High-Dose Prednisone for Treatment of Autoimmune Pancreatitis in a Patient with Coronavirus Disease 2019 (COVID-19) due to Infection with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ADEF 1 **Hammad Liaquat**
BCEF 2 **Brittney Shupp**
CDEF 1 **Sarina Kapoor**
ADEF 1 **Ayaz Matin**

1 Department of Gastroenterology, St. Luke's University Health Network, Bethlehem, PA, U.S.A.
2 Department of Internal Medicine, St. Luke's University Health Network, Bethlehem, PA, U.S.A.

Corresponding Author: Hammad Liaquat, e-mail: liaquathammad@gmail.com
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Patient:	**Male, 53-year-old**
Final Diagnosis:	**Autoimmune pancreatitis type 1 • COVID-19**
Symptoms:	**Abdominal and/or epigastric pain • fever**
Medication:	**—**
Clinical Procedure:	**—**
Specialty:	**Gastroenterology and Hepatology • Infectious Diseases**

Objective: Unusual clinical course

Background: Autoimmune pancreatitis (AIP) is a rare, steroid-responsive disease of the pancreas. Concurrent treatment with immunosuppressants, including corticosteroids, increases the risk of developing a severe form of coronavirus disease 2019 (COVID-19) due to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The World Health Organization (WHO) advises against the use of corticosteroids in patients with SARS-CoV-2 due to their poor outcomes in patients with SARS-CoV and Middle East respiratory syndrome (MERS-CoV), unless these patients require steroid treatment for a coexisting disease.

Case Report: A 53-year old patient was admitted with symptoms and diagnostic findings consistent with AIP. Thorough etiological workup revealed an elevated IgG4 level of 361 mg/dL and significant clinical response to corticosteroid treatment, leading to a diagnosis of AIP. After finishing steroid treatment at home, the patient was readmitted with another episode of AIP complicated by development of acute necrotic collection and COVID-19 while taking a second course of high dose prednisone. The patient was continued on high dose prednisone, started on azathioprine and intravenous meropenem, and underwent CT guided percutaneous drainage. He also received supportive care for COVID-19. After significant clinical improvement, the patient was discharged to quarantine at home, which he completed uneventfully.

Conclusions: Despite the use of corticosteroids due to AIP, this high risk patient recovered from COVID-19 without complications. These findings support the use of corticosteroids when necessary for treatment of coexisting conditions in COVID-19 patients.

MeSH Keywords: Autoimmune Diseases • COVID-19 • Glucocorticoids • Pancreatitis, Acute Necrotizing

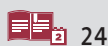**Full-text PDF:** https://www.amjcaserep.com/abstract/index/idArt/926475
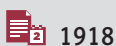
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Background

Autoimmune Pancreatitis (AIP) is a rare but distinct form of pancreatic disease that is responsive to first-line corticosteroids, as well as to immunomodulators [1]. Autoimmune conditions, along with advanced age, male gender, and preexisting comorbidities, are associated with increased risks of mortality and complications in patients with coronavirus disease 2019 (COVID-19) caused by infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [2–4]. Currently, the World Health Organization (WHO) advises against the administration of corticosteroids to patients with SARS-CoV-2 infection due to the poor outcomes observed with corticosteroids in patients with SARS-CoV and Middle East respiratory syndrome (MERS-CoV), unless corticosteroids are necessary for a coexisting disease [5,6]. This report describes a patient with symptomatic, complicated AIP who was receiving treatment with high dose corticosteroids and was diagnosed with COVID-19. This study illustrates the management of a patient with complex SARS-CoV-2 infection and AIP and the outcomes of corticosteroid treatment in this setting.

