, the predicted time to result was four to seven days. Complete blood count (CBC) and complete metabolic panel (CMP) were within normal limits with a normal white blood cell count of 8340/uL and neutrophil composition of 7340/uL. Urinalysis showed ketones greater than 80 mg/dL. Blood glucose was 111 mg/dL on admission.

She was kept overnight for monitoring due to risk of developing diabetic ketoacidosis from acute infection as well as risk for respiratory distress from possible COVID-19 infection with multiple comorbidities. The fetal heart tracing (FHT) was reactive and reassuring for gestational age. She remained afebrile and clinically stable overnight, and was discharged home the next day in stable condition. She and her family were counseled regarding strict home isolation measures.

2.2. Second Hospital Admission

The day after discharge, the patient presented to a local urgent care clinic due to continued fevers. She was diagnosed with mastitis at this facility, and was started on dicloxacillin.

The following day, the patient presented again to the hospital with new-onset nausea, vomiting, and epigastric pain. She also stated that her blood sugars had been greater than 200 mg/dL and difficult to control the night before. She endorsed mild, diffuse, bilateral breast tenderness that had been present for the majority of her pregnancy. She reported no recent trauma, alcohol use, or other new medications. In the setting of pregnancy possibly complicated by COVID-19 with new gastrointestinal symptoms, there was concern for diabetic ketoacidosis, gastroenteritis, sepsis, pancreatitis, or preeclampsia.

Vital signs upon admission were all within normal limits, and stable. She appeared to be very uncomfortable and was nauseated on presentation. Physical exam was remarkable for epigastric tenderness to palpation. The protein/creatinine ratio was elevated at 0.6 but other laboratory results such as CBC, CMP, uric acid, and lactate dehydrogenase were grossly normal and she remained normotensive, excluding the diagnosis of preeclampsia. White blood cell count (WBC) was normal at 6430/uL and creatinine normal at 0.68. Lactate was normal at 0.9 mmol/L. Urinalysis was again remarkable for ketones greater than 80 mg/dL. Evaluation for a biliary cause of pancreatitis was unremarkable with a normal aspartate aminotransferase (23 U/L), alanine aminotransferase (14 U/L), alkaline phosphatase (115 U/L), and bilirubin (0.6 mg/dL). Beta-hydroxybutyrate was elevated at 1.9 mmol/L, but she had a normal anion gap of 9 and normal bicarbonate of 21 mg/dL,

excluding diabetic ketoacidosis. Amylase was normal at 88 U/L but lipase, the more sensitive test for pancreatitis, was elevated to 875 U/L. Triglycerides were mildly elevated at 210 mg/dL. The FHT continued to remain reactive and reassuring for gestational age.

The patient was diagnosed with acute pancreatitis and internal medicine and maternal-fetal medicine staff were consulted. Dicloxacillin was discontinued as there was no evidence of mastitis. An abdominal ultrasound was recommended by internal medicine clinicians. The pancreas was not visualized due to overlying bowel gas. There was no intrahepatic biliary ductal dilation and the common bile duct measured 5 mm. The liver, right kidney, and retroperitoneum were grossly normal with no ascites identified. A computed tomography (CT) scan was not recommended as it would not change clinical management. The patient was made nil per os (NPO), and treated with maintenance intravenous fluids, intravenous anti-emetics, pantoprazole, and fentanyl for pain control. She remained afebrile with acetaminophen and had a maximum temperature of 37.7 °C (99.9 °F).

On hospital day 2, due to continued concern for COVID-19 without an official test result, a chest radiograph was obtained and showed diffuse bilateral infiltrates consistent with a COVID-19 infection. She continued to have a dry cough and subsequently developed dyspnea with a decrease in her oxygen saturation to 88% on room air. She was started on two liters of oxygen via nasal cannula with subsequent improvement in her dyspnea and oxygen saturation to 92%, which is within normal limits for the altitude of the treatment facility. Her T1DM was treated with insulin, per her home insulin pump. She did not require increased insulin at any time during her admission, and had decreased requirements while she was NPO. Lipase trended down and was normal (113 U/L) on hospital day 3. There were multiple unsuccessful attempts to decrease her oxygen during the first two days of her hospital admission.

On hospital days 3–4, she began to tolerate oral intake. She passed her home oxygen test and was discharged home in stable condition. She was again counseled regarding strict quarantine precautions, and to return with any worsening of symptoms. She was educated on how to monitor her oxygen status at home with a pulse oximeter. At home, her oxygen saturation was persistently 83–88%, and she ultimately received home oxygen for approximately one week.

Appropriate personal protective equipment (PPE) was utilized throughout both of her hospital admissions as she remained a person under investigation for COVID-19. The patient's COVID-19 PCR resulted as positive two days after her second hospital discharge and nine days after testing.

2.3. Third Hospital Admission

The patient returned to the hospital at 38 weeks and two days of gestation for a labor evaluation and was diagnosed with preeclampsia without severe features. She was admitted and elected to have a repeat cesarean section. Her pancreatitis and hypoxia had resolved and she had been asymptomatic for over two weeks. She denied any sick contacts and confirmed that she had been in strict social isolation with the exception of routine obstetric appointments.

