Agenesis of the dorsal pancreas presenting with diabetic ketoacidosis – a case report and literature review

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Abstract

Background: Agenesis of the dorsal pancreas (ADP) is clinically rare, and it is usually accompanied by abdominal pain. Various disorders of glucose metabolism associating with ADP have been reported, but there are only two studies reporting a correlation between ADP and DKA in English literature.

Case presentation: We present a case of a patient with ADP accompanied by abdominal pain and diabetic ketoacidosis as the initial clinical presentation. A 30-year-old man presented with a 3-month history of recurrent onset of persistent mild epigastric pain, which worsen when eating. Laboratory tests revealed metabolic acidosis, hyperglycemia, and ketonuria. Phase contrast CT and MRCP showed the absence of the body and tail of the pancreas, as well as the dorsal pancreatic duct. The C-peptide release test indicated β-cell dysfunction. A combination therapy of insulin, pancreatic enzyme supplements, and mosapride citrate were administrated and the pain gradually resolved.

Conclusions: As glucose metabolism disorders can vary across different individuals, we advise clinicians to consider the diagnosis of ADP for a patient who presents with a glucose metabolism disorder accompanied by abdominal pain, pancreatitis or steatorrhea.

Keywords: Agenesis of the dorsal pancreas, Diabetic ketoacidosis, Diabetes mellitus, C-peptide release test

Background

Agenesis of the dorsal pancreas (ADP) is a rare congenital anomaly caused by the failure of the dorsal pancreatic bud to develop the body and tail of the pancreas during embryological development [1]. A key clinical manifestation of ADP is abdominal pain, although ADP often associates with hyperglycemia as a result of β-cell dysfunction and insulin deficiency [2]. However, there are only two studies reporting a correlation between ADP and DKA in English literature [3, 4]. Here, we present a third case of a patient with ADP accompanied by abdominal pain and DKA.

Case presentation

A 30-year-old man referred to our hospital presented with a 3-month history of recurrent onset of persistent mild epigastric pain, which worsen when eating. The patient took a lot of sugary beverages one week before his admission to the hospital. He had no history of diarrhea, dry mouth, polyuria, polydipsia, weight loss, and gastrointestinal disease. The family history was noncontributory. His mother died of gynecological cancer at age 50. His father had no history of hyperglycemia or chronic abdominal pain, and the abdominal CT scan showed a normal pancreas. His only younger sister had no special medical history as well. A physical examination revealed that the patient was in good shape (body mass index 22.7 kg/m²). He was conscious but dehydrated. He had a soft but tender abdomen, and his heart and lung functions were normal. His vital signs were also normal.

Laboratory tests (Table 1) revealed metabolic acidosis with an arterial blood pH of 7.3 and a base excess of −8.9
mmol/L. The random plasma glucose level was 576 mg/dL, with urinalysis revealing glycosuria and ketonuria. The glycated hemoglobin (HbA1c) level was 147 mmol/mol, and the serum lactic acid level was within normal range. Levels of carcinoembryonic antigen and cancer antigen 199 were also within normal ranges. The results of liver function, serum amylase, lipase, C-reactive protein, and microalbuminuria tests, as well as the 24-h urine protein level, were within normal ranges. The patient was negative for the glutamic acid decarboxylase antibody, islet cell antibody, and insulin autoantibody.

The patient was diagnosed with DKA and received standard treatment for the condition, which included intravenous fluids, insulin therapy, and potassium replacement.

DKA resolved gradually after insulin therapy, but the abdominal pain continued. Additional phase contrast CT of the abdomen was performed and revealed an enlarged pancreatic head (Fig. 1A), without the body and tail of the pancreas (Fig. 1B). A further investigation of MRCP revealed the absence of the dorsal pancreatic duct and a short duct of Wirsung running into the major papilla (Fig. 1C). On the basis of these findings, a diagnosis of complete ADP was evident, and we believed that the pain was due to dysfunction of the pancreas. Low-fat diet was recommended, and pancreatic enzyme supplements as well as mosapride citrate were given with meals to facilitate the digestive process. The pain gradually resolved and went away in 7 days after the treatment.

A standard mixed-meal tolerance test was performed one month later to evaluate β-cell function. The fasting C-peptide level was 0.05 ng/mL, and the postprandial C-peptide levels at 1, 2, and 3 h were 0.05, 0.07, and 0.06 ng/mL (normal range, 1.1–4.4 ng/mL), whereas the fasting plasma glucose level was 261 mg/dL, and the postprandial glucose levels at 1, 2, and 3 h were 433, 455, and 433 mg/dL, respectively. According to the patient's medical history and laboratory results, we speculated that the sugary beverages might resulted in high blood glucose, which may contribute to DKA in this patient. According to the ADA’s standard of classification and diagnosis of diabetes, the diagnosis of “Specific types of diabetes due to other causes” was established [1, 2]. The patient received insulin therapy (insulin glargine 12 units at bedtime and biosynthetic human insulin 16 units with meals) and was followed up.