Case Report

A 53-year-old man with no prior medical history was admitted for evaluation of epigastric abdominal pain for 1 day which was radiating to the back, along with nausea. His serum lipase concentration was 2798 U/L and CT of the abdomen showed peripancreatic inflammation, consistent with a diagnosis of AIP. Etiological work up revealed no history of alcohol intake or cigarette smoking, no intake of any medications known to cause pancreatitis or any family history of pancreatitis or pancreatic cancer. He had normal calcium levels, borderline high triglyceride levels, and elevated IgG4 level of 361 mg/dL. Ultrasound and magnetic resonance cholangiopancreatography (MRCP) of his right upper quadrant were unremarkable. He was diagnosed with type 1 AIP due to elevated IgG4 levels, given supportive treatment and started on 40 mg/day prednisone. The patient recovered clinically soon after starting steroid treatment, further confirming the diagnosis of AIP, and he was discharged home. He was prescribed 40 mg/day prednisone for 30 days, followed by dose tapering of 5 mg/day per week.

Although the patient remained asymptomatic during treatment with corticosteroids, he was hospitalized with a second episode of AIP two weeks after completing corticosteroid treatment. He was provided supportive treatment and started on 40 mg/day prednisone. The patient reported improvement in abdominal pain and was able to tolerate a low fat diet. He was discharged from the hospital and prescribed 40 mg/day prednisone for 1 month, followed by dose tapering of 5 mg/day per week. He was also scheduled for an appointment at the gastroenterology clinic within one to two weeks after leaving the hospital.

One week after discharge from the hospitalization, the patient reported fever, a persistent dry cough, and malaise, along with unresolved abdominal pain and the recurrence of nausea. Cobas® SARS-CoV-2 reverse transcriptase-polymerase chain reaction (RT-PCR) testing of a nasopharyngeal swab sample using the automated Cobas® 6800/8800 system showed that he was positive for SARS-CoV-2. He was admitted to the hospital, where he was found to be febrile, tachycardic, and tachypneic with normal blood pressure. Tenderness in the epigastric region was noted. His hematocrit was 35.8%, his white blood cell (WBC) count was 12.32×10³/μL, his blood urea nitrogen (BUN) concentration was 9 mg/dl, his serum lipase concentration was 530 μ/L, and his liver function tests were normal. CT of the abdomen revealed severe pancreatitis along with a multiloculated heterogeneous accumulation of fluid and gas in the pancreatic and peripancreatic tissues, consistent with an infected acute necrotic collection (Figure 1A, 1B). Chest imaging showed bibasilar patchy ground glass opacities (Figure 2A) and the presence of nonspecific linear densities in the lower lung fields (Figure 2B), consistent with COVID-19 pneumonia.

The patient was continued on 40 mg/day prednisone and started on vitamin D3 and plaquenil for COVID-19. He was given single doses of ceftriaxone and flagyl to treat possible infected pancreatic necrosis. One day later, his antibiotic coverage was broadened and he was started on meropenem. The patient remained symptomatic and was unable to resume oral intake. He underwent CT guided percutaneous drainage of the pancreatic necrosis the next day. The following day, his pain improved and his diet was advanced. Following a 4-day course of meropenem and continued clinical improvement, the patient was transitioned to PO bactrim based on culture sensitivities of the pancreatic drainage. Due to the patient's history of AIP relapse despite steroid therapy, 50 mg/day azathioprine was added to his discharge regimen, with a plan to wean off steroids by tapering his dose by 5 mg/day per week. After hospitalization for 7 days, the patient was discharged, prescribed bactrim for two additional days and instructed to quarantine at home. Despite continued high dose corticosteroid use in hospital, the patient did not require oxygen supplementation or experience any further complications from COVID-19.

