

emission tomography–computed tomography, which have alternative diagnostic performance, were unable to detect AIP. This atypical imaging presentation of AIP probably reflects a low activity of pancreatitis. Some reported an AIP patient with atrophic parenchyma.<sup>9,10</sup> Although this entity of atrophy was unclear, they suggested chronic inflammation from AIP or from another etiology, such as alcohol. This was similar to our patient; however, we cannot elucidate the cause for atrophic AIP. This is a potential limitation of our study.

Atypical AIP showing an atrophic parenchyma without pancreatic enlargement is easily overlooked, and it should be examined carefully to detect occult PDAC. Using DWI and repeat biopsy might be useful for the detection of occult cancer in patients suspected of IgG4-RD.

#### ACKNOWLEDGMENTS

The authors would like to thank Editage ([www.editage.com](http://www.editage.com)) for English language editing.

T.I. received a grant (KAKENHI 2019-04-01 to 2022-03-31. 19 K07752) from the Japan Society for the Promotion of Science. The authors declare no conflict of interest.

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## Pancreatic Enzyme Elevation Patterns in Patients With Diabetic Ketoacidosis Does Severe Acute Respiratory Syndrome Coronavirus 2 Play a Role?

#### To the Editor:

In Peru, the current number of confirmed coronavirus disease 2019 (COVID-19) cases exceeds 800,000, with a case fatality rate of 3.9%. This positions our country as one of the most affected by the pandemic worldwide. It is known that diabetes mellitus is a risk factor for the development of severe COVID-19; on the other hand, patients infected with COVID-19 have a higher risk

of developing new-onset diabetes mellitus, thus creating a 2-way relationship.<sup>1</sup>

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has been shown to have a high affinity for the angiotensin converting enzyme 2 receptor, which is used as a gateway.<sup>1,2</sup> The experience published based on the 2002 to 2004 SARS-CoV outbreak, where the pattern of receptor expression in different human organs was studied, showed abundant angiotensin converting enzyme 2 immunostaining in the lungs, kidneys, heart, and pancreatic islets.<sup>3</sup> Moreover, multiple scientific publications have reported a higher incidence of diabetic ketoacidosis in patients with COVID-19, which demonstrates increased morbidity and mortality.<sup>4</sup> It is postulated that the interaction of SARS-CoV-2 and pancreatic cells induces a cytopathic effect in those cells, which can be manifested as increases in serum amylase and lipase levels above the upper limit of normality, with a potential risk of developing acute pancreatitis.<sup>1,4</sup> This pancreatic lesion added to insulin resistance caused by SARS-CoV-2 infection, in the context of a diabetic patient, could imply an increased risk of hyperglycemic crisis.<sup>4</sup>

The revised Atlanta classification published in 2012 continues to be used for the diagnosis of acute pancreatitis, and according to this system, 2 of the following 3 criteria must be met: typical abdominal pain, increases in amylase or lipase levels to more than 3 times the upper limit, and characteristic imaging findings. However, amylase elevation may also be observed in appendicitis, cholecystitis, intestinal obstruction or ischemia, and gynecological diseases; likewise, increased lipase levels may also be seen in kidney disease, appendicitis, and cholecystitis, among other diseases.<sup>5</sup>

Furthermore, it has been reported that the increases in amylase and lipase levels may occur in 16% to 25% of cases of diabetic ketoacidosis, and an increase in lipase is less specific for the diagnosis of acute pancreatitis in the context of diabetic ketoacidosis,<sup>6</sup> which highlights the usefulness of abdominal tomography in these cases.

