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Morphogenic Development of the Pancreas in the Staged Human Embryo

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The Carnegie stage is widely applied in the field of human embryology, and it is more logical to analyze the embryos by this stage than CR length ,or menstrual age. In this study, the early development of the pancreas is studied by tissue observation and reconstruction using serial sections of 33 human embryo ranging from Carnegie stages 11 to 23. The dorsal pancreas develops from the dorsal wall of the duodenum in stage 12, and the ventral pancreas from the proximal part of the cystic primordium in stage 13 or 14 as a single epithelial thickening, but in one case, as a bilateral thickening which contains some isolated spaces. The rotation of the ventral pancreas starts in stage 15, and completes in stage 17. Surrounding connective tissue differentiates in stage 18.

Key Words: Pancreas, development, human, embryo, Carnegie stage

The pancreas develops from two primordia, the ventral and dorsal. Characteristically, the ventral pancreas rotates and fuses with the dorsal pancreas. There are many reports on the development of the human pancreas (Felix, 1892; Piper, 1900; Pearce, 1903; Gage, 1905; Ingalls, 1907; Liu *et al.* 1962). But, most of them mainly dealt with the fetal and histogenic development. The early morphogenic development of the pancreas in the human embryo has been neglected relatively. In addition, because the concept of developmental stage has not been adopted, it is difficult to compare results of one report with an other's.

Accordingly, we used 33 human embryos which had been staged, to clarify the early morphogenic development of the primordia of the panceas and its characteristic features in each stage.

MATERIALS AND METHODS

Serial sections of 33 human embryos ranging from Carnegie stage 11 to 23 were studied from the collection of human embryos in the Department of Anatomy, Yonsei University College of Medicine. Date about the embryos studied are listed in Table 1.

The embryos were embedded in celloidin-paraffin, sectioned at 7~10 μm thickness, and were staind with hematoxylin-eosin. Every second to every fourth section were photographed and printed at an appropriate magnification. Using the blot-

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Table 1. Lists of embryos studied

Weeks	Carnegie stage(cases)
4	11(1) 12(1) 13(3)
5	14(1) 15(3)
6	16(7) 17(2)
7	18(5) 19(1)
8	20(1) 21(2) 22(4) 23(2)

ting papers on which photocopies of the prints were attached, accurate reconstruction models were made. Subsequently details of the pancreas were traced for computer-aided graphic reconstruction(Park *et al.* 1991).

