ACG CASE REPORTS JOURNAL

CASE REPORT | PANCREAS

Type 1 Autoimmune Pancreatitis Unmasked by COVID-19 Vaccine

Erica C. Becker, MD, MPH[1], Osama Siddique, MD[2], Dinesh Kapur, MD[3], Krishna Patel, MD[4], and Vaibhav Mehendiratta, MD[2]

[1]*Department of Internal Medicine, University of Connecticut Health Center*
[2]*Connecticut GI, PC, Division of Gastroenterology, Hartford Hospital, Hartford, CT*
[3]*Eastern Connecticut Hematology and Oncology, Norwich, CT*
[4]*Department of Pathology, Hartford Hospital, Hartford, CT*

ABSTRACT

Autoimmune pancreatitis is a rare fibro-inflammatory disease with 2 distinct subtypes of which each has their own clinical presentation, risk factors, and histopathological patterns. We present a case of newly diagnosed type 1 autoimmune pancreatitis in a symptomatic 54-year-old man with stable ulcerative colitis 1 month after COVID-19 vaccination. Previous reports have indicated that vaccinations can trigger autoimmune disease in predisposed individuals. This case discusses the occurrence of autoimmune pancreatitis triggered after COVID-19 vaccination.

KEYWORDS: pancreatitis; COVID-19 vaccine; type 1 autoimmune pancreatitis; lymphoplasmacytic sclerosing pancreatitis

INTRODUCTION

Type 1 autoimmune pancreatitis (AIP), also known as lymphoplasmacytic sclerosing pancreatitis, is a rare form of idiopathic chronic pancreatitis associated with IgG4-related systemic disease.[1] Type 1 AIP predominantly affects male adults and has multiorgan extrapancreatic manifestations (ie, sclerosing cholangitis, interstitial nephritis, sclerosing sialadenitis, mediastinal fibrosis, and thyroiditis).[2] However, it is much less associated with inflammatory bowel disease compared with type 2 AIP, which is reported to have a least 15% predilection for ulcerative colitis.[2] It is believed that the cause of AIP maybe multifactorial from immunological, genetic, and/or environmental and that an inciting event in genetically predisposed individuals may trigger AIP. To date, there are no reports of vaccine-induced type 1 AIP. We present a case of newly diagnosed type 1 AIP in a 54-year-old man with stable ulcerative colitis 1 month after receiving coronavirus disease 2019 (COVID-19) vaccination.

CASE REPORT

A 54-year-old White man with a history of chronic stable sarcoidosis and ulcerative colitis in surgical remission who presented with a 3-week history of decreased appetite, abdominal pain, fatigue, and 25-pound unintentional weight loss. He reported no history of diabetes, pancreatic cancer, or pancreatic surgery. He was not on any immunosuppressants and had no recent medication changes. He had received the second dose of Pfizer/BioNTech COVID-19 mRNA vaccine approximately 1 month before current presentation. On admission, the patient had vital signs within normal limits. On physical examination, he seemed dehydrated. Computed tomography (CT) was significant for diffusely enlarged pancreas with peripancreatic fat surrounding the tail of the pancreas. He was treated with intravenous fluids and discharged from the emergency department with recommendation to follow-up with his primary care provider.

A few days later, he presented to the emergency department with jaundice and scleral icterus. Laboratory tests were significant for hypovolemia, hyperglycemia, total bilirubin of 10.5 mg/dL (reference range 0.2–1.0 mg/dL), direct bilirubin 7.9 mg/dL (reference range 0–0.2 mg/dL), aspartate aminotransferase of 137 U/L (reference range 10–55 U/L), alanine aminotransferase of 515 U/L (reference range 10–55 U/L), alkaline phosphatase 630 U/L (reference range 45–128 U/L), and lipase 240 U/L (reference range 13–60 U/L). The immunoglobulin G4 (IgG4) level was 287.0 mg/dL (reference range 4.0–86.0 mg/dL). A repeat CT scan

ACG Case Rep J 2023;10:e00950. doi:10.14309/crj.0000000000000950. Published online: January 25, 2023

Correspondence: Erica C. Becker MD, MPH (ebecker@uchc.edu).