Discussion

As the global COVID-19 pandemic unfolds, efforts are being made to identify individuals at highest risk of severe disease and to determine the proper treatment regimens for disease management. Multiple risk factors have been identified and associated with higher morbidity and mortality, especially in
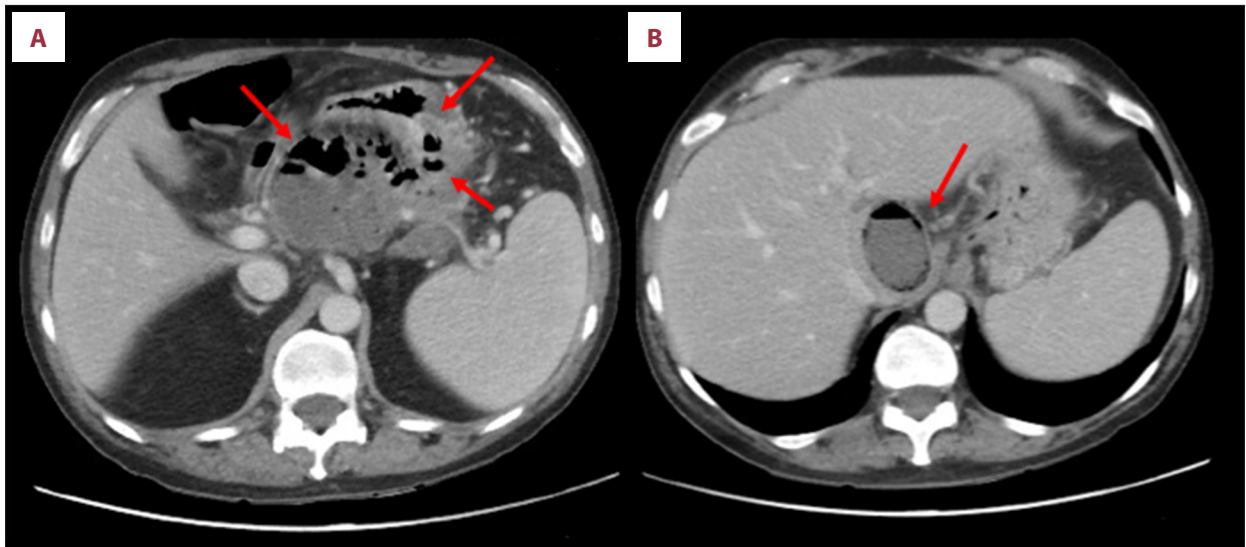
Figure 1. Contrast-enhanced abdominal computed tomography (CT), showing the presence of severe necrotizing pancreatitis with multiloculated collection containing both fluid and gas in pancreatic and peripancreatic tissues (**A, B**).
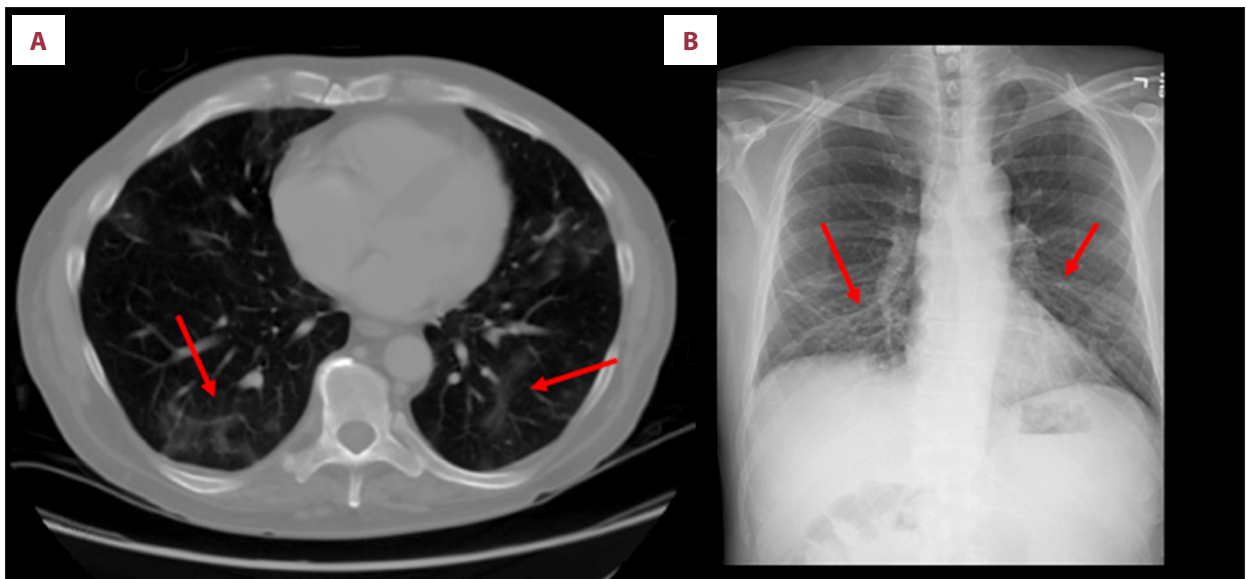