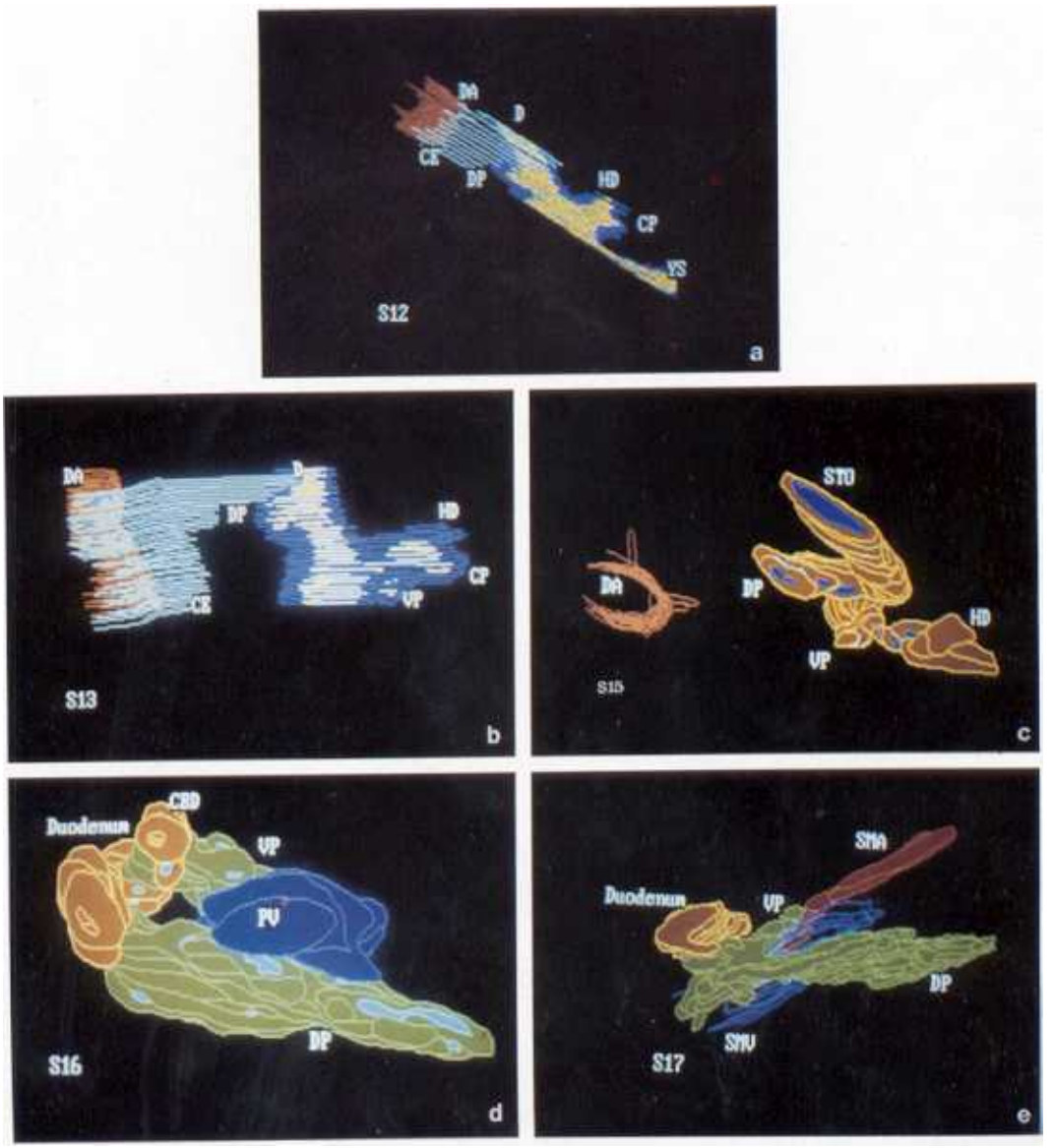

Fig. 1. *Images of computer-aided reconstruction. a. Stage 12. Seen from the right side of the embryo. The dorsal pancreas (DP) is observed. b. Stage 13. Seen from the right side of the embryo. In this case, the ventral pancreas (VP) contains some small spaces which have no connections with the adjacent luman. c. Stage 15. Seen from the right above of the embryo. The ventral pancreas rotates about 90° clockwise. d. Stage 16, The ventral pancreas rotates about 180° clockwise. E. Stage 17. The dorsal and ventral pancreas come in contact. CBD; common bile duct CE; coelomic epithelium, CP; cystic primordium, D; duodenum, DA; dorsal aorta, HD; hepatic diverticulum, PV; portal vein, SMA and SMV; superior mesenteric artery and vein, STO; stomach, YS; yolk sac*

RESULTS

Stage 11

The dorsal and ventral pancreas are not observed.

Stage 12

The dorsal pancreas is observed as an outgrowth from the dorsal wall of the duodenum slightly cranial to the hepatic diverticulum, and extends toward the dorsal mesentery (Fig. 1a). The communication