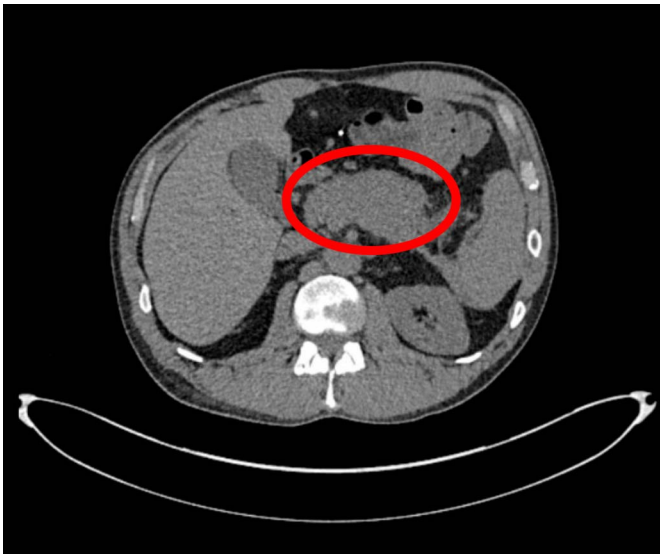

Figure 1. Computed tomography of the abdomen and pelvis revealed (indicated by circle) distended pancreatic parenchyma with peripancreatic stranding with segments of biliary ductal dilation.

demonstrated distended pancreatic parenchyma with peripancreatic stranding with segments of biliary ductal dilation (Figure 1). He underwent a magnetic resonance cholangiopancreatography which showed dilated bile ducts to the level of the head of the pancreas where there was an abrupt truncation of the extrahepatic common duct. The pancreas was diffusely enlarged with some irregular beading and

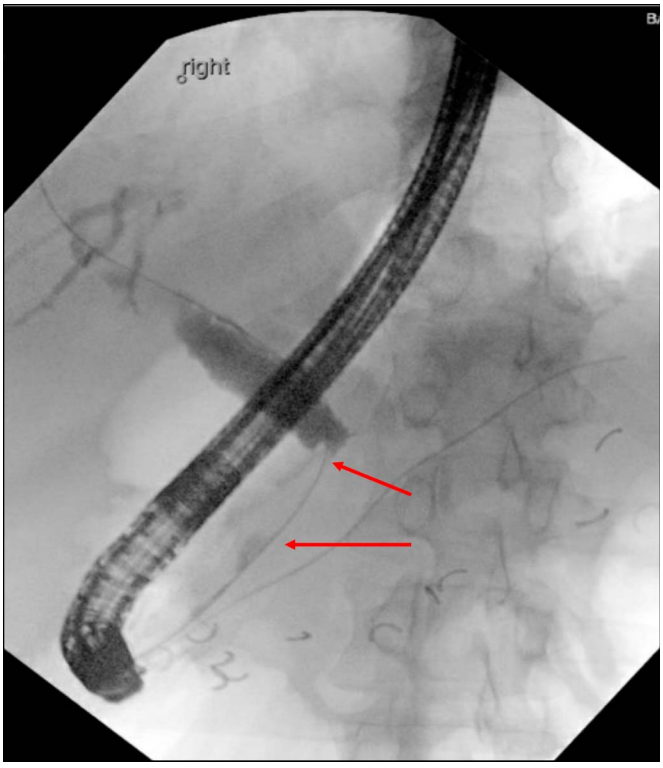

Figure 2. First ERCP with length of stricture marked between the 2 arrows. ERCP, endoscopic retrograde cholangiopancreatography.

