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CASE REPORT

Dorsal pancreatic agenesis: a case report

Agenesia dorsal pancreática: um relato de caso

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ABSTRACT

Pancreatic dorsal agenesis (PDA) is an infrequent and often asymptomatic congenital entity. It may present as an incidental finding of an imaging exam or associated with other conditions such as abdominal pain or discomfort, diabetes mellitus, pancreatitis, exocrine pancreatic insufficiency, tumors, and other malformations. This study presents and discusses the case of a 52-year-old woman, obese, with pre-diabetes and gastroesophageal reflux disease, whose diagnosis of PDA occurred during the investigation of a chronic condition of cholestasis and abdominal discomfort. Magnetic resonance cholangiopancreatography (MRCP) showed an absence of the pancreas body and tail and did not show the corresponding dorsal pancreatic duct. Imaging tests are essential for diagnosing PDA. There is no specific treatment for PDA, so only accompanying conditions are treated when indicated.

Keywords: Pancreas; Pancreatopathies; Congenital abnormalities; Glucose intolerance; Glucose metabolism disorders; Diabetes mellitus; Case report.

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RESUMO

A agenesia dorsal pancreática (ADP) é uma entidade congênita muito rara e muitas vezes assintomática. Ela pode se apresentar como um achado incidental de um exame de imagem ou associada a outras condições como dor ou desconforto abdominal, *diabetes mellitus*, pancreatite, insuficiência pancreática exócrina, tumores e outras malformações. Este estudo apresenta e discute o caso de uma mulher de 52 anos, obesa, com pré-diabetes e doença do refluxo gastroesofágico, cujo diagnóstico de ADP ocorreu durante investigação de um quadro crônico de colestase e desconforto abdominal. A colangiopancreatografia por ressonância magnética (CPRM) mostrou ausência de corpo e cauda do pâncreas e não evidenciou o ducto pancreático dorsal correspondente. Exames de imagem são essenciais para diagnosticar a ADP. Não há tratamento específico para a ADP, de forma que somente as condições que a acompanham são tratadas, quando indicado.

Palavras-chave: Pâncreas; Pancreatopatias; Anormalidades congênitas; Intolerância à glucose; Transtornos do metabolismo da glicose; Diabetes mellitus; Relato de caso.

Introduction

The pancreas is an organ whose formation depends on proper development and fusion of the ventral and dorsal buds[1,2]. In this context, pancreatic dorsal agenesia (PDA) is a malformation characterized by the dorsal bud's absence or congenital regression. It is pretty rare, with about 100 reported cases in the literature since the first description in an autopsy in 1911[1,3-18]. However, it is worth remembering that the exact frequency is unknown, with the number of cases being higher, considering that not all PDA cases are published and that this malformation is not systematically tracked[5]. Furthermore, some differential cases, especially pancreas pseudoagenesis, may have been mistakenly classified as PDA[15,19].

Most cases are asymptomatic and incidentally found in imaging tests such as ultrasonography (USG), computed tomography (CT), magnetic resonance (MR), magnetic resonance cholangiopancreatography (MRCP), and endoscopic retrograde cholangiopancreatography (ERCP)[5,9,11-13,15,17,19,20]. Despite this, this condition may be associated with nonspecific abdominal symptoms, dysglycemia, diabetes mellitus, pancreatic tumors, pancreatitis, pancreatic pseudocyst, enlarged pancreatic head, and exocrine pancreatic insufficiency[2,4-9,11-19].

Given this, we aim to present and discuss a case of PDA in the light of the available scientific literature to contribute to a better understanding of PDA by medical professionals.

Case Report

After we explained the purpose of this case report and stated our professional secrecy guarantee, the patient signed the consent term. The present case report was analyzed and approved by the Research Ethics Committee of the Federal University of Uberlândia under the CAAE (from the Portuguese *Certificado de Apresentação de Apreciação Ética*, meaning Ethical Appraisal Presentation Certificate) number 50166021.0.0000.5152 and the consubstantiated declaration number 4.922.097.

