Pancreas – Pathological Practice and Research

Editor

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Preface

The pancreas lies deep in the body. It is a calm, silent organ located behind the stomach, with much hope and possibilities for solving the physiological and pathological problems of its behavior. Because the pancreas is a complicated organ, it is important in an anatomical and embryological sense, and because of its frequent age-related lesions. It develops from two buds fused into a single organ with a ductal system, close to the biliary tract and duodenum. Both mucous-cell hyperplasia, which corresponds to PanIN-1, and cystic dilatation of the branch pancreatic duct, relevant to branch-duct-type intraductal papillary-mucinous tumors, frequently occur in elderly persons, resulting in the modification of the tissue surrounding it, i.e. atrophy. Moreover, pathological changes in the pancreas are focal or patchy in nature (i.e. normal tissue is found adjacent to the affected foci), especially in non-tumorous lesions, but not homogeneous and diffuse in the case in the liver.
Nowadays, many different imaging methods and approaches allow the form of the pancreas and its parenchyma to be seen in detail and in repetition or sequence, while the problems posed by biopsy specimens, apart from the risk involved in obtaining the sample, are of sampling error and small sample size because of unequally distributed foci or sparing neighboring areas in the whole organ, as mentioned above.

When doing a pathological study of the pancreas, my colleagues and I appreciate not only the pancreas itself, in a morphological sense, but also its relationship with its neighboring organs such as the duodenum, biliary tract (especially in the pancreatico-choledocho-ductal junction) and liver, and its developmental and anatomical characteristics.

Here, my colleagues and I describe a number of pathological changes in the behavior of the pancreas based on our experience and knowledge. Our opinions may include those which differ from established ones. They are to stimulate discussion resulting from detailed histopathological or clinicopathological observations.

I offer my deep appreciation of my fellow department members as well as my publisher Karger for their kind assistance and consideration in publishing this book.

My hope is that this book will be a useful reference source for all those who wish to investigate and practice research in pancreatology.

Koichi Suda, Tokyo
Development of the Pancreas with Relation to Its Paired Ventral Anlagen

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Abstract

In order to understand the anatomical variations and congenital anomalies of the pancreas, many of which have practical surgical implications, it is important to realize that this organ originates from two separate embryonic anlagen: a ventral and a dorsal primordium. An annular pancreas is a rare malformation, and it is generally accepted that the ring formation originates from a single ventral pancreas, as suggested by Lecco. However, an annular pancreas may also originate from paired ventral pancreata, thus supporting Baldwin’s hypothesis. Here, we attempt to clarify the pathogenesis of the annular pancreas.

An annular pancreas is a rare malformation in which a band of pancreatic tissue surrounds the descending portion of the duodenum, either completely or incompletely, and is in continuity with the head of the pancreas. The anomaly is often discovered incidentally and/or at autopsy. Some patients with this anomaly develop duodenal stenosis, obstructive jaundice and pancreatitis; however, many remain asymptomatic and the anomaly is only discovered accidentally in adulthood.

Many infants with this anomaly also have various other congenital anomalies such as Down’s syndrome, malrotation, esophageal atresia, duodenal atresia, duodenal diverticulum, pancreas divisum, imperforate anus and congenital heart disease. The diagnosis is usually obtained by endoscopic retrograde cholangiopancreatography (ERCP) and/or histological analyses. Although several theories have been proposed to explain the origins of annular pancreas, the pathogenesis is still controversial [1–4]. It is generally accepted that the ring formation originates from the ventral pancreas, as suggested by Lecco and Baldwin [1, 2]. The difference between Lecco’s and Baldwin’s hypotheses is
whether the ventral pancreatic anlage is single or paired. On the basis of embryologic analyses, many gastroenterologists and pathologists have come to believe that the ventral pancreatic anlage is initially paired, with the left lobe normally disappearing during development, as described by Odgers [5]. However, the histogenesis of the ventral pancreatic anlage is also controversial because most of the resected and/or autopsied annular pancreata that have been investigated histopathologically support Lecco’s hypothesis. We present an annular pancreas that was investigated histopathologically and immunohistochemically, which supports Baldwin’s hypothesis with reference to the histogenesis of the ventral pancreatic anlage [6].