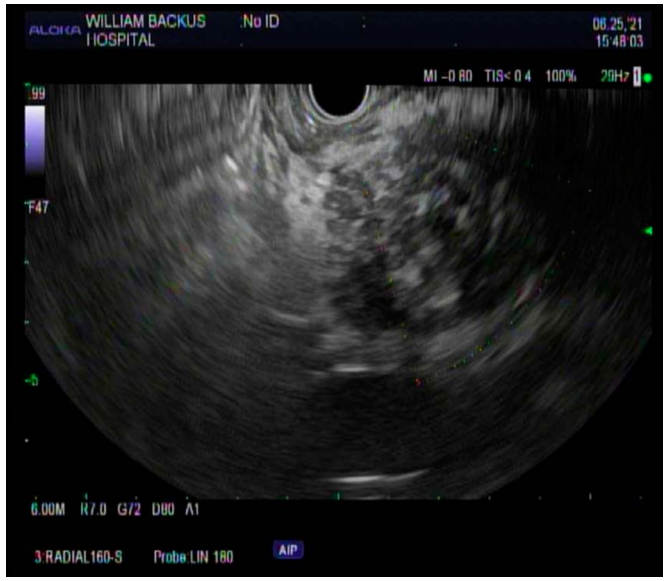

Figure 3. Hypoechoic gland with hyperechoic foci without shadowing.

narrowing of the main pancreatic duct. Minimal amount of peripancreatic fluid pattern was noted. On endoscopic retrograde cholangiopancreatography (ERCP), the lower third of the main bile duct contained a single severe stenosis 20–25 mm in length and a biliary stent was placed (Figure 2). Brush cytology from the common bile duct was negative for malignancy. Endoscopic ultrasound was performed and pancreatic parenchyma was diffusely abnormal with lobularity, generalized hypoechoic gland, and hyperechoic foci without shadowing (Figure 3). The pancreatic duct was irregular in contour. Fine needle biopsies were obtained from the pancreatic body (Figures 4). Immunohistochemical tests showed IgG and IgG4 positive plasma cells (Figures 5). There were 18 IgG4-positive plasma cells with a calculated IgG-IgG4 ratio of 0.7, which is suggestive of an IgG4-related chronic pancreatitis, also known as type 1 AIP. Inflammatory cells consisted predominantly of lymphocytes and plasma cells and occasional eosinophils.

The patient was started on a 3-week prednisone taper starting with 40 mg. Repeat laboratory work showed normalization of liver enzymes and IgG4. Repeat magnetic resonance cholangiopancreatography showed strictures in the distal common bile duct with interval improvement. Repeat ERCP showed improvement of the lower third of the main bile duct with a focal area of stenosis at 8 mm in length (Figure 6). Two biliary stents were placed for serial dilation. On the 9-month follow-up, he had gained his weight back and reported complete resolution of abdominal pain and fatigue.

DISCUSSION

Both vaccine-induced acute hepatitis and pancreatitis have been reported occurring 2–3 days after receiving Pfizer/