Figure 2. (**A**) Contrast-enhanced chest computed tomography (CT) showing bibasilar infiltrates in the lower lung fields and (**B**) chest x-ray showing nonspecific linear densities in lower lung fields. Both of these images are consistent with COVID-19 pneumonia.

critically ill patients. Although the median age of patients with this disease has been shown to be approximately 56 years, individuals aged ≥64 years are at greatest risk for contracting this disease and experiencing complications from it [3,7]. Additionally, data from the Centers for Disease Control and Prevention have shown that individuals aged ≥45 years are at higher risk for hospitalization and ICU admission [2]. COVID-19 has also been shown to affect minorities more than white people, a difference likely due to disparities in healthcare, while also affecting males more than females [3]. However, one of the most significant risk factors associated with development

of severe disease is having preexisting conditions, including cardiovascular disease, hypertension, diabetes, chronic lung disease, cancer, and diseases that require immunosuppressant therapy, such as corticosteroids [4,8]. AIP is a rare autoimmune disease that requires treatment with corticosteroids, placing these patients at greater risk of complications and mortality due to COVID-19.

AIP is a steroid responsive, pancreatic disease that is often evaluated and diagnosed after exclusion of other causes. There are two forms of AIP, characterized by the presence of

Table 1. Studies demonstrating outcomes of corticosteroid use in patients with severe acute respiratory syndrome (SARS-CoV) and Middle East respiratory syndrome (MERS-CoV).

Outbreak	Participants	Methods	Outcomes related to steroid use	Ref
SARS-CoV	117 previously healthy patients with confirmed diagnosis of SARS-CoV	Compared weekly qualitative CoV RT-PCR assays, chest XR, SARS-COV serology, and daily plasma SARS-CoV RNA concentrations between those who received hydrocortisone 100 mg q 8 hrs *vs.* placebo group	Early hydrocortisone initiation led to delayed viral clearance	[12]
	Compared 15 patients diagnosed with SARS related psychosis to 30 age and sex matched SARS control subjects with no diagnosis of psychosis	Reviewed the clinical data of SARS patients requiring psychiatric consultation and compared them with the charts of the control group to investigate risk factors	Higher rates of psychosis associated with higher cumulative corticosteroid doses	[14]
	133 confirmed SARS patients, including 95 who were prescribed glucocorticoids	Reviewed the clinical data of SARS patients to determine fasting plasma glucose (FPG) levels and associated risk factors	Elevated FPG and diagnosis of steroid-induced diabetes were associated with increased doses and duration of corticosteroids	[15]
	40 hospitalized patients with confirmed SARS infection	3 months following discharge, SARS patients on corticosteroids were evaluated by MRI to detect avascular necrosis of the femoral head and with ultrasound of the left heel to determine osteoporosis	Increased cumulative dosing of corticosteroids led to higher incidence rates of osteoporosis and avascular necrosis	[16]
MERS-CoV	309 patients who met the MERS eligibility criteria, excluding patients with a history of chronic corticosteroid use	Analyzed the recorded data from a retrospective cohort hospital study involving 14 tertiary care hospitals in Saudi Arabia and compared corticosteroid use and viral RNA clearance in groups that were and were not treated with corticosteroids group	Corticosteroid use had no effect on 90-day mortality but was associated with delayed MERS-CoV RNA clearance	[13]