**Embryological Development**

In order to understand the anatomical variations and congenital anomalies of the pancreas, many of which have practical surgical implications, it is important to realize that this organ originates from two separate embryonic anlagen: a ventral and a dorsal primordium. On or about the 24th day of gestation, the diverticulum begins to bud from the ventral surface of that part of the primitive digestive tube which is destined to later become the duodenum. This hepatic anlage invades the ventral mesentery and later develops into the liver, bile ducts, and gallbladder. Some two days later (26th day of gestation), a similar diverticulum emanates from the dorsal surface of the digestive tube. In normal pancreatic development, the pancreas arises from the dorsal and ventral anlagen in the 4-week embryo (fig. 1). The ventral anlage consists of two buds, a right and left lobe, and they arise on each side of the common bile duct, as described by Odgers [5]. The left lobe of the ventral pancreatic anlage disappears rapidly. This develops into the dorsal anlage of the pancreas, growing rapidly within the dorsal mesentery. The smaller ventral pancreatic anlage buds a little later from the hepatic diverticulum on the 32nd day (fig. 2) [7].

A series of rapid development changes (elongation of the hepatic anlage to from the bile duct, disappearance of the ventral mesentery, rapid growth of the left wall of the duodenum) leads to a rotation of the common bile duct, together with the ventral pancreatic anlage, into a dorsal position behind the primitive superior mesenteric vessels.

Thus, the dorsal and ventral portions of the pancreas come into close contact by the 37th day of gestation. While these two portions and their drawing ducts begin to amalgamate, the right leaf of the dorsal mesentery fuses with the posterior abdominal wall, thus determining the retroperitoneal position of the pancreas and three-quarters of the duodenum. This avascular plane, the fascia of Treitz, separates the posterior aspect of the pancreas from the abdominal...
By the end of the 7th week of gestation, with the embryo only about 13 mm long, gross morphological development of the pancreas is largely complete. The ventral anlage now comprises the uncinate process and most of the pancreatic head. Its duct (the duct of Wirsung) fuses with the duct of the dorsal anlage and drains into the duodenum together with the common bile duct.
The dorsal anlage constitutes the body and tail of the pancreas and the crani- nal part of the head. The distal part of its duct joins that draining the ventral anlage, although its proximal portion (the duct of Santorini) either drains into the duodenum through a minor papilla or drains retrogradely into the the duct of Wirsung; in some cases it degenerates completely.

The functional development of the pancreas into an exocrine and endocrine gland occurs much later. Secretory acini first appear at the ends of ducts in the third gestational month. Trypsin is formed at about 22 weeks, but full exocrine function is not achieved until six months after birth [8].

Primary islet cells, which probably originate from the neural crest (as do other cells of the APUD system) appear in the 8th week, but are gradually replaced by secondary islets from the third gestational month onwards. Insulin may be detected from the end of the third month, but full endocrine function is not established until after birth.

**Paired Ventral Pancreatic Anlage and Annular Pancreas**

An annular pancreas is a rare malformation and its pathogenesis is still controversial. In the normal course of development between the 8- and 12-mm stages (sixth week), the common duct and the right portion of the ventral primordium are carried dorsally around the circumference of the duodenum to lie adjacent to the dorsal pancreas. This rotation is the result of duodenal growth, during which all enlargement is from the ventral side only. The duct of the longer, dorsal pancreas anastomoses with that of the ventral pancreas to form the main pancreatic duct (duct of Wirsung), which opens into the common duct. If the proximal portion of the dorsal primordium duct persists, it forms an accessory duct (duct of Santorini). How this normal pattern is altered to produce an annular pancreas is not clear, and a number of explanations have been proposed. Tieken’s theory suggests that hypertrophy of both lobes occurs, and that these eventually coalesce to form a ring; Lecco’s theory proposes adhesion of the distal tip of the ventral primordium to the duodenal wall prior to its migration; Baldwin’s theory is based on persistence of a hypothetical left lobe assuming that the ventral lobe is originally a paired structure; while Erimoglu’s theory involves the formation of a ring by fusion of aberrant pancreatic tissue from the duodenum [1–4]. It is now generally accepted that the ring formation originates from the ventral pancreas, as suggested by Lecco (fig. 3) [2]. However, on the basis of clinicopathological analyses of pancreata with pancreaticobiliary maljunctions, many gastroenterologists and pathologists have come to believe that the ventral pancreatic anlage is initially paired, and that the left lobe normally disappears over time, as shown by Odgers [5, 9, 10].
With improvements in imaging techniques such as computed tomography, ERCP and magnetic resonance cholangiopancreatography (MRCP), annular pancreata are being recognized with increasing frequency. Most cases have been diagnosed by ERCP and/or MRCP, although some have been discovered incidentally during surgery or autopsy [11–13]. At present, if patients with an annular pancreas have no symptoms or related complications such as weight loss due to pyloric stenosis, severe abdominal pain, obstructive jaundice or a pancreaticobiliary maljunction, etc., they are followed up conservatively. Therefore, annular pancreas case reports with a histological analysis are still rare. As most resected and/or autopsied annular pancreata that have been investigated histopathologically support Lecco’s hypothesis [14, 15], there is a discrepancy between histopathological analyses of the annular pancreata and clinicopathological analyses of pancreata with a pancreaticobiliary maljunction, i.e. the former support Lecco’s hypothesis of a single ventral pancreas, while the latter support Baldwin’s hypothesis of paired ventral pancreata [3, 6, 14, 15]. Whether the ventral pancreatic anlage is single or paired is the most basic and important embryological point in understanding the pathogenesis of annular pancreas [16–20], because many researchers have come to believe that if the left lobe of the ventral pancreatic anlage does not disappear a pancreaticobiliary maljunction occurs [21, 22]. However, Nobukawa and colleagues and Muraoka and colleagues reported a case with an annular pancreas with