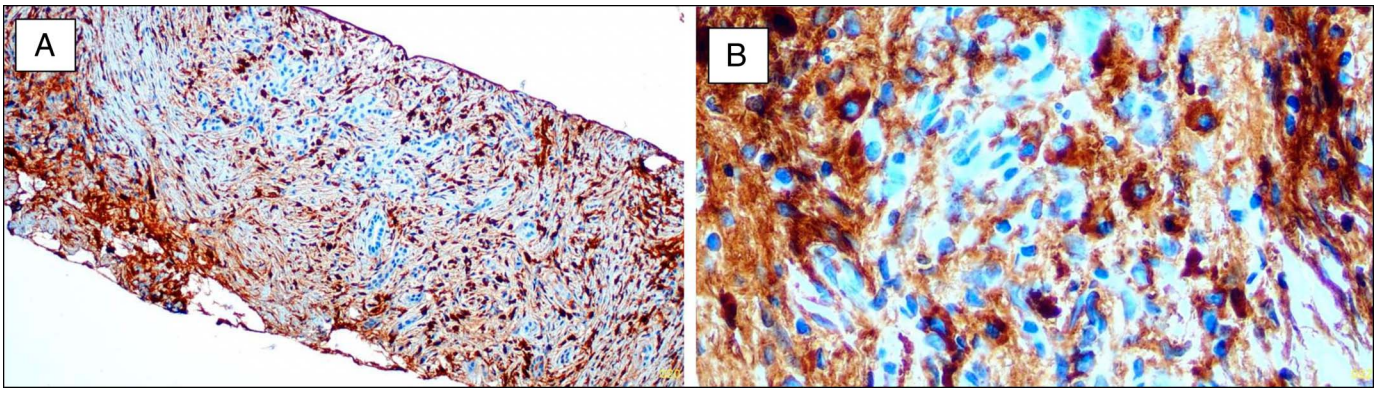

Figure 4. (A) Low-power (×4) hematoxylin and eosin (H&E) stained slide of immunoglobulin G4 (IgG4)-related chronic pancreatitis. Histopathological image of pancreatic parenchyma with dense storiform fibrosis and lymphoplasmacytic infiltrate. (B) High-power (×40) H&E stained slide of IgG4-related chronic pancreatitis. Histopathological image of pancreatic parenchyma with duct centric lymphoplasmacytic infiltrate.

BioNTech COVID-19 mRNA vaccine.[3,4] To date, there have been 3 publications regarding possible COVID-19 vaccine-induced autoimmune hepatitis (AIH); this is the first case documented regarding AIP (Table 1).

McShane et al (2021) reported a case of Moderna COVID-19 mRNA vaccine-induced AIH with symptoms occurring 4 days after vaccination. The mechanism of action was believed to be through immune system activation and of autoreactive lymphocytes leading to the development of autoimmune disease; however, as eosinophils were seen on histopathology, it unknown whether the patient was presenting with AIH or AIH features because of drug or toxin-induced liver injury.[5] Bril et al (2021) reported a case of Pfizer/BioNTech COVID-19 mRNA vaccine-induced AIH who developed symptoms 1 week after vaccination. Similarly, to the case by McShane et al, this patient's histopathology was also significant for eosinophils, which have been documented in cases of AIP, but are more commonly found in drug or toxin-induced liver injury.[6] Rocco et al (2021) reported an 80-year-old woman who developed AIH 1 week after obtaining Pfizer/BioNTech COVID-19 mRNA vaccine. Like the other patients, she had no history of liver disease or triggering factors. All patients improved with a steroid taper.[5–7]

Our case suggests a temporal association between COVID-19 vaccination and AIP, although a cause effect relation cannot be definitely established. We considered other triggers and confounding factors for AIP. Laboratory results were not indicative of other inciting factors. He had no allergies. He had not received any other recent vaccinations. In addition, he was not on any medications that have been linked to induction of autoimmune conditions or had any recent medication changes. Our patient was the appropriate age and had ulcerative colitis, thus the correct demographic for developing AIP. He may have been genetically predisposed, and the vaccination triggered the immune system. Like the other cases of vaccine-induced AIH, no other confounding risk factors were identified. We acknowledge and cannot completely exclude the possibility of AIP occurring by chance or secondary to genetic or environmental factors. However, we are reassured that the patient did not have any symptoms concerning for AIP before presentation. Although most cases of vaccine-induced autoimmune disease

