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Agenesis or pseudoagenesis of the dorsal pancreas

Agenesia ou pseudoagenesia do pâncreas dorsal

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A B S T R A C T

The authors present an evidence-based case report of a patient with agenesis or pseudoagenesis of the dorsal pancreas.

CASE REPORT

A 57-year-old woman was referred in 2007 for assessment of jaundice of cholestatic pattern. The patient's vital signs and physical examination were unremarkable. Laboratory test results were normal except for elevated total bilirubin level, 6.4 mg/dL (direct bilirubin level, 5.8 mg/dL**)**. In her past medical history, she reported anything remarkable until 1995, when she developed acute biliary pancreatitis, characterized by abdominal pain accompanied by vomiting, diarrhea, and elevated serum pancreatic amylase (5,000 IU/L). Abdominal ultrasonography (US) showed gallstones. At that occasion, she underwent a conventional open cholecystectomy to prevent another episode of acute biliary pancreatitis. Routine perioperative cholangiography did not visualize the pancreatic duct.

During the hospitalization, an abdominal ultrasonography showed dilated bile ducts and stones in the choledochal duct. A computed tomography (CT) did not reveal the pancreatic corpus or tail (Figures 1). An endoscopic retrograde cholangiopancreatography (ERCP) was carried out with stones removal. It was not possible to perform a pancreatography, and the minor papilla was not visualized even after careful examination. The major papilla was normal. A conservative management was instituted, since dorsal pancreas agenesis is quite consistent with a normal life. She was discharged three days later.

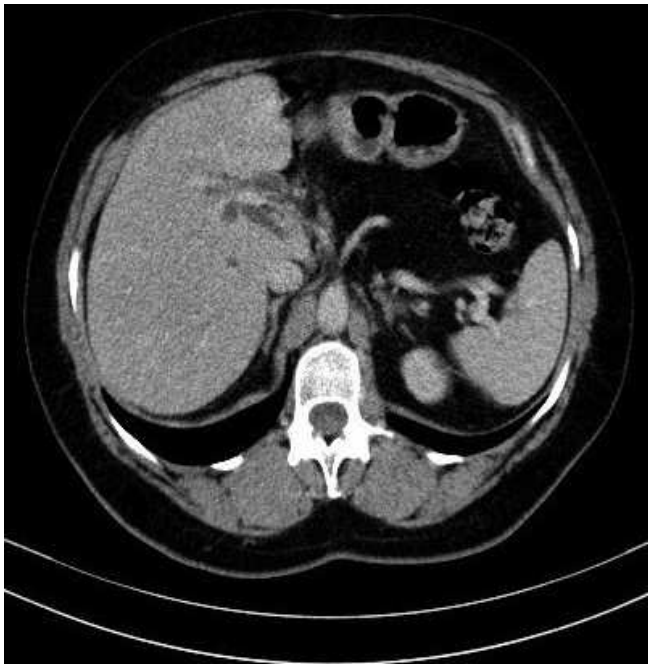

Figure 1 - *Computed tomography did not reveal the pancreatic body or tail.*

Formulating the questions

It is frequently written that the first step in evidence based practice is to turn the clinical problem into an answerable question. This proved more difficult than we first thought – as we wanted answers to several clinical questions –, involving quite a different way in thinking the anatomical-pathological-physiological questions and formulating empirical ones. We wanted to use an evidence based approach to guide our assessment and management, so we considered five issues: frequency, etiology, clinical manifestations, diagnosis and association with other diseases[1].

Searching for evidence

We searched PubMed (March 2015) with the terms "Pancreas/abnormalities" OR "dorsal pancreas agenesis" OR "short pancreas" OR "pancreas hypoplasia" (articles published in the last 10 years), which yielded 421 references. Browsing these titles, we limited our search to

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case reports. We also searched the references list of each case report selected for full reading.

We also searched PubMed for published articles with the search terms "dorsal pancreas agenesis", "short pancreas", and "pancreas hypoplasia". All papers identified were English or German (full-text papers, case reports, and letters to the editor). The references lists of identified articles were searched for further papers.

How common is agenesis of the body and tail of the pancreas?

In 1911 the first description of agenesis of the dorsal pancreas was published as an autopsy finding.

The exact prevalence of agenesis of the dorsal pancreas is not known. From 1913 through 2006, only 20 cases have been reported in the literature. Complete agenesis is actually quite rare, with a total of 16 cases reported in that period. Agenesis of the dorsal pancreas may be complete or partial, the latter being more frequent. In the complete dorsal pancreatic agenesis, the minor papilla, the accessory pancreatic duct (duct of Santorini) and the body and tail of the pancreas are absent; whereas in partial agenesis, the minor papilla, the duct of Santorini and body are present.

