Scientific Research Publishing

Open Journal of Nephrology, 2025, 15(2), 174-179
https://www.scirp.org/journal/ojneph
ISSN Online: 2164-2869
ISSN Print: 2164-2842

Acute Autoimmune Pancreatitis and Interstitial Nephritis, due to IgG4 Disease, Following Pfizer-BioNTech COVID-19 Vaccination

—IgG4 Disease Following COVID-19 Vaccination

Kamel El-Reshaid[1*], Abdulmohsen Al-Bader[2]

[1]Department of Medicine, Faculty of Medicine, Kuwait University, Kuwait City, Kuwait
[2]Department of Medicine, Farwania ENT & ICU units, Kuwait City, Kuwait
Email: *kamel@hsc.edu.kw

How to cite this paper: El-Reshaid, K. and Al-Bader, A. (2025) Acute Autoimmune Pancreatitis and Interstitial Nephritis, due to IgG4 Disease, Following Pfizer-BioNTech COVID-19 Vaccination. *Open Journal of Nephrology*, **15**, 174-179.
https://doi.org/10.4236/ojneph.2025.152017

Received: April 6, 2025
Accepted: May 19, 2025
Published: May 22, 2025

Abstract

Background: Immunoglobulin G4-related disease (IgG4-RD) is a multi-organ, fibro-inflammatory condition characterized by triad of; 1) lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, and increased $IgG4^+$ plasma cells, 2) elevated serum IgG4 levels, and 3) good response to Corticosteroids. Its etiology is uncertain. **Case:** A 60-year-old man developed persistent acute pancreatitis for 1 month following Pfizer-BioNTech COVID-19 vaccination. Moreover, he had progressive acute renal failure. Computerized tomography of abdomen and pelvis did not show abnormality, especially in the peripancreatic region. Moreover, endoscopic ultrasonography did not show pancreatic lesions. His kidney biopsy showed acute interstitial nephritis with a heavy IgG4-plasma cell infiltrate. Autoimmune workup was negative except for high IgG4 at 1963 g/L (N: 0.039 - 0.864) with IgG4/IgG ratio at 0.16. Hence, diagnosis of IgG4-RD was established. He was treated with Prednisone 1 mg/kg for 1 month which was tapered till discontinuation by 3rd month. His clinical picture, biochemical indices and IgG4 level returned to normal by 2nd week. Such improvement persisted up to 2 years. **Conclusion:** Overt IgG4 disease with acute pancreatitis and interstitial nephritis can be triggered by COVID-19 vaccination that is amenable to Corticosteroids. It confirms the autoimmune etiology of IgG4-RD triggered by COVID-19 vaccine in a genetically predisposed patient.

Keywords

Autoimmune, Corticosteroids, Genetic-Predisposition, IgG4, Interstitial Nephritis, COVID-19 Vaccine, Pancreatitis, Triggers

1. Introduction

Immunoglobulin G4-related disease (IgG4-RD) is a multi-organ, fibro-inflammatory condition characterized by the triad of 1) lymphoplasmacytic infiltrate, storiform fibrosis, obliterative phlebitis, and increased $IgG4^+$ plasma cells, 2) elevated serum IgG4 levels, and 3) good response to Corticosteroids. Virtually any organ can be involved, but the most commonly involved are the pancreas, kidneys, orbital adnexal structures, salivary glands, and retroperitoneum. Its lesions, including inflammatory pseudotumors, are often misdiagnosed as tumors, infections and sarcoidosis [1]. Hence, its exact epidemiology is not known. However, a retrospective study, between 2009 and 2021, noted that its 1) incidence had increased from 0.78 to 1.39 per 100,000 person-years, 2) point prevalence was 5.3 per 100,000 persons in 2019, and 3) mortality at 3.4 per 100 person-year. Historically, the disease was initially reported by Sarles *et al.* in 1961 as a case of pancreatitis with hypergammaglobulinemia [2]. Subsequently, Yoshida *et al.* proposed the concept of autoimmune pancreatitis (AIP) in 1995, followed by Hamano *et al.* defining it as IgG4-RD in 2001, and Kamisawa disclosing its systemic nature by reporting on its multiple extra-pancreatic lesions [3]. The etiology is unclear, yet its dramatic response to Corticosteroids indicated its autoimmune pathophysiology [4]. In our case report, we describe a patient who had developed such pancreatitis with acute interstitial nephritis following COVID-19 vaccination that may have triggered such autoimmune disease.