Discussion and conclusions

The pancreas develops from the ventral and dorsal buds, which fuse during the seventh week of gestation. The ventral bud gives rise to the uncinate process, post-inferior portion of the head, and Wirsung duct, whereas the dorsal bud, which drains into the minor papilla through the Santorini duct, gives rise to the upper head, body and tail [5]. Monogenic mutations in insulin promoter factor 1 [6], pancreas associated transcription factor 1 [7], and transcription factor-2 / hepatocyte nuclear factor-1 homeobox B [8] have been reported to associate with pancreatic agenesis, multigenic traits are likely to contribute to this disorder. However, one limitation should be noted that we didn’t have genetic analysis in the presented case as the patient refused DNA sequencing test.

We reviewed the articles published between January 2008 and August 2019 and 75 cases of ADP were identified. Of the 75 cases, 53 cases that had been reported by Cienfuegos were excluded from the study [9]. Clinical presentation, pancreas imaging, and gene mutation results were extracted and summarized (Table 2). Although the majority of ADP patients are asymptomatic, abdominal pain is the most common reported symptom. The abdominal pain may contribute to the dysfunction of the sphincter of Oddi and/or chronic pancreatitis accompanied by an elevated pancreatic intra-ductal pressure [10]. In this case, we at first believed that the pain was caused by DKA. However, the abdominal pain continued after rectifying the DKA, indicating that the abdominal pain was caused by ADP.

Patients with ADP may also present with disorders of glucose metabolism, such as insulin-dependent diabetes, high-fasting blood glucose levels, and non-insulin-dependent diabetes [11]. According to the published reports, approximately 50% of patients with ADP also have concomitant hyperglycemia [12]. Although β-cell dysfunction is often indicative of hyperglycemia, there are only two studies reporting a correlation between ADP and DKA [3, 4]. Four cases of ADP, including the present one, had reported C-peptide test results, three of which showed low levels of fasting and postprandial C-peptide associated with β-cell dysfunction [13, 14], and one case showed detectable C-peptide level of 0.47

| Table 1 Laboratory results of this patient |
|--------------------------------------------|
| Results | Reference Range | Units |
| White blood cell counting | 8.7 | 3.5–9.5 | 10⁹/L |
| Neutrophils | 50.1 | 40–75 | % |
| C reactive protein | 0.3 | 0–8 | mg/L |
| Serum bilirubin | 11.4 | 5.1–19.0 | μmol/L |
| Serum albumin | 37.1 | 40–55 | g/L |
| Serum alkaline phosphate | 48 | 35–100 | U/L |
| Serum aspartate | 16 | 13–35 | U/L |
| Serum amylase | 75 | 35–135 | U/L |
| Fasting plasma glucose | 576 | 70–110 | mg/dL |
| HBA1c | 147 | 16–42 | mmol/mol |
nmol/L [3]. Therefore, low insulin levels underlie most of the glucose metabolism disorders, as islets and β-cells are located in the tail of the pancreas [15, 16]. Previous studies have reported variations in the severity of high-fasting blood glucose disorders and insulin-dependent diabetes [12, 17], indicating that there are many degrees of β-cell dysfunction in patients with ADP.

Other abdominal symptoms including pancreatitis and steatorrhea have also been reported [18, 19]. The reported incidence of pancreatitis was 30% [12], but it is

