Case Series

Prolonged hyperglycemia in three patients with type 2 diabetes after COVID-19 infection: A case series

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Abstract

Three independent cases of adult patients are described who had relative control of their type 2 diabetes prior to infection with COVID-19. Each of the described patients had different levels of severity of COVID-19 but all experienced significant and prolonged hyperglycemia for at least 1–2 months after resolution of their COVID-19 infection. Two of the three patients required intensifying insulin regimens for two months after COVID-19 infection. The case study helps to inform primary care providers about the possible need for the intensification of antihyperglycemic medications for several weeks to months after the resolution of COVID-19 infection to minimize prolonged hyperglycemia.

Keywords: COVID-19, hyperglycemia, inflammation, type 2 diabetes

Introduction

Stress-induced hyperglycemia is well-known as an adaptive response and expected during times of infection.[1] However, this is believed to be a transient response that resolves upon improvement of the infection. Unfortunately, there is increasing evidence related to the possibility of a prolonged inflammatory response in patients who have recovered from COVID-19 infections.[2] There is also concern that COVID-19 may cause damage to beta-cells resulting in relative insulin deficiency and acute hyperglycemia.[2] Finally, there have been reports of increased insulin resistance for critically ill patients with type 2 diabetes which may further complicate hyperglycemia management.[3] In the case series described herein, two questions are raised:

1. Does COVID-19 have lingering hyperglycemic effects in patients with underlying type 2 diabetes?
2. What is the most appropriate treatment in the primary care setting to manage hyperglycemia in these patients after acute COVID-19 infection has resolved?

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Case Presentations

Case #1

A 47-year-old Hispanic female with a history of type 2 diabetes mellitus (diagnosed in January 2018) was diagnosed with COVID-19 on April 23, 2020 and was subsequently noted to have an elevated hemoglobin A1c (Hgb A1c) level of 12.1% on May 6, 2020 that was a 4.9% increase from her most recent in-clinic Hgb A1c eight months earlier. Hemoglobin A1c history in 2019 was 6.3% (4/2019), 8.2% in (8/2019) and 7.2% in (9/2019) [Figure 1]. Her only other chronic medical condition includes intermittent asthma for which she does not take medications. Diabetes medications at the time of COVID-19 infection included oral metformin 1,000 mg twice daily and sitagliptin 100 mg daily. She had been on this metformin dose since her diabetes diagnosis and the sitagliptin dose had been consistent for the prior 10 months. The patient's medications had not changed since her previous Hgb A1c in September 2019

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and both her reported history and documented prescription refill history indicated good adherence to her metformin and sitagliptin. She denied other medication changes or change in dietary habits in the interim and received no medication therapy for her COVID-19 infection. Upon following-up with her primary care provider in May 2020 after receiving her COVID-19 diagnosis, no changes were made to her medications despite the Hgb A1c level of 12.1% because the elevation in blood glucose was believed to be related to COVID-19 and likely temporary. The patient was asymptomatic with her COVID-19 infection; however, it is notable that she had an elevation in transaminases after her diagnosis. These were previously normal in April 2019. Hemoglobin A1c was repeated in June 2020 and noted to be further increased at 13.0%. At that point, she was scheduled for instruction on insulin initiation with a plan to begin insulin detemir 10 units once daily. The patient attended her appointment for insulin instruction at the end of July and at that time was not checking her blood glucose regularly. She had two fasting blood glucose readings from the previous week and reported those to be 120 mg/dL and 290 mg/dL. Given that she had not been checking her blood glucose consistently and these readings were quite discrepant, we asked her to check fasting blood glucose daily and planned to follow up in one week by telephone to determine whether basal insulin was truly necessary. One week later, the patient was scheduled in clinic for a different reason and reported fasting blood glucose consistently <200 mg/dL. Hemoglobin A1c was 9.1% on August 6, 2020 and the decision was made to continue monitoring on current medications without starting insulin. Unfortunately, this patient did not attend her most recent visit to follow up in September 2020.

Case #2

A 48-year-old Hispanic female with type 2 diabetes mellitus (diagnosed in 2014) was diagnosed with COVID-19 on June 2, 2020. She was seen in the emergency department on June 6, 2020 for shortness of breath and admitted for COVID-19–related pneumonia. She was also found to have a blood glucose >300 mg/dL and hyponatremia. She was noted to have a Hgb A1c level of 11.1% in the hospital (which was a 2.6% increase from her most recent in-clinic Hgb A1c three months earlier). Hemoglobin A1c history was 8.8% (November 15, 2019), 8.8% (January 27, 2020), and 8.5% (February 24, 2020) [Figure 1]. Other chronic conditions include obesity, dyslipidemia, and dysthymia. Upon admission to the hospital, she reported stopping all of her medications upon diagnosis of COVID-19 as she was afraid of hypoglycemia due to her acute illness. Previously her antihyperglycemic medications included: Insulin glargine 40 units once daily, insulin lispro 45 units twice daily with meals, metformin 1,000 mg twice daily, pioglitazone 45 mg once daily, and dulaglutide 1.5 mg once weekly. Refill history dates support non-adherence with metformin and pioglitazone during the time of COVID-19 infection. While in the hospital, she was given IV fluids and acetaminophen for fever/symptom management and basal and bolus insulin were restarted although at lower doses due to her decreased appetite. She was not treated with steroids. She was discharged home on June 9, 2020 with doxycycline to complete her treatment for community-acquired pneumonia. She followed-up with her primary care clinician who subsequently further titrated her insulin. On August 14, 2020, she returned for another Hgb A1c and it was 11.4% on insulin glargine 55 units once daily and insulin lispro 40 units twice daily in addition to metformin, pioglitazone, and dulaglutide. Her insulin was titrated by 10–15% and she returned one month later (9/11/20) and her Hgb A1c was still 11.4%, despite reporting adherence to medications and taking higher insulin doses prior to her COVID-19 infection.