The patient, a 52-year-old Brazilian female diagnosed with gastroesophageal reflux, grade 1 obesity (weight = 89kg; height = 1.68m; body mass index = 31.53kg/m^2), and prediabetes, and using metformin for about a year, attended a radio imaging service to investigate chronic cholestasis due to complaints of abdominal discomfort and reflux for approximately two years. This discomfort was in the upper abdomen, especially in the right hypochondrium, accompanied by a distention sensation. It occurred continuously, with worsening in a prone position and after meals, and improved with the use of bromopride and pantoprazole twice per day. In recent months, she has enhanced by adopting a healthier diet and losing weight, including reducing the need for these medications and starting to use them once a week. She mentioned beer consumption of approximately 1,400mL per day and up to 6,300mL once a week from 30 to 51 years old. She currently claims to ingest a can or two of beer on weekends. She has

also been using bupropion to control anxiety for about six months. She denies smoking and a history of gallstones and pancreatitis. As for family history, she had a father with diabetes, a drinker, and a former smoker, who died at the age of 52 from pancreatic cancer.

The tests previously performed by the patient showed: mild neutropenia (neutrophils = 1154/mm³) and mild anisocytosis on blood count; moderate hepatic steatosis on total abdominal ultrasound; moderate erosive esophagitis (grade B in Los Angeles classification), grade 1 hiatal hernia, and mild antral enanthematous gastritis on upper gastrointestinal endoscopy; fasting glucose (103mg/dL) and HbA1c (6.0%) in glucose intolerance levels; normal or near-normal plasma levels of direct (0.23mg/dL), indirect (0.38mg/dL) and total (0.61mg/dL) bilirubin; plasma levels ranging from average to slightly increased of the liver enzymes, aspartate aminotransferase (35U/L) and alanine aminotransferase (51U/L); and elevated levels of the canalicular enzymes, gamma-glutamyl transferase (GGT) (248U/L), and alkaline phosphatase (AP) (148U/L).

In this context, a magnetic resonance cholangiopancreatography (MRCP) detected the absence of the pancreas body and tail (Figure 1) and no evident dorsal pancreatic duct (Figure 2), findings compatible with pancreatic dorsal agenesis.

Discussion

In humans, the ventral and dorsal buds of the endoderm of the foregut originate the pancreas[1,4-8,10,15,16,19,21]. The dorsal bud drains through Santorini's dorsal pancreatic duct and minor papilla, forming the anterosuperior part of the head, neck (also called isthmus), body, and tail of the pancreas. The ventral bud, directly related to the common bile duct, drains through Wirsung's ventral pancreatic duct and generates most of the pancreatic head and the uncinate process[1,4,5,7,8,12,14-19,21].

During the gestation 7th week, the ventral bud rotates close to the duodenum and fuses with the dorsal bud, allowing fusion of the ventral Wirsung and dorsal Santorini ducts at the level of the head of the pancreas and the formation of the mature gland[1,2,4,6-8,10,14,16,18-20]. It is noteworthy that, in this process, the ventral and dorsal ducts form the main pancreatic duct (Wirsung), while the proximal segment of the dorsal duct degenerates or generates the accessory pancreatic duct (Santorini), draining directly into the duodenum through the minor papilla or ending on a blind bottom[1,2,19].

PDA characterizes by the dorsal bud's absence or congenital regression and occurs in two forms: partial or complete. In complete PDA, the minor papilla, the dorsal duct of Santorini, the neck, body, and tail are absent. In the partial form, the neck, a variable amount of pancreas body, the minor papilla, and a remnant of the dorsal duct of Santorini are present[10,11,15-17,19,20].

Although the genetic factors associated with PDA are not well understood, the occurrence of familial cases suggests a genetic predisposition, and studies carried out in mice reveal that mutations in the enzyme retinaldehyde dehydrogenase 2 (Raldh2) and the H1xb9 gene or retinoic acid deficiency generate PDA[5,9]. In addition to this, other studies have found that PDA and pancreatic exocrine dysfunction occur in the presence of mutations in the HNF1B gene, which acts in the regulation of pancreatic development[6,9,17]. Some studies also point to overexpression of the Sonic Hedgehog (SHH) protein and exacerbating a signaling pathway leading to PDA[4]. Other hypotheses to explain the genesis of PDA are the involvement of the developing pancreas by ischemic aggression[4,11,17,19] or the occurrence of an anomalous arrangement along the left-right axis[21].