| Studies         | Clinical presentation                                                                 | Pancreas imaging                                      | Gene mutation                                |
|-----------------|---------------------------------------------------------------------------------------|-------------------------------------------------------|---------------------------------------------|
| Devarbhavi PK   | Diabetic ketoacidosis                                                                   | Short pancreatic tail                                 | Not assessed                                |
| Sohn TS [4]     | Severe hypertriglyceridemia, and acute pancreatitis                                    | Pancreas tail and dorsal pancreatic duct were not visualized | Not assessed                                |
| Caetano LA [5]  | Maturity onset diabetes of the young                                                   | Caudal pancreatic agenesis                            | Heterozygous variant in PDX1                |
| Caetano LA [5]  | Impaired glucose tolerance                                                             | Short pancreas tail                                   | Heterozygous variant in PDX1                |
| Cienfuegos JA   | DM, mucinous cysts and chronic calcific non-alcoholic pancreatitis                    | Mucinous cysts                                        | Not assessed                                |
| Liang K [14]    | DM                                                                                    | Normal shape of pancreatic head                       | Not assessed                                |
| Erotokritou A   | DM, nonspecific abdominal symptoms                                                    | Neuroendocrine tumor                                  | Not assessed                                |
| Kawasaki S [19] | Pancreatitis, Peutz-Jeghers syndrome                                                  | Normal shape of pancreatic head                       | Not assessed                                |
| Alexander E [21]| Pancreatic head cancer, obstructive jaundice                                           | Hypo-vascular lesion in the head                      | Not assessed                                |
| Suh PS [22]     | DM                                                                                    | Cystic mass lesion                                    | Not assessed                                |
| Suh PS [22]     | DM                                                                                    | Calcified cystic mass                                 | Not assessed                                |
| Riguetto CM [23]| DM, heterotaxy syndrome                                                               | Enlarged pancreas head                                | Not assessed                                |
| Sonkar SK [24]  | DM, recurrent loose stool and abdominal pain                                         | Agenesis of dorsal pancreas                           | Not assessed                                |
| Jain A [25]     | DM, recurrent upper abdominal pain, fatigue                                           | Pancreatic body and tail were not visible in MRCP     | Not assessed                                |
| Rodrigues P [26]| Neuroendocrine tumor                                                                  | Nodular-lesion on pancreas head                       | Not assessed                                |
| Chhabra P [27]  | Epigastric pain aggravated by meals                                                    | Normal shape of pancreatic head                       | Not assessed                                |
| Mustafa K [28]  | DM, polysplenia, Kartagener syndrome, polycystic kidney disease.                     | Hypertrophied ventral pancreas                        | Not assessed                                |
| Kabnurkar R [29]| Carcinoma of tongue                                                                  | Normal shape of pancreatic head                       | Not assessed                                |
| Saikaly E [30]  | Mucinous adenocarcinoma and cystic teratoma                                            | Complex cystic lesion                                 | Not assessed                                |
| Shahzad R [31]  | No                                                                                   | Agenesis of dorsal pancreas                           | Not assessed                                |
| Robert AP [32]  | Right iliac fossa pain                                                                | Normal shape of pancreatic head                       | Not assessed                                |
| Nassif S [33]   | Pancreatic neuroendocrine tumor, endometrial stromal sarcoma                           | Mass at the neck of the pancreas                      | Not assessed                                |

Fig. 1 Contrast abdominal computed tomography scan showed the pancreatic head (a, red arrow), whereas the pancreatic body and tail are absent (b, red arrow). Magnetic resonance cholangiopancreatography demonstrated the absence of the dorsal pancreatic duct (c, red arrow).
unclear whether the high frequency of pancreatitis in ADP patient was due to the requirement of imaging procedure for patient with pancreatitis. Steatorrhea in ADP patient was due to exocrine pancreatic insufficiency. Although the prevalence is much less common, most of the cases had concomitant hyperglycemia [18].

Imaging modalities are essential in the diagnosis of ADP, with ultrasonography as the most commonly used approach for evaluating abdominal pain and other abdominal symptoms [20]. However, interference from the superimposed gas in the stomach and duodenum limits its usefulness in the detection of pancreatic anomalies [14]. Both CT and MRCP are reliable modalities to confirm the absence of the body and tail of the pancreas and to differentiate this condition from other disorders such as peripancreatic lymphadenopathy and anatomic variations. ERCP and MRCP can also be used to confirm the absence of the dorsal duct system. In summary, MRCP is a noninvasive approach with no risk of exposure to radiation, and we recommend it as the first choice for patients with ADP.

As glucose metabolism disorders can vary across different individuals, we advise clinicians to consider the diagnosis of ADP for a patient presenting with a glucose metabolism disorder accompanied by abdominal pain, pancreatitis or steatorrhea.

Informed consent was obtained from this patient for publication of this case history and associated images were provided.

Abbreviations
ADP: Agenesis of the dorsal pancreas; CT: Computed tomography; DKA: Diabetic ketoacidosis; Dm: Diabetes mellitus; ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography

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Author’s contributions
TY led the conception and design, review of the literature, and drafted the manuscript. XY interpreted data and revised the manuscript. LW collected data and revised the manuscript. JM discussed the data and revised the manuscript. All authors read and approved the final manuscript.

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Ethics approval and consent to participate
Informed consent was obtained from this patient for publication of this case history and associated images were provided.

Consent for publication
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Competing interests
The authors declare that they have no competing interests.

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