Some cases of pancreatic injury have been reported in patients with COVID-19, and of these, some meet the criteria for acute pancreatitis.<sup>7–10</sup> One of the first case series, published by Wang et al,<sup>7</sup> reported that, of 52 patients with COVID-19, 17% had elevated amylase and/or lipase levels, which appeared to be signs of more serious disease on admission. In another series of 71 patients with COVID-19, 9 had elevated lipase on admission, but the increase was greater than 3 times the upper limit in only 2 of those cases; both presented with diarrhea, and 1 had active enterocolitis based on tomography, which suggests that the

**TABLE 1.** Clinical and Biochemical Characteristics of Patients With Diagnosis of Diabetic Ketoacidosis Upon Admission

| Sex | Age, y | Severity of DKA | COVID-19 Diagnosis | Typical Abdominal Pain    | Blood Test Upon Admission |  |                |          |          |          |           |              |             |              | Acute Pancreatitis            |     |
|-----|--------|-----------------|--------------------|---------------------------|---------------------------|--|----------------|----------|----------|----------|-----------|--------------|-------------|--------------|-------------------------------|-----|
|     |        |                 |                    |                           | pH                        | HCO <sub>3</sub> <sup>-</sup> , mmol/L | Glucose, mg/dL | AST, U/L | ALT, U/L | ALP, U/L | GGTP, U/L | Amylase, U/L | Lipase, U/L | Abdominal CT |                               |     |
| 1   | Male   | 31              | Severe             | No                        | No                        | 6.9                                    | 5.6            | 888      | 17       | 24       | 107       | 20           | 361         | 396          | Edematous pancreas            | Yes |
| 2   | Male   | 66              | Mild               | No                        | No                        | 7.26                                   | 20.5           | 506      | 48       | 92       | 121       | 96           | 413         | 2421         | Edematous                     | Yes |
| 3   | Male   | 66              | Severe             | Yes (ELISA)               | No                        | 7.05                                   | 8.6            | 781      | 45       | 78       | 224       | 122          | 54          | 284          | No abnormalities              | No  |
| 4   | Male   | 36              | Severe             | No                        | Yes                       | 6.99                                   | 6.1            | 683      | 17       | 28       | 92        | 86           | 87          | 14,172       | No abnormalities              | Yes |
| 5   | Male   | 73              | Mild               | Yes (RT-PCR)              | No                        | 7.3                                    | 18.6           | 699      | 28       | 28       | 150       | 156          | 51          | 315          | Hypotrophic pancreas          | No  |
| 6   | Male   | 62              | Severe             | No                        | No                        | 7.27                                   | 13.7           | 260      | 44       | 57       | 165       | 216          | 600         | 4837         | Edematous pancreas            | Yes |
| 7   | Male   | 62              | Moderate           | Yes (suggestive chest CT) | No                        | 7.3                                    | 14.6           | 1218     | 35       | 18       | 210       | 23           | 37          | 106          | No abnormalities              | No  |
| 8   | Male   | 48              | Moderate           | No                        | No                        | 7.23                                   | 11             | 305      | 15       | 16       | 47        | 25           | 159         | 1004         | Diffuse edema of the pancreas | Yes |
| 9   | Female | 36              | Severe             | Yes (RT-PCR)              | No                        | 6.8                                    | 2.5            | 420      | 22       | 11       | 149       | 20           | 622         | 15           | No abnormalities              | No  |
| 10  | Male   | 40              | Moderate           | No                        | No                        | 7.24                                   | 10.6           | 341      | 17       | 28       | 92        | 86           | 89          | 143          | No abnormalities              | No  |
| 11  | Male   | 63              | Moderate           | No                        | No                        | 7.25                                   | 11.6           | 1046     | 40       | 97       | 120       | 109          | 146         | 353          | No abnormalities              | No  |
| 12  | Male   | 15              | Moderate           | No                        | Yes                       | 7.1                                    | 8              | 637      | 28       | 28       | 321       | 16           | 64          | 25           | No abnormalities              | No  |
| 13  | Male   | 45              | Severe             | No                        | Yes                       | 6.9                                    | 10.5           | 1072     | 15       | 13       | 120       | 72           | 86          | 558          | No abnormalities              | No  |

Source: Data were obtained from the Endocrinology Inpatient Department, Guillermo Almenara National Hospital, March to July 2020. Reference values: amylase, 30–110 U/L; lipase, 23–300 U/L.