2. The Case

A 60-year-old man presented with epigastric pain for 1 month. The pain was persistent, dull-aching in character, radiating to the back. Pain was worse on lying down and after fatty meals. It was associated with nausea and vomiting that did not relieve the pain. The patient did not have previous significant medical illness, surgery, allergy and chronic intake of medications and alcohol. He just had 1 dose of Pfizer-BioNTech COVID-19 vaccine 1 month prior to his presentation for recent COVID-19 epidemic. Family history was irrelevant. On his initial physical examination, he was in distress of epigastric pain that had required Paracetamol and Codeine to relive. His body weight was 84 kg, blood pressure was normal and he was afebrile. Systemic examination did not show abnormality except for mild epigastric tenderness. He had normal peripheral leucocytic and platelets counts. Hemoglobin was normal. Serum sugar, electrolytes and liver functions were normal. Serum amylase and lipase were elevated at 240 IU/L (N: 26 - 100) and 354 IU/L (N: 13 - 160), respectively. Lipid profile was normal. Serum urea and creatinine were elevated at 10 mmol/L and 180 umol/L, respectively. Serum creatinine phosphokinase was normal. Urine routine and microscopy did not show abnormality. Ultrasound and computerized tomography of the abdomen and pelvis did not show abnormality, including the pancreas (**Figure 1**). Moreover, upper gastrointestinal endoscopy did not show; 1) gastric and duodenal lesions, and 2) its

associated ultrasound did not disclose pancreatic lesions (Figure 2). However, percutaneous kidney biopsy showed acute interstitial nephritis with heavy IgG4-plasma cells infiltrate in the fibroinflammatory areas (Figure 3). Furthermore; autoimmune work up showed; 1) polyclonal gammopathy, on serum electrophoresis, with high isolated high IgG4 at 1963 g/L (N: 0.039 - 0.864) with IgG4/IgG ratio at 0.16, 2) normal serum complements (C3 & C4) were normal, and 3) negative ANA, anti-ds DNA, ANCA, anti-GBM antibodies, anti-CCP, HIV, hepatitis B surface antigen and anti-HCV antibodies. Hence, diagnosis of IgG4RD disease with AIP and interstitial nephritis (AIN) was established. Initially, he was treated with Prednisone 60 mg daily that resulted in improvement of his epigastric pain within 3 days. By 2 weeks, serum amylase, lipase, urea, creatinine as well as IgG4 levels decreased to normal. Hence, the initial dose of Prednisone was maintained for 4 weeks followed by gradual tapering till discontinuation by 3 months. After 2 years of follow up the patient remained stable without 1) recurrence of clinical pancreatitis, 2) increase in serum amylase, lipase, creatinine and IgG4 levels, and 3) pancreatic abnormality on CT scan of the abdomen. Moreover, he did not have malabsorptive features, hemoglobin A1c and C-peptide insulin remained normal.

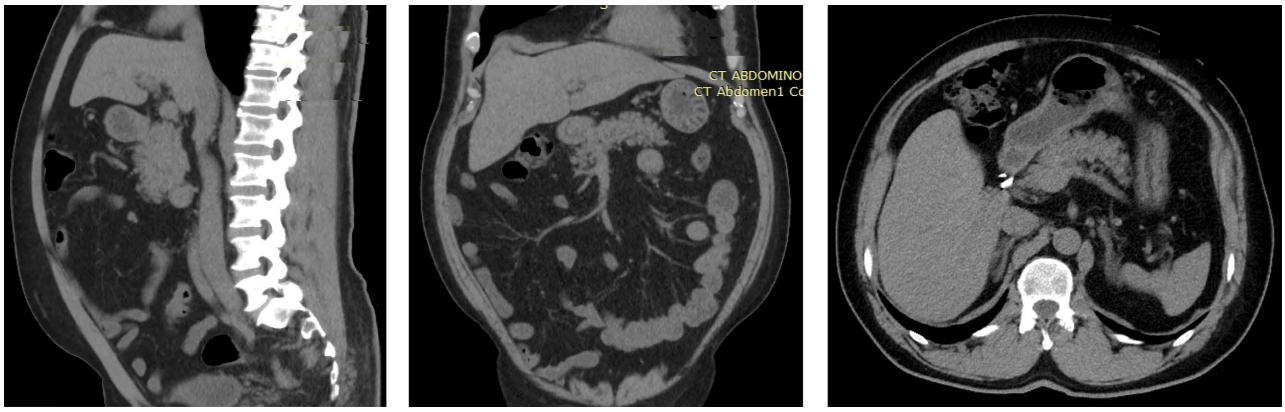

Figure 1. Computerized tomography of the abdomen and pelvis showing normal pancreas in all radiological views.

