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Case report

Acute pancreatitis complicated with diabetic ketoacidosis following COVID-19 mRNA vaccination: a case report

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Abstract

Objective: Since the onset of the coronavirus disease 2019 (COVID-19) pandemic, COVID-19 vaccination has substantially reduced mortality and hospitalization rates worldwide, with rare adverse events reported in clinical settings. Herein, we present a case of acute pancreatitis complicated by diabetic ketoacidosis (DKA) following the third COVID-19 vaccination dose.
Patient: A 72-year-old male with a history of diabetes mellitus developed generalized fatigue, mild epigastric pain, nausea, and frequent vomiting after receiving the COVID-19 vaccine.
Results: Blood analysis revealed elevated levels of pancreatic enzymes, hyperglycemia, and acidemia. Computed tomography revealed evidence of acute pancreatitis, leading to a diagnosis of both DKA and acute pancreatitis. Treatment with a large volume of saline and intravenous insulin improved both DKA and acute pancreatitis. After a thorough examination, no other factors capable of causing acute pancreatitis were identified. Hence, we concluded that acute pancreatitis was induced by COVID-19 vaccination.
Conclusion: Acute pancreatitis is a rare but potentially life-threatening adverse event associated with COVID-19 vaccination. Delaying the treatment or diagnosis of acute pancreatitis can increase mortality risk in patients with both acute pancreatitis and DKA. Hence, it is crucial for healthcare professionals to consider the potential occurrence of acute pancreatitis and DKA following COVID-19 vaccination.

Key words: coronavirus disease 2019 (COVID-19) vaccination, acute pancreatitis, diabetic ketoacidosis, potential adverse events

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic has had a serious negative impact on individuals globally, causing more than 17 million deaths worldwide[1, 2]. Vaccination against COVID-19 has contributed substantially to controlling the pandemic and reducing mortality and hospitalization rates[2–4]. However, vaccination has been associated with concerns regarding potential side effects[5, 6]. Adverse events due to the COVID-19 vaccine include gastrointestinal symptoms such as nausea, vomiting, and abdominal pain, as well as pain at the injection site and fever[5, 6]. Additionally, acute pancreatitis has been reported as a rare adverse event associated with COVID-19 vaccination[7]. However, owing to the widespread administration of COVID-19 vaccinations, it is essential to remain vigilant regarding uncommon adverse events. Moreover, acute pancreatitis can be complicated by diabetic ketoacidosis (DKA), depending on the patient's clinical condition[8]. Herein, we report a rare case of acute pancreatitis complicated by DKA following a third dose of the Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccination.

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Case Report

A 72-year-old male with a history of diabetes mellitus was admitted to our hospital with generalized fatigue, mild

epigastric pain, nausea, and frequent vomiting without fever. He had received a third dose of Pfizer-BioNTech BNT162b2 mRNA COVID-19 vaccine six days prior. Nausea and frequent vomiting appeared two days after vaccination. Although he had received six previous doses of COVID-19 vaccines, this was the first time that he experienced adverse effects post-vaccination. He denied consuming spoiled or raw food and had not traveled recently. Moreover, there were no local outbreaks or reports of patients with similar symptoms. His diabetes mellitus was managed with oral hypoglycemic agents, including empagliflozin, glimepiride, metformin hydrochloride, and oral semaglutide, with no changes in his medication regimen over the past year. However, the control of diabetes mellitus was suboptimal (HbA1c, 7.2%).

Upon admission, vital signs revealed a blood pressure of 144/105 mmHg, heart rate of 120 beats per minute, and body temperature of 36.0°C. A blood analysis revealed elevated pancreatic enzymes (serum amylase 1,252 IU/L and lipase 996 U/L), hyperglycemia (547 mg/dL), acidemia with increased anion-gap (pH 7.22, HCO_{3-} 8.3, $PaCO_2$ 20.9, anion-gap 14.5), and renal dysfunction (serum creatinine 1.03 mg/dL, blood urea nitrogen 58.0 mg/dL) without elevation of hepatobiliary enzymes (aspartate aminotransferase 10 IU/L, alanine aminotransferase 15 IU/L, serum total bilirubin 0.8 mg/dL). Urinalysis was positive for ketone bodies (3+). Computed tomography (CT) revealed the presence of an increased adipose tissue concentration around the pancreatic head (Figure 1). These findings were suggestive of DKA and acute pancreatitis with acute kidney injury. The patient had no history of recreational drug, alcohol, or cigarette use. He had no history of over-the-counter medication use, trauma, hereditary disorders, or autoimmune disease. Biochemical tests showed no evidence of autoimmune disease (antinuclear antibody, <1:40; IgG, 1,387 ng/dL; and IgG4, 104 ng/dL). Blood triglyceride levels were within the normal range (121 mg/dL). Magnetic resonance cholangiopancreatography detected no signs of carcinoma, cholelithiasis, or pancreaticobiliary maljunction on day 8 of hospitalization (Figure 2). Based on these findings, the patient was diagnosed with DKA complicated by acute pancreatitis