ALP indicates alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CT, computed tomography; DKA, diabetic ketoacidosis; ELISA, enzyme-linked immunoSorbent assay; GGTP, gamma-glutamyltransferase; RT-PCR, reverse transcription–polymerase chain reaction.

lipase elevation and associated symptoms; her presentation was compatible with acute pancreatitis, which evolved favorably with fasting.<sup>9</sup> A family is also described, in which 5 members who tested positive for SARS-CoV-2 infection; of these, 3 required admission to the intensive care unit for severe respiratory compromise, and 2 were diagnosed with severe acute pancreatitis.<sup>10</sup>

Based on our experience in the endocrinology inpatient department of a social security hospital in Peru from March 2020 to July 2020, we have treated 13 patients with diabetic ketoacidosis with remission criteria, of whom 6 were severe cases, 5 were moderate cases, and 2 were mild cases; overall, we registered 12 patients with recent-onset diabetes. Likewise, 9 patients presented with high levels of amylase and/or lipase on admission, tomographic signs of acute pancreatitis were observed in 4 patients, and 5 patients met the criteria for acute pancreatitis. Abdominal pain was not a common feature because this symptom was present in only 3 cases, 1 of which met the criteria for acute pancreatitis. Four patients had diagnosis of COVID-19, none of them had pancreatic abnormalities by tomography, only 1 had a significant elevation of amylase, but none met the criteria for acute pancreatitis (Table 1).

Finally, according to these data, we cannot conclude that SARS-CoV-2 has contributed to pancreatic injury in patients with diabetic ketoacidosis. The increase in amylase and lipase levels occurred more frequently in our patients than expected according to the literature, but this does not seem to be related to COVID-19. In addition, we suggest that diabetic ketoacidosis may be a frequent clinical presentation of new-onset diabetes.

*The authors declare no conflict of interest.*

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elevation of this enzyme may be due to the enteric involvement of the virus, although this elevation can also be explained by other

causes.<sup>8</sup> Other published cases include a 26-year-old woman with no evidence of respiratory symptoms who presented with

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## A Novel Strategy of Endoscopic Ultrasonography-Guided Pancreatic Duct Drainage for Pancreatic Fistula After Pancreaticoduodenectomy

### To the Editor:

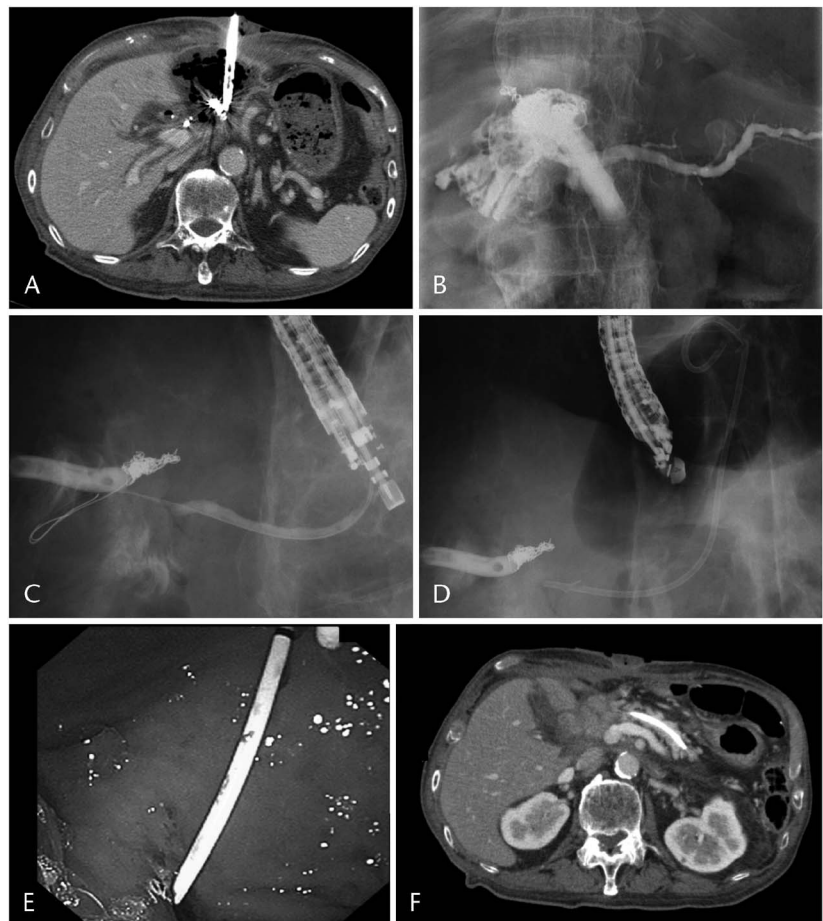
Postoperative pancreatic fistula (POPF) is a common and potentially life-threatening complication after pancreaticoduodenectomy.<sup>1,2</sup> The optimal treatment for the International Study Group for Pancreatic Fistula–defined pancreatic fistula is not well defined.<sup>2</sup> For decades, primary catheter drainage has been becoming a less invasive alternative to reoperation. However, current treatments require patients to withstand prolonged, uncomfortable percutaneous drainage and are exposed to the risk of bleeding and infection.<sup>3</sup> Herein, we report a case of refractory POPF after pancreaticoduodenectomy that was successfully managed by endoscopic ultrasonography (EUS)-guided pancreatic duct drainage (EUS-PD).