There is usually no clinical manifestation associated with PDA, still, when present, it is variable and nonspecific and may include abdominal pain or discomfort (most common), especially in the upper abdomen, meteorism, pancreatitis, diabetes mellitus, duodenal obstruction, bile duct obstruction, and malabsorption with steatorrhea caused by exocrine pancreatic insufficiency[1,4,5,7,9-19]. Abdominal pain or discomfort and meteorism could be explained by different factors, such as lack of papillary muscles, sphincter of Oddi dysfunction, intestinal obstruction, concomitant pancreatitis, exocrine pancreatic dysfunction, diabetic autonomic neuropathy, and, in some instances, malignancy[2,6,8,9,16,17]. Many studies reported the occurrence of acute pancreatitis by several mechanisms, such as sphincter of Oddi dysfunction, compensatory pancreatic head hypertrophy, increased secretion of pancreatic juice, and pancreatic duct hypertension[7-9,16,17,19]. Pancreatitis in PDA can be clinical or subclinical, which is reinforced by cases described in the literature of pancreatic pseudocysts without a previous history of pancreatitis[15].

Particularly concerning dysglycemia, PDA can act as a contributing factor in the development of hyperglycemia and diabetes mellitus (DM) since the pancreatic beta cells, which secrete insulin, are located predominantly in the body and, above all, in the tail of the pancreas body[1,6-9,15-21]. This association is very noticeable since the occurrence of hyperglycemia is described in approximately 50% of PDA cases, with about half of them requiring insulin therapy[8,9,13,14,16,18,19,21].

Some of these reports also demonstrated low levels of C-peptide, which is a laboratory indicator of dysfunction and deficiency of pancreatic beta cells, a deficit that presents itself to varying degrees in patients with PDA[8,18]. In addition, a reduction in islet cell mass, glycogen synthesis, and glycogenolysis was reported along with an increase in gluconeogenesis and hepatic insulin clearance in a family with agenesis of the dorsal pancreas, which may favor progression to pre-diabetes and DM[21].

In the case in question, multiple factors may have contributed to the development of the present glycemic disorder, such as bad previous lifestyle habits, obesity, genetic predisposition, and PDA. The meteorism that the patient experiences can either be part of the dyspeptic condition resulting from the gastroesophageal reflux disease or be a symptom associated with PDA.