extrapancreatic involvement and histological appearance [1,9]. Type 1 AIP, also called lymphoplasmocytic sclerosing pancreatitis (LPSP), is a systemic form of the disease that usually involves multiple organs and is associated with elevated IgG4 levels. Type 2 AIP, also called idiopathic duct centric pancreatitis (IDCP), is localized to the pancreas and is characterized by granulocyte epithelial lesions (GEL) due to infiltration of neutrophils into the pancreatic ductal epithelium. These two forms of AIP are similar, in that both are responsive to first-line corticosteroids, as well as to immunomodulators. Type 1 AIP usually presents in men aged >60 years as painless obstructive jaundice, with acute pancreatitis and presentation in younger persons considered rare. The diagnosis of AIP requires the presence of one or more components of the HISORt criteria (histology, characteristic findings on imaging, elevated IgG4 levels, involvement of other organs, and/or response of disease to corticosteroid usage) [1]. Our patient had elevated IgG4 levels and responded to corticosteroid therapy, factors consistent with a diagnosis of Type I AIP.

Our patient had severe AIP, complicated by the presence of an acute necrotic collection. In addition to inpatient treatment with high dose corticosteroids, he was managed by percutaneous drainage and treatment with antibiotics. This regimen is the most frequently used minimally invasive form of therapy, especially when compared with endoscopic drainage, because percutaneous drainage is successful in avoiding open necrosectomy, which is associated with higher morbidity and mortality rates [10]. If necessary, patients can be treated with additional minimally invasive procedures, such as endoscopic drainage to treat necrotic collections. These procedures are accompanied by the continued use of corticosteroids, which reduce pancreatic inflammation. Nevertheless, uncontrolled AIP and corticosteroids, which increaseing co-morbidity burden and immunosuppression, respectively, place individuals at increased risk of severe COVID-19 infection [4,8]. Relatively little is known about the impact of gastrointestinal and liver diseases, specifically autoimmune conditions, on COVID-19 patients [11]. Because AIP is rare, it has not yet been implicitly discussed as

Table 2. Studies demonstrating outcomes of corticosteroid treatment in patients with coronavirus disease 2019 (COVID-19) due to infection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).

Outbreak	Participants	Methods	Outcomes related to steroid use	Ref
SER-CoV-2	138 hospitalized patients with confirmed COVID-19 infection, including 45% who received methylprednisolone	Reviewed clinical data of COVID-19 patients to identify, analyze, and compare patient characteristics and treatment outcomes	No effective outcomes were observed	[7]
	41 hospitalized patients with confirmed COVID-19 infection, including 22% who received methylprednisolone	Reviewed clinical data of COVID-19 patients to identify, analyze, and compare patient characteristics, radiographic features, and laboratory data	Methylprednisolone was administered if patient was diagnosed with severe community acquired pneumonia, but no effective outcomes were observed	[22]
	201 hospitalized patients with confirmed COVID-19 infection, including 30.8% who received methylprednisolone	Reviewed clinical data of COVID-19 patients to identify, analyze, and compare patient characteristics, radiographic features, and laboratory data	Death rates in ARDS patients who did and did not receive methylprednisolone were 46% and 61.8%, respectively	[23]
	15 hospitalized patients with critical COVID-19 pneumonia admitted to the ICU	Initiated corticosteroid treatment after ICU stay of an average of 9.5 days and followed up on patient outcomes	Use of corticosteroids did not improve ICU mortality. No conclusion on corticosteroid usage could be reached due to small sample size and lack of a matched control group	[21]
	46 hospitalized patients with severe COVID-19 pneumonia, including 26 who received extra low-dose methylprednisolone treatment	Compared the clinical outcomes of patients receiving low dose methylprednisolone treatment with a control group that received the same treatment regimen without methylprednisolone	Use of low dose and short term methylprednisolone treatment early in the disease course was associated with better outcomes in severe COVID-19 patients including shorter supplemental oxygen use, reduced need for mechanical ventilation, and shorter ICU and hospitalization stay	[20]

a comorbid condition in COVID-19 patients, making management of this patient more complex and empiric.