A 78-year-old man underwent pancreaticoduodenectomy with lymph node dissection for distal bile duct cancer (T1bN0M0,

stage IA). A reconstruction procedure was performed with the modified Child method. The pancreatic parenchyma was soft and an endo-to-side pancreaticojejunostomy was accomplished by duct-to-mucosa anastomosis (modified Blumgart technique) with a 4-Fr external stent and 2 closed suction drains at the ventral and dorsal sides. His turbid drainage juice contained amylase of greater than 10,000 IU/mL on postoperative day (POD) 3. Both drains were removed on POD 22/25, respectively, after the drainage amount decreased and inflammation improved; however, a percutaneous drainage was added because fluid collected at the pancreatic anastomotic site on POD 29. Three weeks later, a ruptured pseudoaneurysm of common hepatic artery

developed and was successfully treated by transcatheter arterial embolization using coiling. The characteristics and amount of drainage did not change with a beige-colored, digestive juice of greater than 200 mL/d despite 3 months of percutaneous drainage (Fig. 1A). In addition, the pancreatic duct was clearly described, although not dilated, by contrast examination from percutaneous drain (Fig. 1B).

The procedure of EUS-PD via transgastric approach was performed on POD 90. The distal part of the main pancreatic duct (MPD) was punctured with a 19-gauge needle under EUS guidance using a convex array echoendoscope (GF-UCT260-AL5; Olympus Medical Systems, Tokyo, Japan), followed by the insertion of a 0.025-in guide



**FIGURE 1.** A, A contrast-enhanced computed tomography image showing fluid collection of the POPF, which was percutaneously drained from the epigastric region with beige-colored, digestive juice of greater than 200 mL/d. B, A fluoroscopic image of the pancreatic duct, which was clearly described, although not dilated, by contrast examination from the percutaneous drain. C, A fluoroscopic image of the EUS-guided transgastric approach showing the pancreatic duct of 2 mm in size that was punctured with a 19-gauge needle at the distal pancreas through the posterior gastric wall under EUS guidance using a convex array echoendoscope. D, A fluoroscopic image after placement of a 7-Fr single pigtail type plastic stent from the posterior gastric wall to the pancreatic duct. E, An endoscopic image showing a deployed 7-Fr single pigtail type plastic stent in the pancreatic duct. F, A computed tomography image taken 1 week after EUS-guided drainage showing considerable shrinkage of the fluid collection by POPF.