![Fig. 3. Sections of annular pancreata, as suggested by Lecco. An infantile (a) and an adult annular pancreas (b). HE.](image-url)
The persistence of the left lobe of the ventral pancreatic anlage which did not cause a pancreatobiliary maljunction [6, 23, 24]. The histogenesis of the ventral pancreatic anlage has not yet been clarified, and not even in the most recent textbooks of embryology [25–27].

Our evaluations revealed that the ring formation originated from the left lobe of paired ventral pancreata (fig. 4), thus supporting Baldwin’s hypothesis. It was proved that persistence of the left lobe of paired ventral pancreata was not associated with occurrence of a pancreatobiliary maljunction.

References

Development of the Pancreas


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Abstract

Recently, various reduction resections of the pancreas have been performed. The vascular anatomy of the pancreas is unique and complicated, it is therefore especially important for surgeons to understand it.

The vascular anatomy of the pancreas is unique, and complicated compared with other organs. Only surgeons with sufficient knowledge of the vascular anatomy of the pancreas should perform reduction surgery. In this paper, the vascular anatomy of the pancreas together with its embryological and anatomical development and implications for reduction surgery is documented.

The Blood Supply of the Pancreas

Arteries

The pancreas, in particular its head, has an abundant blood supply basically derived from the celiac axis and the superior mesenteric artery (SMA). In fact, the collateral pathways between these two arteries are so efficient that the cut surface of the pancreas removed en bloc using the Whipple procedure will often continue to bleed until the very last jejunal branch (and the proximal jejunal artery itself) has been divided. The general pattern of the arterial blood supply and anatomy of the pancreas is shown in figure 1.

The pancreatic head and uncinate process receive arterial blood from two pairs of pancreatoduodenal (PD) arcades. The superior PD arteries, the anterior and posterior, arise from the gastroduodenal artery (GDA) (either separately or...
Fig. 1. Vascular anatomy (autopsied pancreas). a Gross appearance. b Horizontal section of the entire infantile pancreas on pancreatic polypeptide staining. The lines indicate the boundaries between the head, body, and tail. c Anterior PD arcade, SMA, and SMV are shown on the front of the pancreas. d Posterior PD arcade, SMA, SMV, SA, and SV are shown on the back of the pancreas. e The appearance of the vascular anatomy after removal of the pancreatic head. AIPDA = Anterior inferior pancreatoduodenal artery; ASPDA = anterior superior pancreatoduodenal artery; CA = celiac artery; CBD = common bile duct; CHA = common hepatic artery; DPA = dorsal pancreatic artery; GCT = gastrocolic trunk; GDA = gastroduodenal artery; IMV = inferior mesenteric vein; J-1 = first branch of jejunal artery; LGA = left gastric artery; LNs = lymph nodes; PIPDA = posterior inferior pancreatoduodenal artery; PSPDA = posterior superior pancreatoduodenal artery; PV = portal vein; RGEA = right gastro-epiploic artery; SA = splenic artery; SMA = superior mesenteric artery; SMV = superior mesenteric vein; SV = splenic vein.