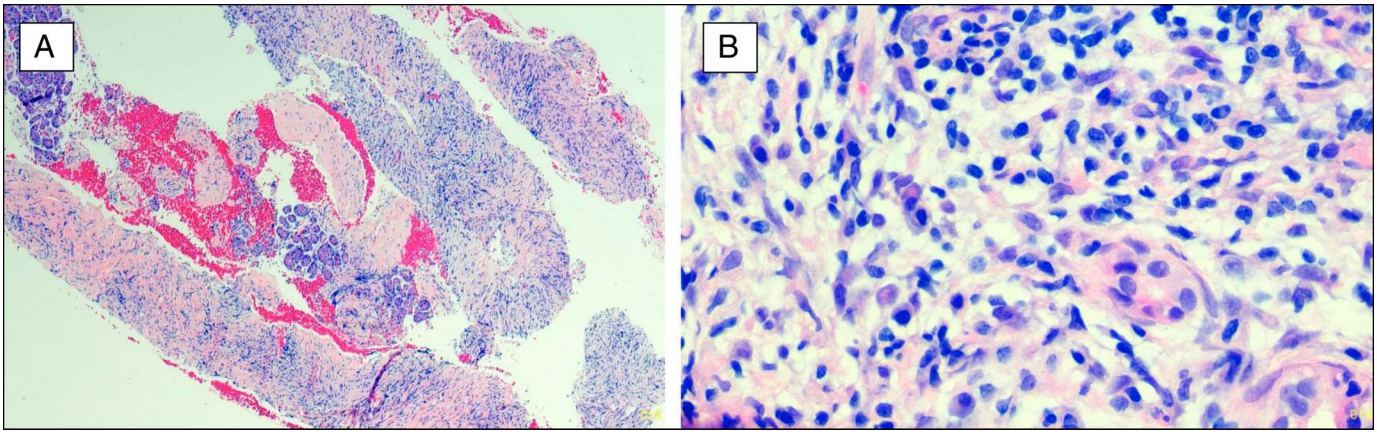

Figure 5. (A) Medium-power (×10) immunohistochemical positivity for IgG on plasma cells. (B) High-power (×40) immunohistochemical positivity for IgG4 on plasma cells.

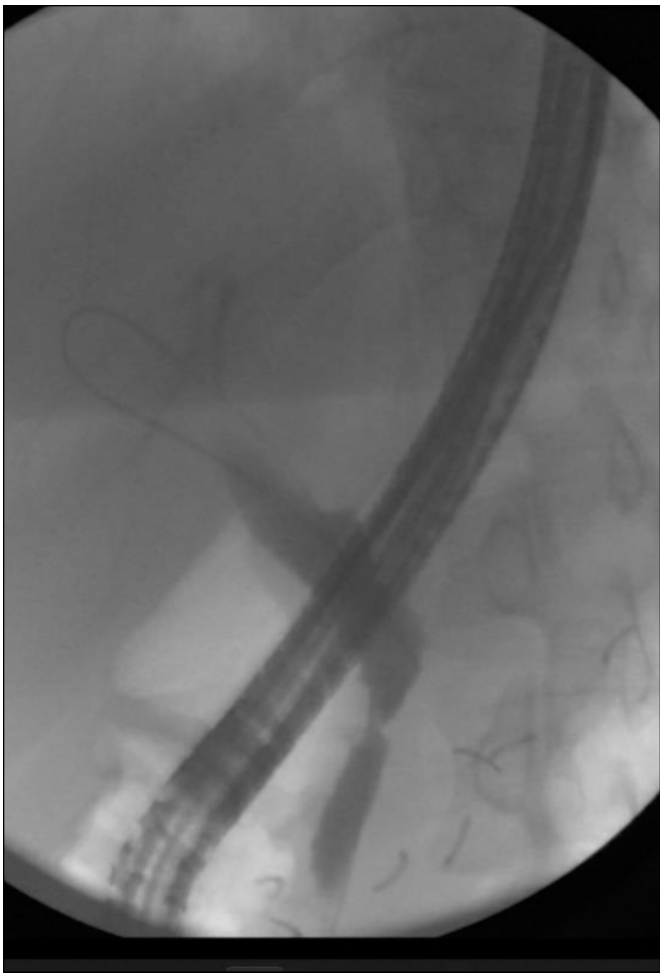

Figure 6. Repeat ERCP with much improved stricture. ERCP, endoscopic retrograde cholangiopancreatography.

have been reported within a few days of vaccination, there are reports of immune-mediated disease occurring 3–4 weeks postvaccination. For example, Patrizio et al (2021) documented an occurrence of Graves' disease and autoimmune diabetes mellitus 4 weeks after vaccination.[8] In addition, it has been reported that Guillain-Barre syndrome, an acute autoimmune demyelinating polyneuropathy, can occur few weeks postvaccination.[9]

Fortunately, the patient did not have any known symptoms to the initial COVID-19 vaccine. However, the lack of complication from the initial vaccination does not exclude the second vaccination as a trigger. There have been other cases documenting COVID-19 vaccine-induced autoimmune disease occurring after the second vaccination. For example, King et al (2022) reported immune thrombocytopenic purpura occurring after the second COVID-19 vaccination in a patient who reported no complications after the initial vaccination.[10,11] In our case, we cannot verify whether this was just idiosyncratic or concurrent doses triggering an eventual autoimmune flare.