Infectious disease clinicians recommended another COVID-19 PCR test, which returned positive. This result was four weeks after the first positive COVID-19 test and symptom onset. Staff wore appropriate PPE during the hospitalization. Shared decision making with the patient and pediatric team was implemented with regard to care for the newborn. Following an uncomplicated hospital course, both the patient and her infant were discharged home in stable condition.

3. Discussion

The patient presented early in the COVID-19 course in the authors' geographic area and was the first confirmed case on the authors'

urban labor and delivery unit. This patient's COVID-19 course lasted approximately two weeks and was complicated by acute pancreatitis.

Pancreatitis commonly presents with nausea and vomiting. It is diagnosed based on acute epigastric pain with tenderness to palpation, and is accompanied by elevations in amylase or lipase up to three times the upper limit of normal. Imaging studies are not required to make the diagnosis. However, if amylase or lipase are less than three times the upper limit of normal, a contrast-enhanced computed tomography (CT) scan can be performed to evaluate other possible etiologies. Additionally, amylase has a shorter half-life, of 10 h, and does not remain elevated, while lipase will remain elevated for longer, which contributes to the increased sensitivity of lipase in diagnosing pancreatitis [13]. Normoamylasemia is also a common finding in acute pancreatitis. Although this patient had a lipase level just under three times the upper limit of normal, a CT scan was not performed due to the high clinical suspicion for acute pancreatitis. The imaging results would not have changed the clinical management and would have exposed the patient and her fetus to radiation.

Common etiologies of pancreatitis were ruled out by her clinical presentation, laboratory studies, and history. A normal triglyceride level excluded hypertriglyceridemia-induced pancreatitis. The patient's history of prior cholecystectomy, along with lack of common bile duct dilation on ultrasound and normal bilirubin, excluded gallstone-induced pancreatitis. She had a normal calcium level, which excluded hypercalcemia as the cause. She also had no recent alcohol intake, trauma, or medications that increase susceptibility to pancreatitis. Although her symptoms started shortly after taking dicloxacillin, there is no evidence that this medication induces pancreatitis or causes elevations of serum amylase or lipase.

Lipase may be elevated by sources other than pancreatitis, such as renal impairment or acute kidney injury (AKI), obstruction of the biliary tract, neoplasia, peritonitis, and DKA [14]. These etiologies of elevated lipase were excluded by clinical presentation and laboratory evaluation. Although the patient was at risk for developing DKA due to her T1DM, this syndrome was ruled out due to the normal anion gap, bicarbonate, and serum glucose levels. Additionally, she did not require any increased insulin throughout her treatment. Lastly, her symptoms resolved with pain medicine, pantoprazole, anti-emetics, remaining NPO until she could advance her diet as tolerated, and intravenous fluids. As a result, the patient was diagnosed with acute pancreatitis from an infectious source, specifically COVID-19.

Multiple studies have now implicated angiotensin-converting enzyme 2 (ACE2) receptors as key players in the pathophysiology of COVID-19 [15,16]. These receptors are also known to exist in the pancreas, and are thought to offer protection against acute inflammation [17,18]. It has been proposed that after COVID-19 binds to these receptors, inflammatory markers are released. Furthermore, this patient's health was complicated by T1DM, which causes chronic inflammation in the pancreas and increases the risk for pancreatitis. Although her T1DM was well controlled on an insulin pump, it is conceivable that her pancreatic ACE2 receptors could be compromised by her chronic condition, making her more susceptible to this acute inflammation from COVID-19 [19].

This case reviews the unique course of a pregnant woman with PCR confirmed COVID-19 infection who presented with acute pancreatitis. While COVID-19 has not been specifically identified to cause pancreatitis in humans, this study proposes COVID-19 as the inciting cause for a presentation of acute pancreatitis in a pregnant patient. In addition, her viral positivity more than four weeks from presentation has implications for the management of previously symptomatic COVID-19 patients later in pregnancy and for their neonates in the postpartum period. We hope that this study will contribute to the fund of knowledge regarding COVID-19 in pregnancy.

Contributors

Sarah R. Rabice was responsible for data collection, writing, research of the case report, and review of the manuscript, and made substantial contributions to the conception and design of the case report.

Paulina C. Altshuler contributed to data collection, writing, literature review, and revision of the manuscript, and made substantial contributions to the conception and design of the report.

Claire Bovet materially participated in data collection and article preparation, and critically revised the article for intellectual content.

Cathlyn Sullivan provided important clinical intellectual content.

Amjy J. Gagnon contributed to the drafting and review of this manuscript, and the conception and design of the report.

All authors saw and approved the final version.

Conflict of Interest

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

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Patient Consent

Written informed consent was obtained from the patient for the use of her medical history and clinical presentation addressed in this case report.

Provenance and Peer Review

This case report was peer reviewed.

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