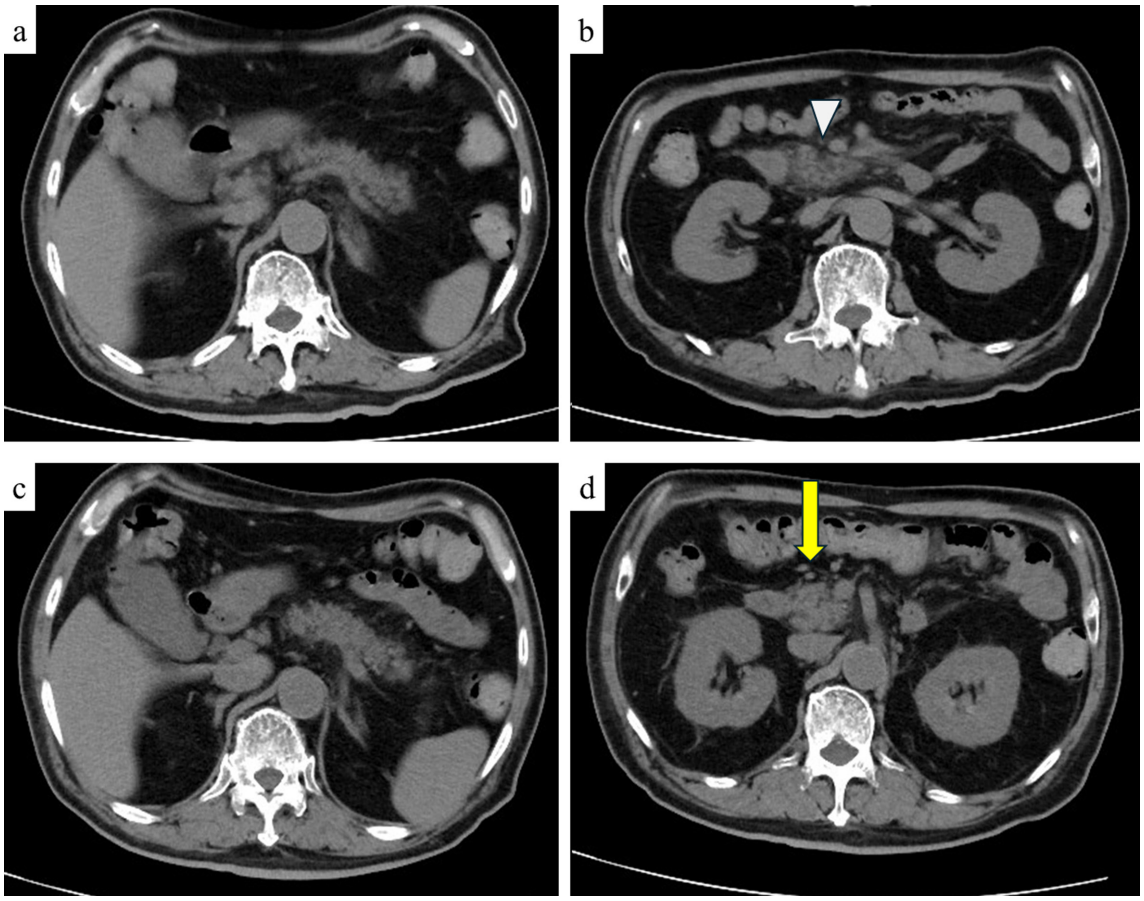

Figure 1 Computed tomography (CT) depicting the clinical progression of acute pancreatitis. On day 1 of hospitalization, CT imaging shows a localized increase in adipose tissue concentration around the pancreatic head (arrowhead) (a, b). On day 3 of hospitalization, the increase in adipose tissue concentration around the pancreatic head (arrow) has almost completely resolved (c, d).

following COVID-19 vaccination.

Initially, a large volume of saline (1 L/h) and intravenous short-acting insulin (0.1 U/kg) were administered. Thereafter, we continued administering intravenous insulin and aggressive fluid therapy, along with electrolyte correction for serum potassium and phosphorus. Intravenous insulin administration and fluid therapy likely contributed to the improvement in DKA. Similarly, acute pancreatitis can be managed by fasting and aggressive fluid therapy. Pancreatic enzyme levels gradually normalized by day 7 of hospitalization, as evidenced by the laboratory results. CT imaging revealed an improvement in the adipose tissue concentration around the pancreas by day 4 of hospitalization. Eventually, the patient required subcutaneous insulin injections to control diabetes mellitus and was discharged without complications on day 32 of hospitalization (Figure 3).