Table 1. Review of autoimmune hepatitis and autoimmune pancreatitis cases in patients with recent COVID-19 vaccination

Reference	Diagnosis	Sex/age	Vaccine
Bril et al 2021	Autoimmune hepatitis	F/35	Pfizer/BioNTech mRNA
McShane et al 2021	Autoimmune hepatitis	F/71	Moderna mRNA
Rocco et al 2021	Autoimmune hepatitis	F/80	Pfizer/BioNTech mRNA
Becker et al 2022	Autoimmune pancreatitis	M/54	Pfizer/BioNTech mRNA

It is important to consider that the COVID-19 vaccine could be the inciting factor for type 1 AIP in patients with genetic predisposition. Furthermore, it is unclear at this time whether patients should obtain additional doses of the vaccination once diagnosed with AIP. However, owing to the risks of COVID-19 infection and ongoing mandates, physicians should continue to discuss benefits and risks of vaccination with patients and to monitor for symptoms if vaccination is pursued.

DISCLOSURES

Author contributions: E. Becker wrote the manuscript. O. Siddique, D. Kapur, K. Patel, and V. Mehendiratta revised the manuscript for intellectual content. E. Becker, O. Siddique, D. Kapur, K. Patel, and V. Mehendiratta approved the final manuscript. V. Mehendiratta is the article guarantor.

Financial disclosure: V. Mehendiratta is consultant for Boston Scientific.

Informed consent was obtained for this case report.

Received June 7, 2022; Accepted December 5, 2022

REFERENCES

1. Martins C, Lago P, Sousa P, et al. Type 2 autoimmune pancreatitis: A challenge in the differential diagnosis of a pancreatic mass. *GE Port J Gastroenterol* 2017;24(6):296–300.
2. Masood M. Autoimmune pancreatitis: What we know so far. *JGH Open* 2022;6(1):3–10.
3. Garrido I, Lopes S, Simoes MS, et al. Autoimmune hepatitis after COVID-19 vaccine - more than a coincidence. *J Autoimmun* 2021;125:102741.
4. Ozaka S, Kodera T, Ariki S, Kobayashi T, Murakami K. Acute pancreatits soon after COVID-19 vaccination: A case report. *Medicine* 2022;101(2):e28471.
5. McShane C, Kiat C, Rigby J, Crosbie O. The mRNA COVID-19 vaccine-a rare trigger of autoimmune hepatitis. *J Hepatol* 2021;75(5):1252–4.
6. Bril F, Al Diffalha S, Dean M, Fettig DM. Autoimmune hepatitis developing after coronavirus disease 2019 (COVID-19) vaccine: Causality or casualty? *J Hepatol* 2021;75(1):222–4.
7. Rocco A, Sgamato C, Compare D, Nardone G. Autoimmune hepatitis following SARS-CoV-2 vaccine: May not be a casuality. *J Hepatol* 2021;75(3):728–9.

8. Patrizio A, Ferrari SM, Antonelli A, Fallahi P. A case of Graves' disease and type 1 diabetes mellitus following SARS-CoV-2 vaccination. *J Autoimmun* 2021;125: 102738.
9. Patel SU, Khurram R, Lakhani A, Quirk B. Guillain-Barre syndrome following the first dose of the chimpanzee adenovirus-vectored COVID-19 vaccine, ChAdOx1. *BMJ Case Rep* 2021;14(4):e242956.
10. King ER, Towner E. A case of immune thrombocytopenia after BNT162b2 mRNA COVID-19 vaccination. *Am J Case Rep* 2021;22: e931478.
11. Chen Y, Xu Z, Wang P, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. *Immunology* 2022;165(4):386–401.