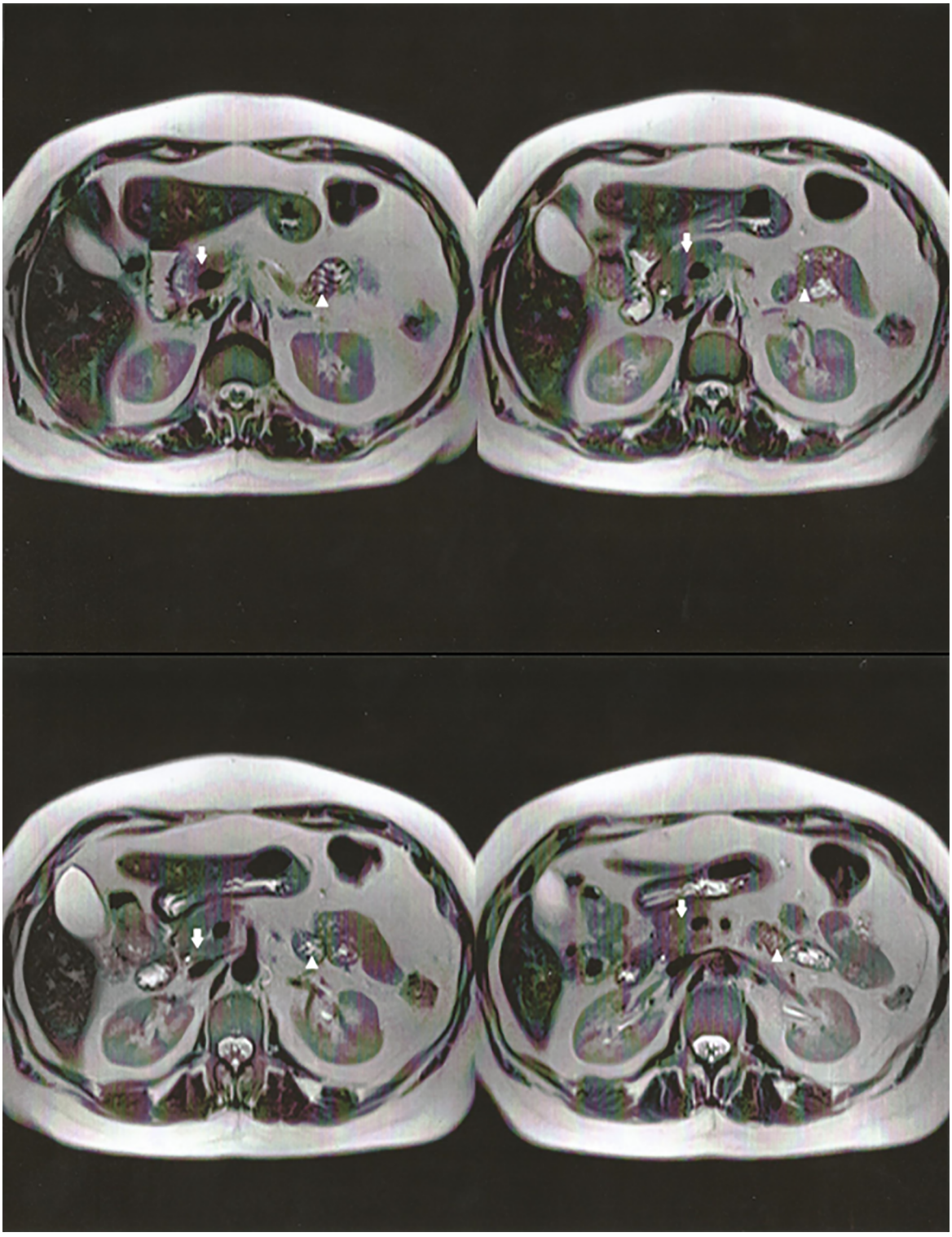


Figure 1. Serial sequences in the axial section show the pancreatic head and the uncinate process with the typical morphology and sign (arrow). The rest of the pancreas is not seen. A loop of the small bowel is seen in the pancreatic bed anterior to the splenic vein − bowel-dependent sign (arrowhead).

More rarely, such agenesis can be associated with pancreatic neoplasms, perhaps because of an increased risk of chronic pancreatitis, which, in turn, is a risk factor for pancreatic tumors, although more studies are needed to clarify the mechanisms involved[5,9,15,17]. There are also reports of PDA along with other congenital anomalies, including heterotaxy, cardiac septal defects, coarctation of the aorta, tetralogy of Fallot, pulmonary stenosis, polycystic kidney disease, horseshoe kidney, unilateral renal agenesis, Kartagener syndrome, intestinal malrotation, Hirschsprung's disease, polysplenia, ectopic spleen, choledochal cyst, biliary atresia, vaginal atresia, and ectopic ovary, so there is