Case #3

A 45-year-old Hispanic male with type 2 diabetes mellitus (diagnosed May 2019) was diagnosed with COVID-19 on July 31, 2020. He was subsequently hospitalized (August 9, 2020–August 15, 2020) for one week for acute hypoxic respiratory failure secondary to COVID-19. During hospitalization, he was started on remdesivir for five days, and received plasma therapy. He was also started on a dexamethasone taper which he continued as outpatient untill September 2, 2020. Hemoglobin A1c history was 7.4% (January 13, 2020) on metformin 1,000 mg twice daily [Figure 1]. As an inpatient, he received sliding scale insulin and was told to hold his metformin upon discharge until August 24 due to receiving contrast dye. Upon follow-up with his primary care clinician on August 18, he reported a fasting blood glucose of 200–300 mg/dL and was referred to a clinical pharmacist for initiation of insulin. Insulin glargine 10 units at bedtime was started on August 20, 2020 and metformin was reinitiated at 500 mg twice daily on August 25, 2020. On September 15, 2020, the patient was taking 1,500 mg/day of metformin and insulin glargine 20 units once daily; patient reported 100% adherence and was very motivated to get blood glucose under control. He reported the most recent fasting blood glucose of 146 and 148. Unfortunately, the patient did not show up to his most recent appointment for a Hgb A1c recheck.

Discussion

The first patient had type 2 diabetes that was well controlled on two oral medications eight months prior to developing COVID-19.

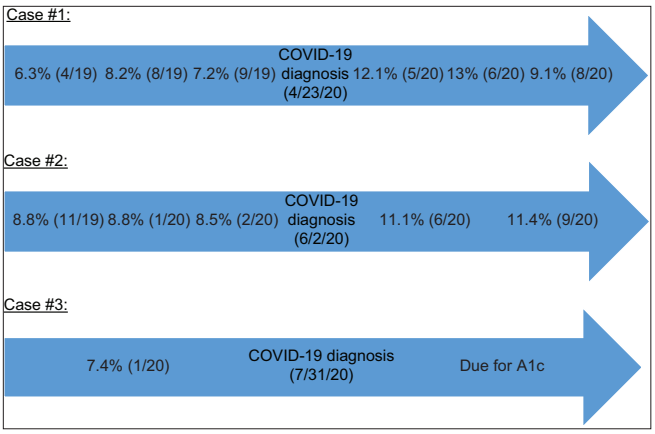

Figure 1: Timeline of A1c trends and COVID-19 infection

Thirteen days after testing positive for COVID-19, her A1c was drawn and was found to have increased dramatically by 4.9%. While there are several potential explanations for worsening control including natural progression of her chronic disease, the patient denied changes in diet or exercise and refill history suggested that the patient had continued to take her oral antihyperglycemic medications reducing the likelihood for these to be potential reasons for the abrupt change in Hgb A1c control. Two months later, despite (inadvertently) not starting insulin or making changes to her antihyperglycemic medications, Hgb A1c began to trend down (improvement by 3.0%) although was still not back to her goal of <7%. This case study presents a clinical dilemma for primary practice clinicians who are following-up with patients after resolution of acute COVID-19 infection. In particular for patients who were previously well-controlled with oral agents alone, is insulin necessary to return to euglycemia or will patients return to baseline control without intensification of medication and how long will this take?

The second patient had type 2 diabetes that was not well controlled but stable approximately three months prior to her diagnosis of COVID-19. The patient admitted to stopping her medications upon her COVID-19 diagnosis which certainly contributed to her acute hyperglycemia upon hospital admission. However, two months later, despite restarting all of her home medications and further intensifying insulin doses, her Hgb A1c had actually trended upward and not improved. This case study demonstrates the potential for a prolonged inflammatory response and/or increased insulin resistance that may be further contributing to hyperglycemia for several weeks to months after resolution of COVID-19 infection.

The third patient had well-controlled type 2 diabetes using metformin only prior to his COVID-19 infection. The patient received a steroid which undoubtedly contributed to his acute hyperglycemia. However, he was not discharged home on insulin from the hospital despite requiring this inpatient. His follow-up with primary care was essential to starting basal insulin in order to better manage this steroid-induced hyperglycemia. Two weeks after the steroid was stopped, the patient's fasting blood glucose readings were improving although still not back to goal despite adherence with basal insulin and reinitiation of metformin. This case demonstrates the necessity of close blood glucose monitoring and primary care follow-up after hospital discharge as he required insulin to return to euglycemia. Yet, this was not given upon hospital discharge suggesting that the medical team did not believe his hyperglycemia would persist.

This case series demonstrates three different patients who had prolonged hyperglycemia lasting up to several months post COVID-19 infection. Two of the three patients required intensifying their antihyperglycemic medications by their primary care team in order to better control their hyperglycemia. Primary care clinicians must recognize that hyperglycemia secondary to COVID-19 infection may not resolve immediately on its own, despite resolution of infection. Close monitoring of blood glucose and Hgb A1c may be needed to help guide intensification of medications.

Conclusion

Patients diagnosed with COVID-19 may have a prolonged inflammatory response with an increased risk of acute hyperglycemia secondary to relative insulin deficiency and/or increased insulin resistance from this novel virus. Primary care clinicians will be responsible for close monitoring of patients with type 2 diabetes after resolution of COVID-19 infection and must recognize that some patients may require intensification of their antihyperglycemics for several weeks to months after infection.

Declaration of patient consent

Institutional IRB approval was received as exempt research was approved with waiver of consent as this was a retrospective review of existing patient data (926-20-EX).

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Nil.

Conflicts of interest

There are no conflicts of interest.

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