When one considers the criterion for dorsal pancreas agenesis as the absence of pancreatic tissue above the pancreatic artery, either on computed tomography (CT) or as an anatomopathological finding, one finds around 50 patients over the last 100 years. But, with the development of new image diagnostic techniques, many authors advised that the diagnosis of dorsal pancreas agenesis should only be firmed if there is the absence of the pancreatic duct of Santorini during either ERCP, magnetic nuclear resonance (MNR) or as an anatomopathological finding[2-7].

Another curious findings are the pseudo-agenesis of the dorsal pancreas and pancreatic distal lipomatosis. Pseudo-agenesis is a clinical scenario that may follow a necrohemorrhagic pancreatitis, which could be responsible for the partial destruction of the pancreatic tissue, its atrophy and its substitution by fat. Some cases could have been misdiagnosed as dorsal pancreas agenesis, given the higher prevalence of pancreatitis. However, in such cases it is possible to identify the duct of Santorinni[5].

What causes the agenesis of the dorsal pancreas?

The name pancreas is derived from the Greek words *pan* and *creas*, meaning all and flesh, respectively.

The origin of dorsal pancreas agenesis consists in the absence or regression of the embryonic dorsal bud, which arises from the posterior duodenal wall. This dorsal bud usually provides the isthmus, body and tail of the pancreas and the cranial part of the head; the caudal part of the head, the retro-duodenal process, is supplied by the ventral bud, which is sometimes duplicated.

The pancreas presents a complicated embryogenesis between the 5th and the 7th week of gestation. At the 6-7th week, the ventral pancreas fuses with the dorsal one. During the fusion, the ventral and the dorsal ducts form the main pancreatic duct. The accessory pancreatic duct is formed from the portion of the dorsal bud, which gives rise to the upper pancreatic head.

The causes of agenesis of the dorsal pancreas are unknown. A primary dysgenesis of the dorsal pancreatic bud and an ischemic insult to the developing pancreas are possible explanations.

Family cases have been reported in the literature, but the genetic transmission remains unclear. One report of dorsal pancreatic agenesis inherited by 2 sons from their mother clearly suggests a genetic etiology, with an X-linked or autosomal-dominant mode of transmission[3].

What are the clinical manifestations of the dorsal pancreas agenesis?

Most cases of dorsal pancreas agenesis are likely asymptomatic because of the functional reserves of the exocrine and endocrine pancreas, and the diagnosis is usually made incidentally on abdominal imaging during evaluation for an unrelated issue. However, abdominal pain with or without recurrent acute pancreatitis, weight loss with or without diabetes mellitus, and jaundice are the most commonly reported indicators of dorsal pancreatic agenesis. Hyperglycemia is found in around 50% of patients with dorsal pancreas agenesis, suggesting that it may cause diabetes mellitus[2,8]. Exocrine pancreatic insufficiency is not common, because this condition is avoided if there is only 10% of functioning pancreatic tissue. The relationship between agenesis of the dorsal pancreas and exocrine pancreatic insufficiency remains unclear; only one case has been reported up to 2006[9].

Some authors suggest that abdominal pain is more common in patients with partial agenesis, and diabetes mellitus is more common in patients with complete agenesis of the dorsal pancreas.

Abnormalities of the bile duct system have been found in several cases, and there are reports of other congenital anomalies, such as polysplenia syndrome, and pancreatic tumors[3,8].

Pancreatic agenesis is a rare cause of neonatal diabetes mellitus, characterized by severe intrauterine growth retardation, early onset of permanent neonatal diabetes mellitus, failure to thrive due to lack of pancreatic exocrine dysfunction, and associated malformations mainly of the heart or the biliary tract. Neonatal diabetes in association with pancreatic agenesis is a rare condition that has been reported only in 15 cases in the literature up to 2008[10].

Is the complete agenesis of the dorsal pancreas associated with other diseases?

Of the 14 reported patients (1913 through 1999) with complete agenesis of the dorsal pancreas,

nine had diabetes mellitus, while only one had chronic pancreatitis.

Most likely, diabetes mellitus develops because most of the â cells of the islets of Langerhans are located in the absent pancreatic body and tail[3].

More then 50% of patients with this agenesis of the dorsal pancreas were hyperglycaemic. It is known that the majority of islets are located in the pancreatic tail, and that â cells of the dorsal pancreas respond better to glucose stimulation. It is thus believed that agenesis of the dorsal pancreas may cause diabetes mellitus. The most common way to Type 1 and 2 diabetes is a decrease in â cell mass. It seems that, as in dorsal pancreas agenesis, the decreased â cell mass and the limited *in vivo* replication capacity of â-cells after surgical resection lead to diabetes mellitus in a high number of affected patients[8].

This anomaly may be complicated by recurrent acute and chronic pancreatitis (calcified or non-calcified). The explanation for the association between pancreatitis and dorsal pancreas agenesis is far from clear. There are two suggested causes for the pathogenesis of pancreatitis in dorsal pancreatic agenesis: first, sphincter of Oddi dysfunction; and second, elevated intrapancreatic ductal pressures in the compensating hypertrophied remnant ventral pancreas[3].