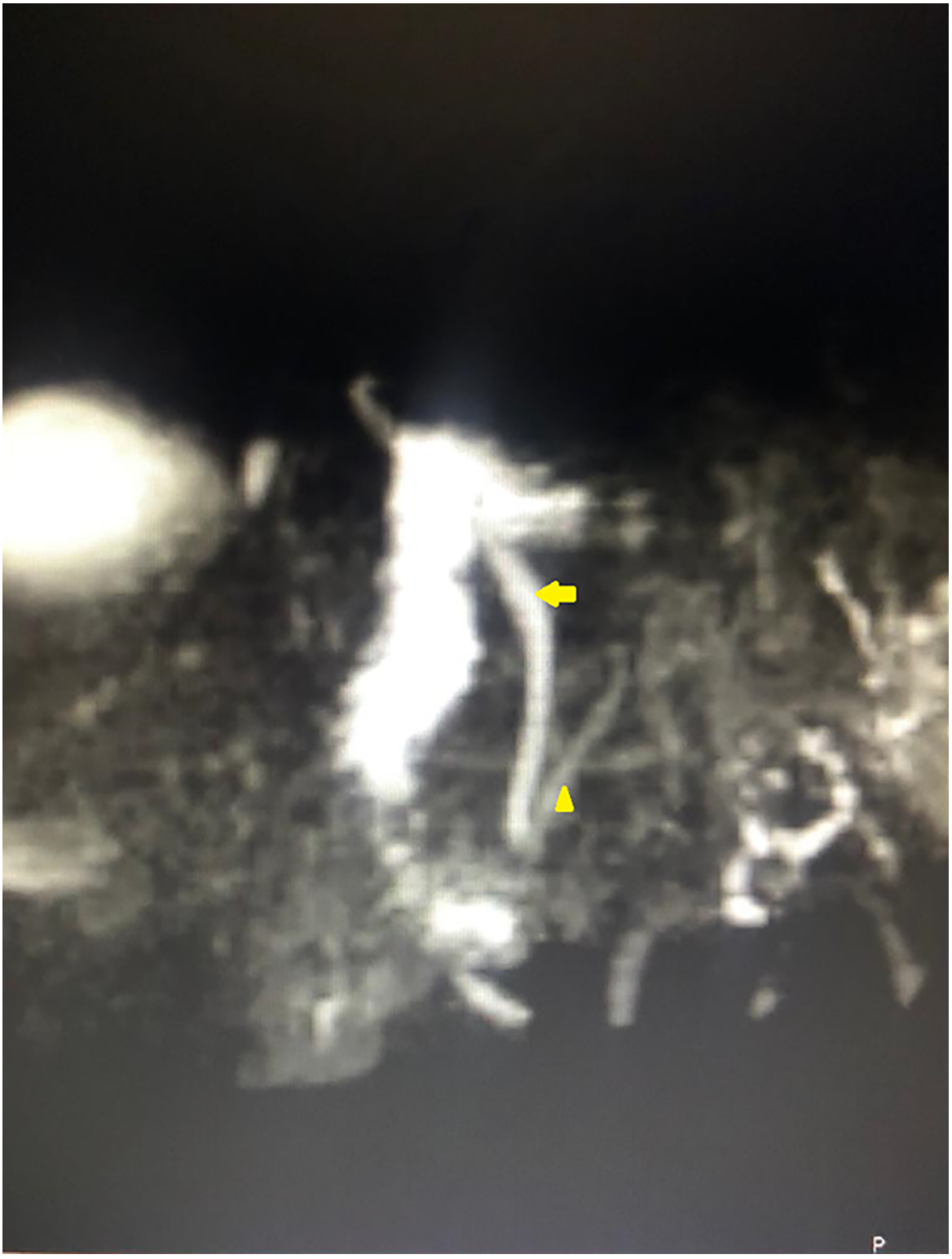


Figure 2. MRCP (Magnetic Resonance Cholangiopancreatography) image shows the common bile duct (arrow) and Wirsung's ventral duct (arrowhead). The dorsal pancreatic duct is not evidenced.

a possibility of syndromes encompassing PDA as research advances[3,4,7-11,14,16,17,19,20].

Depending on the nonspecific or absent clinical character, the diagnosis of PDA is mainly based on imaging exams. In this sense, USG is one of the first modalities involved, as it is commonly requested in medical practice, including the investigation of abdominal pain[3,7,11,16,18]. However, USG is quite limited by intestinal gas or morbid obesity, being an insensitive test to detect PDA and other pancreatic anomalies[3,7-9,11,16-19]. Unlike USG, CT and MR easily

identify the absence of the body and tail of the pancreas, with a standard or slightly enlarged pancreatic head[2,4,8,9,16,18]. CT shows the defective part of the pancreas and presents corresponding signs, such as the stomach-dependent sign or the intestine-dependent sign, which indicate the occupation of the distal pancreatic bed, anterior to the splenic vein, by the stomach or by the intestine, respectively[3,7,11,13,14,16]. MR also shows analogs of these signals[16].