Discussion

Vaccination is essential in the fight against infectious diseases, including COVID-19. Notably, COVID-19 vaccination markedly reduced mortality and hospitalization rates during the COVID-19 pandemic era[3]. However, COVID-19 vaccination may lead to potential adverse events, including gastrointestinal symptoms such as acute pancreatitis[6, 7, 9]. In real-life scenarios, conditions such as DKA can develop concurrently when a patient with diabetes mellitus develops acute pancreatitis[10]. Given its notable benefits to public health, vaccination is crucial for the collective well-being. Thus, clinicians must remain alert to any potential adverse effects to ensure patient safety and health.

Since the onset of the COVID-19 pandemic, a new cause of acute pancreatitis has been identified, and several studies have reported a potential link between acute pancreatitis and vaccination[7]. Acute pancreatitis can be triggered by various factors, including bile duct obstruction, trauma, cig-

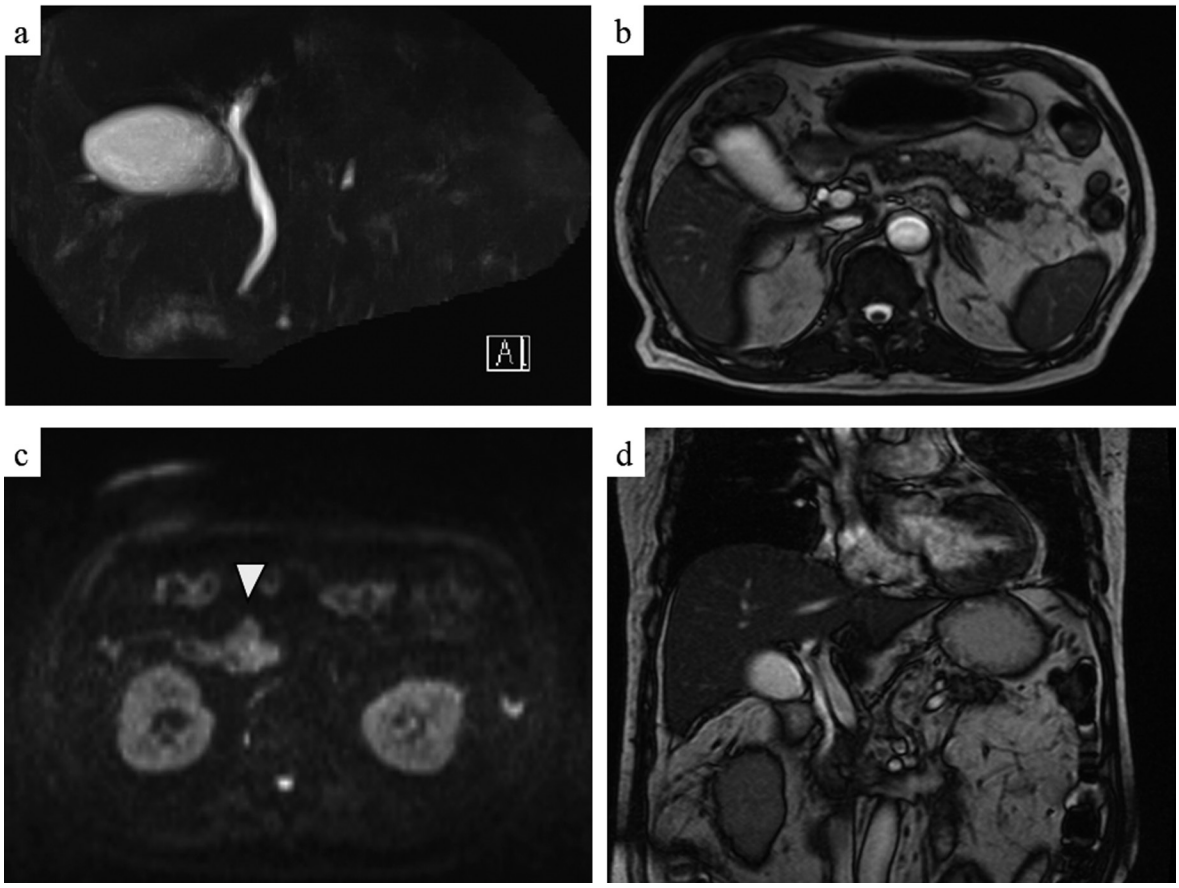

Figure 2 On day 8 of admission, MRCP shows no evidence of biliary tract obstruction, carcinoma, or cholelithiasis as causes of acute pancreatitis (a). T2-weighted MRI images show a small cyst in the pancreatic body (b, d). Diffusion-weighted magnetic resonance imaging highlights a high-intensity area at the pancreatic head (arrowhead), suggesting the patient suffered from acute pancreatitis (c). MRCP: Magnetic resonance cholangiopancreatography; MRI: magnetic resonance imaging.