Currently, the WHO advises that corticosteroids not be administered to patients with COVID-19, but does allow for their use in patients with preexisting conditions. Judicious use of steroids in the setting of COVID-19 was originally suggested in response to poor outcomes in previous viral outbreaks. such as SARS-CoV and MERS-CoV [5]. Although corticosteroids have been tested due to their potential ability to prevent inflammatory lung injury, their use was not advantageous and led to serious adverse reactions (Table 1). Patients with SARS-CoV and MERS-CoV who were treated with corticosteroids had higher plasma viral loads, suggesting delayed viral clearance due to corticosteroid impairment of the host immune system [5,12,13]. In addition, SARS-CoV patients treated with higher cumulative doses of corticosteroids were found to be more likely to develop complications, such as

psychosis, diabetes, osteoporosis and avascular necrosis [14–16]. Systemic reviews of previous viral outbreaks and during the current SARS-CoV-2 pandemic have found that corticosteroid use was not advantageous in the past and requires further research to warrant their use for treatment of SARS-CoV-2 [17–19].

Few studies to date have investigated steroid use in COVID-19 illness, with those studies limited by small sample sizes and inconclusive or conflicting results (Table 2). In one study, a short course of low dose methylprednisolone improved outcomes in severe COVID-19 patients in the ICU by shortening supplemental oxygen use, reducing the need for mechanical ventilation and shortening ICU and hospitalization stay when compared with a control group [20]. Another study found that steroid treatment failed to show benefits in 15 critically ill patients with COVID-19 pneumonia [21], whereas other studies did not report definitive results [7,22,23]. Most of these studies are

similar, in that they involve small sample sizes and administration of corticosteroids to critically ill patients, suggesting that they may be somewhat limited by the potential of confounding bias. Overall, these studies do not provide sufficient evidence to support routine corticosteroid use in COVID-19 [5,6]. However, the National Institute for Health and Care Excellence (NICE) has developed guidelines to specifically assist in the management of gastrointestinal and liver diseases during the COVID-19 pandemic [24]. These guidelines recommend that oral or rectal corticosteroids to treat compelling gastrointestinal or liver conditions not be discontinued when a patient is diagnosed with COVID-19. These guidelines are in accordance with WHO recommendations that allow for corticosteroid treatment of preexisting conditions in COVID-19 patients.

The outcomes of past studies, as well as the scarcity of data regarding steroid use in SARS-CoV-2 infected patients, have helped in the formulation of WHO recommendations on corticosteroid use in COVID-19 patients. The findings in our patient provide evidence supporting current WHO recommendations on the judicious use of corticosteroids for the treatment of preexisting conditions such as AIP in COVID-19 patients.

Conclusions

Corticosteroids are the first line of treatment for AIP. Little is known about the use of steroids to treat COVID-19 patients. Although corticosteroids resulted in poor outcomes in previous SARS-CoV and MERS-CoV outbreaks and are not recommended for use in patients with COVID-19, our patient did not experience additional COVID-19 complications despite having multiple risk factors (age >45 years, male gender, comorbidity due to uncontrolled AIP and steroid immunosuppression) associated with poor outcomes. The findings in our patient provide evidence supporting current recommendations that steroid therapy be administered for co-existing diseases in patients with COVID-19.

Department and Institution where work was done

Gastroenterology Department, St. Luke's University Health Network, Bethlehem, PA, U.S.A.

Conflict of interest

None.

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