It is noteworthy that USG, CT, and MR are tests that suggest PDA because ERCP or MRCP is necessary to confirm such a diagnosis. Such studies provide more detailed information regarding the anatomy and morphology of the pancreatic ducts, with high value for identifying the (partial or complete) forms of PDA and for ruling out differential diagnoses[1,3,4,9,11,14-16,18,19]. However, considering the costs involved, some researchers question the need to perform ERCP or MRCP in cases suggestive of PDA without associated diseases or symptoms[8,17].

Most reports describe ERCP as the gold standard exam. However, it is operator-dependent, requires exposure to ionizing radiation and contrast, in addition to presenting a risk of causing pancreatitis by catheterization of the minor papilla. Thus, MRCP is often chosen since it is non-invasive, without ionizing radiation, does not require contrast infusion, and has good diagnostic accuracy, mainly when used with three-dimensional or dynamic reconstructions with secretin injection. MRCP is also helpful in cases where ERCP cannulation was impossible[1,4,7,11,14,15,18-20]. Some authors also point to endoscopic ultrasound, a minimally invasive valuable procedure in the cytological investigation of pancreatic tumors, as a potential option to establish PDA diagnosis[2,4,7,11,16,19].

On imaging examination, pancreatic pseudoagenesis, distal pancreatic adipose replacement, periportal lymphadenopathy, and anatomical variations are examples of differential diagnoses concerning PDA[2,3,5,8-16,19]. Pseudoagenesis of the pancreas, in particular, is characterized by atrophy of the dorsal pancreas secondary to pancreatitis so that it closely resembles PDA at first sight[2,15,16,19].

On both CT and MR, abundant fat tissue is seen anterior to the splenic vein in cases of distal pancreatic adipose replacement, and pancreatic atrophy, similarly, can also present with fat replacement in this same region[3,9,13,19]. When possible and pertinent, the analysis of the dorsal duct of Santorini is part of the diagnostic differentiation, as this structure is absent or considerably shortened in PDA, whereas it is usually present in conditions such as pancreatic adipose replacement and pancreas pseudoagenesis[10,15,16,19].

There is no specific treatment for PDA, so only accompanying conditions are treated when indicated[4,9,17]. Depending on the predominant type of DM and the degree of insulin deficiency due to the loss of beta cells in the dorsal pancreas, exogenous insulin can be considered a primary or complementary therapeutic option in cases of DM and PDA to obtain adequate glycemic control[8,9,14,18,21]. Regarding abdominal pain or discomfort and meteorism related to PDA, reports, and articles describe improvement or disappearance of these symptoms with the prescription of low-fat diets, gastrokinetics, analgesics, and supplemental pancreatic enzymes[1,2,9,16,18]. The clinical improvement or resolution with these enzymes suggests that these symptoms are related to some degree of exocrine pancreatic dysfunction[9].

Concerning follow-up, this is not well defined in PDA, as there are authors who advocate screening for pancreatic tumors in all patients diagnosed with PDA[4,5], while others claim that it is necessary to weigh the risk of mental stress, the additional costs, and benefit of detecting the tumor early[16].

This study has limitations considering the lack of follow-up, besides being intrinsically observational and descriptive, with a low level of evidence and without the capacity to establish associations. On the other hand, it has, as strengths, the contextualization of a clinical case and the discussion based on the available scientific literature.

Conclusion

Different genetic, embryological, and pathological factors are potentially involved in the genesis of PDA, a condition that still lacks better understanding. PDA is very rare and often asymptomatic but may occasionally be associated with symptoms and diseases such as blood glucose disorders, meteorism, abdominal pain, steatorrhea, pancreatitis, and, more rarely, pancreatic neoplasms and congenital anomalies. Image exams are essential to suggest and confirm the diagnosis of PDA. However, its use for diagnostic confirmation in cases suggestive of PDA without associated symptoms or diseases is questionable, given the uncertain cost-benefit. Considering its rarity and non-specificity, in the absence of associated clinical relevance conditions that require therapeutic approach, it has no specific treatment or well-deemed follow-up, and pancreatic tumor screening in patients with PDA is controversial.

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Authors' Contribution

We describe contributions to the papers using the taxanomy (CRediT) provided below: *Conceptualization, Investigation, Methodology, Visualization & Writing – review & editing: IMG; RR; NPS. Project administration, Supervision & Writing – original draft*: IMG; RR; NPS.

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