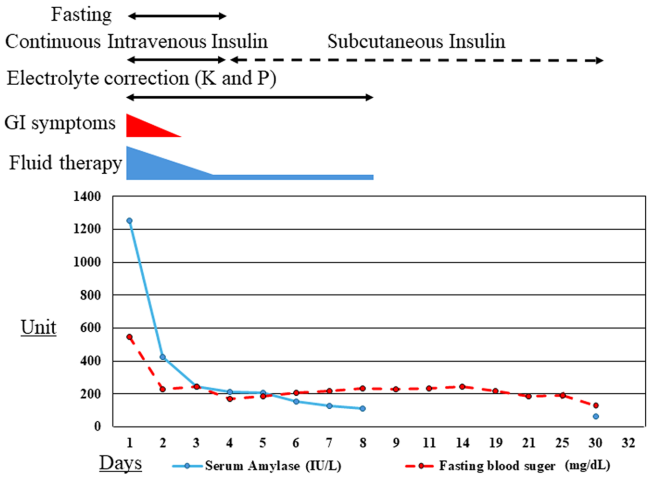

Figure 3 The clinical course of the patient following hospitalization. Initially, the patient was administered a large amount of saline (1 L/h) and intravenous short-acting insulin (0.1 U/kg). In addition, he required continuous intravenous insulin and fluid therapy, along with electrolyte correction. Pancreatic enzyme levels gradually returned to the normal range by day 7. Upon clinical improvement, including stabilization of blood sugar and acidemia (blood pH >7.3), continuous intravenous insulin was switched to subcutaneous insulin, and fasting was ended. Electrolyte correction was maintained with both oral and intravenous supplementation after breaking the fast. The patient was eventually discharged without complications, continuing on subcutaneous insulin therapy.

arette smoking, alcohol consumption, and hypertriglyceridemia[11, 12]. However, the etiology of acute pancreatitis following COVID-19 vaccination remains unclear. The prevailing hypothesis is the molecular mimicry theory, which suggests that the similarity in amino acids between the vaccine and body antigens triggers an autoimmune response[7, 9, 13]. The time from COVID-19 vaccination to the onset of acute pancreatitis can range from several hours to one month[7]. Gastrointestinal symptoms following COVID-19 vaccination are generally reported to be relatively mild[5, 6, 14]. A previous study has indicated that DKA symptoms may obscure the presence of acute pancreatitis[8]. Accordingly, the occurrence of acute pancreatitis following COVID-19 vaccination may be overlooked and underreported. However, acute pancreatitis can lead to fatal clinical conditions, such as multiple organ dysfunction and DKA[10, 12]. Therefore, healthcare professionals need to be fully aware of the potential adverse events despite the rarity of these conditions.

DKA is one of the most serious complications of diabetes mellitus[15]. DKA can be triggered by acute stress, such as infection and surgery; direct injury, such as acute pancreatitis; and poor medication adherence. Uncontrolled diabetes mellitus is a risk factor for DKA[16]. Delaying the treatment or diagnosis of DKA is associated with a significant risk of mortality[15]. Notably, the combination of acute pancreatitis DKA is more likely to escalate into severe clinical conditions such as systemic inflammatory response syndrome and acute kidney injury[10]. Therefore, when a patient with diabetes mellitus receives a COVID-19 vaccination, it is necessary to carefully monitor the occurrence of gastrointestinal symptoms to detect any potential adverse events promptly. Patients with DKA should be treated rapidly with adequate fluid therapy and blood sugar control via IV insulin infusion.

Conclusion

Acute pancreatitis is a rare but important adverse event of COVID-19 vaccination, potentially leading to a life-threatening condition complicated by DKA. Therefore, the possibility of acute pancreatitis should be considered when examining patients with gastrointestinal symptoms following COVID-19 vaccination. Furthermore, medical professionals need to be aware that patients with diabetes mellitus may experience DKA accompanied by acute pancreatitis to avoid missing the optimal timing for treatment.

Conflict of interest: The authors declare no conflicts of interest associated with this study.

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Ethics approval and consent to participate: Ethical approval was obtained from the Ethics Committee of the Japanese Red Cross Society Koga Hospital (approval number: 23-12). Informed consent was obtained from all the participants involved in this study.

Consent for publication: Written informed consent was obtained from the patient for the publication of this case report.

Data availability statement: The anonymized patient data used in this study are included in the text.

Author contributions: All authors contributed to the conception and design of this study. YW wrote the first draft of the manuscript. All authors commented on the manuscript. All authors have read and approved the final version of the manuscript.

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