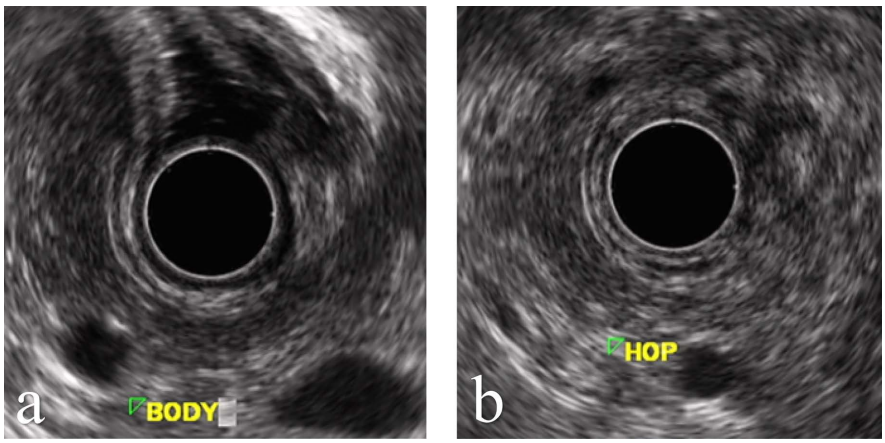

Figure 2. Endoscopic ultrasound of body (a) and head (b) of the pancreas that did not show lesions.

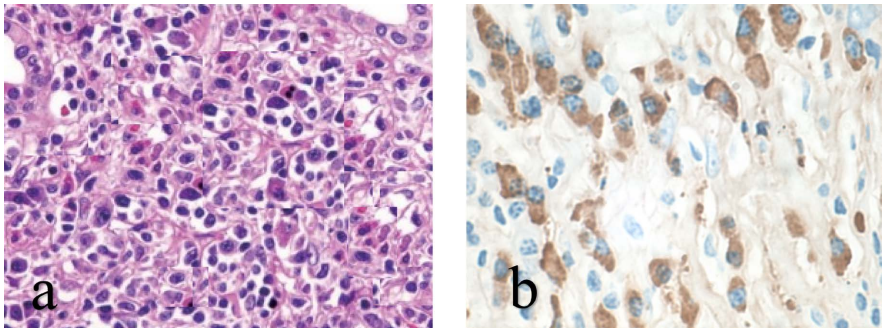

Figure 3. Photomicrograph of a kidney biopsy showing: (a) Acute interstitial nephritis with infiltration of lymphocytes, eosinophils and plasma cells (H&E ×400) and (b) Many of those plasma cells were IgG4-positive in fibroinflammatory areas (IgG4, ×400).

3. Discussion

Acute pancreatitis (AP) is an inflammatory process affecting the pancreas. It is characterized by severe epigastric pain, 3X upper limit of normal increase serum amylase and lipase and radiological evidence of pancreatic oedema or/or necrosis [5]. In 2019, its global age-standardized incidence rate was 34.8/100,000 [6]. The mortality of AP ranges from 3% in patients with mild edematous pancreatitis to as high as 20% in patients with pancreatic necrosis [7]. The most common causes of acute pancreatitis are gallstones (20% - 70%) followed by alcohol-use (30%). [8]. Other notable causes are metabolic (hypercalcemia, hypertriglyceridemia), drug-induced, autoimmune, post-endoscopic retrograde cholangiopancreatography, trauma, infectious, congenital or genetic, and idiopathic. The rate of occurrence of each etiology of acute pancreatitis varies across geographic regions and socioeconomic strata [8]. High-index of suspicion is indicated in early diagnosis and skilled management (treatment and prevention) is essential in preventing long-term sequelae viz. diabetes and malabsorption. In this case report, we presented a patient with AIP and AIN following COVID-19 vaccination, indicating a cause-and-effect phenomenon. The latter was supported by lack of history, biochemical and autoimmune workup for the common etiologies of both diseases viz. alcohol, metabolic, infectious, obstructive and chronic autoimmune ones. Though he presented with clinical and biochemical evidence of AP; he did not have significant radiological evidence of pancreatic lesions nor florid/progressive disease. Hence, etiological diagnosis was established by kidney biopsy that showed typical lesions of IgG4-RD and specifically high serum IgG4 levels with high IgG4/total IgG ratio [9]. Fortunately, the patient improved clinically, biochemically and serologically with 3-month therapy with corticosteroid. Moreover, disease-recurrence and resurge of IgG4 levels were not observed over 2-year of follow up indicating clear triggering by the vaccine. Review of the literature indicated: frequent surge of IgG4 following COVID-19 vaccination yet 5 cases had documented IgG4-disease of whom 1 with interstitial nephritis [10]. The latter phenomenon indicates disease-triggering in genetically predisposed patients for such disorder. Interestingly, previous data on IgG4 surge following vaccination did not