Abnormalities of the bile duct system have been found in several cases in the literature (common embryological origin of the pancreas and bile duct system from the distal foregut). In some of the reported patients, additional congenital anomalies were found (ectopic spleen, duodenal malrotation, intestinal malrotation, heterotaxy syndrome, left-sided gallbladder, choledochal cyst, annular pancreas, vaginal atresia, coarctation of the aorta, atrioventricular septal defects; anomalous pulmonary veins drainage, pulmonary stenosis, Tetralogy of Fallot, and anatomical variant of the abdominal arteries or veins), but there was no consistent pattern resulting in a syndromic diagnosis. Few cases of dorsal pancreas agenesis are associated with polysplenia syndrome.

A very limited number of pancreatic tumors (n = 4) have been found in association with agenesis of the dorsal pancreas, including solid papillary and pseudopapillary tumors and adenocarcinomas[3].

Does this patient have complete agenesis of the dorsal pancreas?

Complete agenesis of the dorsal pancreas is a rare pancreatic anomaly. Differential diagnosis is necessary to distinguish this entity from pancreatitis and various other pancreatic anomalies. Partial agenesis of the dorsal pancreas has been described, in which the pancreatic body and the main dorsal duct of the Santorini remain. Autodigestion of pancreatic tissue (pseudo-agenesis) due to pancreatitis should also be excluded. The pseudo-agenesis may be associated with ventral pancreas hypertrophy.

Prior to 1979, agenesis of the dorsal pancreas was diagnosed only after laparotomy or at autopsy. The preoperative diagnosis of pancreatic agenesis is difficult, with various imaging techniques being used. Ultrasonography may not visualize the body and tail of the pancreas due to interference of overlying bowel gas or technical failure. Understanding the detailed information of the pancreatic duct on CT is difficult. The three-dimensional (3D) CT reconstruction, especially using the volume rendering technique, and the MRI are very helpful for assessing this entity, despite not being strictly necessary to confirm the diagnosis. ERCP, an invasive, operator-dependent procedure, is useful for obtaining information about the pancreatic duct, but this is an invasive method, and locating and cannulating the minor papilla are sometimes difficult. Because magnetic resonance cholangiopancreatography (MRCP) clearly reveals the pancreatic major and accessory ducts, this technique is useful for the diagnosis of pancreas abnormalities, and, in recent years, has been used as a non-invasive alternative to ERCP, but the latter is still the gold standard. So, to differentiate complete versus partial agenesis of the dorsal pancreas, ERCP is necessary to define absence of the dorsal ductal system, of the accessory duct and of the minor papilla.

Although MRCP can diagnose dorsal agenesis of the pancreas, considerations of cost, availability, and the recent advancement in 3-dimensional imaging capability of a CT scan rendered it the initial diagnostic modality of choice.

Nowadays, the diagnosis is based on four imaging studies: transabdominal US, CT, MRCP and, the gold-standard, ERCP. Sometimes the ability of such studies is limited to distinguishing agenesis of the dorsal pancreas from another congenital abnormalities.

Recently, endoscopic ultrasonography (EUS) has been shown to be useful in the diagnosis of agenesis of the dorsal pancreas. The role of EUS in its identification has not been evaluated, but it may be as good as ERCP[10].

In our patient, pancreatic tissue was present in the pancreatic head, but the distal pancreas was absent on CT scans. Further, the pancreatic accessory and dorsal duct system were not observed in ERCP.

Whether the present patient had agenesis or pseudo-agenesis is a matter of speculation as there is no definite diagnostic test, just non-conclusive classic imagines studies.

DISCUSSION

How has an evidence based approach helped? The main difference was the change in clinical thinking that allowed us to break away from the pathological-anatomical-physiological approach and adopt an empirical one. These steps are not easy. Searching the published

reports is still awkward and time consuming. Some answers are difficult to find. How long, for example, should we carry on looking before concluding that there seems to be no published work to guide us?

We report a case of a patient with a probable agenesis of the body and tail of the pancreas, who was referred to our institution in order to treat cholestatic jaundice due to choledocal stones. The distal pancreas was absent on CT scans. It was not possible to identify the accessory pancreatic and dorsal duct system during ERCP, and the MRCP was not available. Taking into account her past medical history of previous pancreatitis, a pseudoagenesis (resulting from a severe necrohemorrhagic pancreatitis) could not be ruled out. However, based on the medical reports, she had not presented severe pancreatitis in the past, but only mild clinical manifestations. To our knowledge, this is the first evidence based case report published in our country.

R E S U M O

Os autores apresentam um relato de caso baseado em evidência de uma paciente com agenesia ou pseudoagenesia de pâncreas dorsal.

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