offer patients-immunity for covid disease. On the contrary, it was associated with high-risk of future infections, tumors, and autoimmune disorders viz. pancreatitis, myasthenia gravis, systemic lupus erythematosus, myocarditis and sudden cardiac death [11]. Another unique observation in our patient is lack of pancreatic lesions, by CT and endoscopic ultrasonography, despite his AP [1].

4. Conclusion

Our findings confirm the autoimmune nature of IgG4-RD, its potential for triggering by COVID-19 vaccine in genetically predisposed individuals and the efficacy of early-implementation of short-course of Corticosteroid-therapy.

Author's Contributions

Prof. Kamel El-Reshaid conceived the study, participated in its design, and drafted the manuscript. Dr. Abdulmohsen Al-Bader participated in the study design, follow-up of patients, data collection and tabulation of data.

Data Availability Statement

The data provided in the current review are available from the references.

Conflicts of Interest References

All authors have read and approved the final version of the manuscript. The authors declare no conflicts of interest regarding the publication of this paper.

References

[1] Stone, J.H., Zen, Y. and Deshpande, V. (2012) IgG4-Related Disease. *New England Journal of Medicine*, **366**, 539-551. https://doi.org/10.1056/nejmra1104650

[2] Sarles, H., Sarles, J., Muratore, R. and Guien, C. (1961) Chronic Inflammatory Sclerosis of the Pancreas—An Autonomous Pancreatic Disease? *The American Journal of Digestive Diseases*, **6**, 688-698. https://doi.org/10.1007/bf02232341

[3] Nambiar, S. and Oliver, T.I. (2025) IgG4-Related Disease. StatPearls Publishing.

[4] Kamisawa, T., Okazaki, K., Kawa, S., Shimosegawa, T. and Tanaka, M. (2010) Japanese Consensus Guidelines for Management of Autoimmune Pancreatitis: III. Treatment and Prognosis of AIP. *Journal of Gastroenterology*, **45**, 471-477. https://doi.org/10.1007/s00535-010-0221-9

[5] Ortiz Morales, C.M., Girela Baena, E.L., Olalla Muñoz, J.R., Parlorio de Andrés, E. and López Corbalán, J.A. (2019) Radiology of Acute Pancreatitis Today: The Atlanta Classification and the Current Role of Imaging in Its Diagnosis and Treatment. *Radiología* (*English Edition*), **61**, 453-466. https://doi.org/10.1016/j.rxeng.2019.06.005

[6] Li, C., Jiang, M., Pan, C., Li, J. and Xu, L. (2021) The Global, Regional, and National Burden of Acute Pancreatitis in 204 Countries and Territories, 1990-2019. *BMC Gastroenterology*, **21**, Article No. 332. https://doi.org/10.1186/s12876-021-01906-2

[7] Werge, M., Novovic, S., Schmidt, P.N. and Gluud, L.L. (2016) Infection Increases Mortality in Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis. *Pancreatology*, **16**, 698-707. https://doi.org/10.1016/j.pan.2016.07.004

[8] Gapp, J., Tariq, A. and Chandra, S. (2023) Acute Pancreatitis. StatPearls Publishing.

[9] Culver, E.L. and Bateman, A.C. (2013) General Principles of IgG4-Related Disease. *Diagnostic Histopathology*, **19**, 111-118. https://doi.org/10.1016/j.mpdhp.2013.01.003

[10] Aochi, S., Uehara, M. and Yamamoto, M. (2023) IgG4-Related Disease Emerging after COVID-19 mRNA Vaccination. *Internal Medicine*, **62**, 1547-1551. https://doi.org/10.2169/internalmedicine.1125-22

[11] Uversky, V., Redwan, E., Makis, W. and Rubio-Casillas, A. (2023) IgG4 Antibodies Induced by Repeated Vaccination May Generate Immune Tolerance to the SARS-CoV-2 Spike Protein. *Vaccines*, **11**, Article No. 991. https://doi.org/10.3390/vaccines11050991