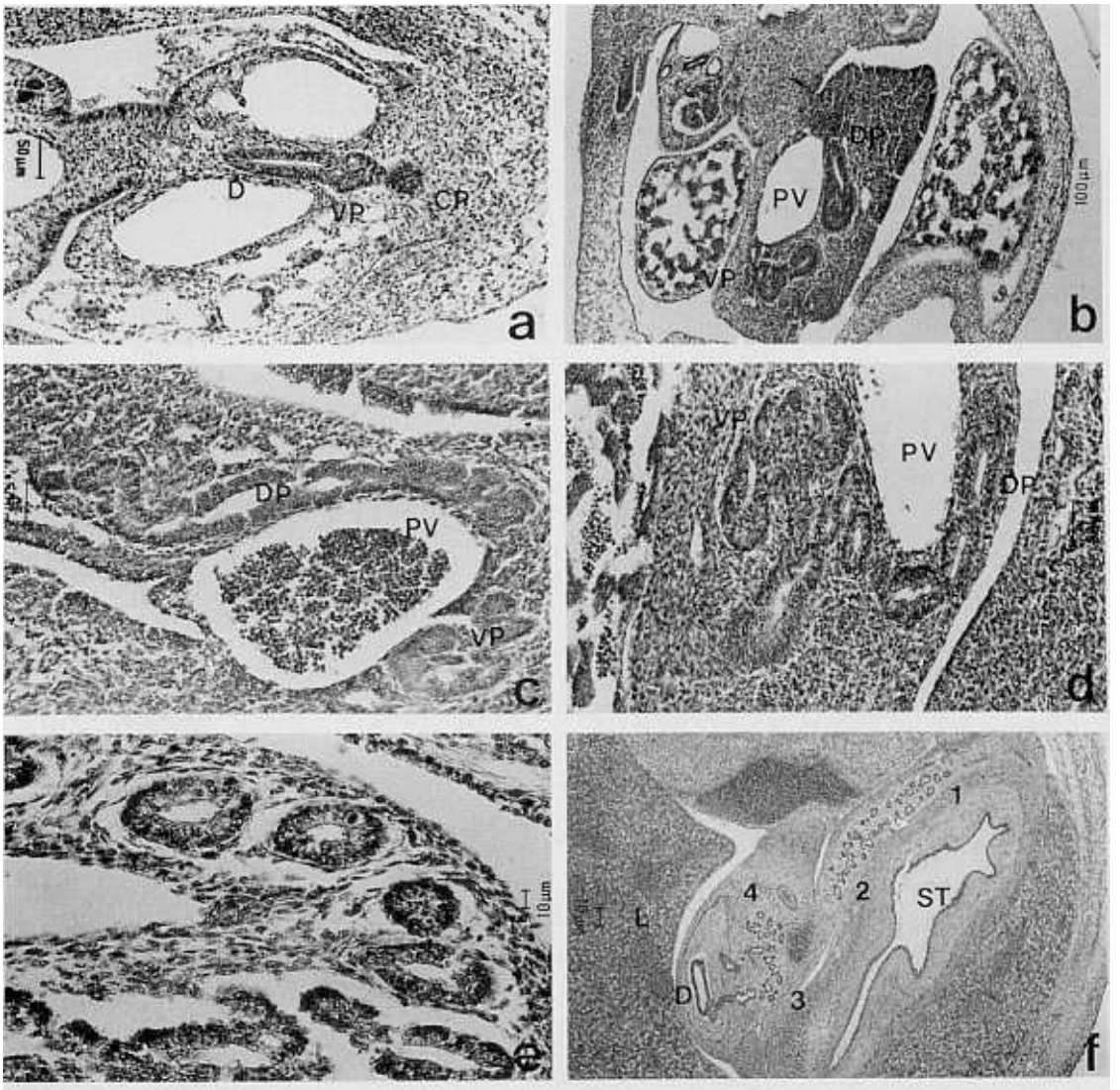

Fig. 2. Sections through the developing pancreas. a. Stage 13. In this case, the ventral pancreas (VP) is composed of an epithelial thickening and isolated spaces. b. Stage 15. Characteristically the ventral pancreas never extends beyond the ventral wall of the portal vein. c. Stage 16. The dorsal pancreas (DP) exhibits a tortuous appearance. d. Stage 17. The branching of the lumen of the dorsal panceas is apparant. e. Stage 18. The connective tissues are differentiating between the branches of the duct. f. Stage 20. The tail (1), body (2), head (3) and uncinate process (4) of the pancreas are discernable. CP; cystic primordium, D; duodenum, L; liver, PV; portal vein, ST; stomach

of the lumen of the dorsal pancreatic primordium with the duodenum is wide. In all sections, the lumen of the dorsal pancreas continues with the duodenum. The lumen and epithelium of the dorsal pancreas are slightly constricted at the junction with the duodenum.

Stage 13~14

The communication between the dorsal pancreas and the duodenum is constricted, so in some sections, the lumen of both is characteristically separated by epithelium.

In some cases, the ventral pancreas is observed as an epithelial thickening from the caudal wall of the proximal part of the hepatic diverticulum(Fig. 1b). In one case, the ventral pancreas contains some small spaces which have no connections with the adjacent lumen (Fig , 2a).

Stage 15

The dorsal pancreas forms an elongated mass extending almost to the attachment of the dorsal mesentery. In sections, some lumens are observed due to its branching. The ventral pancreas rotates about 90° clockwise when viewed from above (Fig. 1c). The ventral pancreas is less developed than the dorsal. Characteristically the ventral pancreas never extends beyond the ventral wall of the portal vein (Fig. 2b).

Stage 16

In sections, the dorsal pancreas exhibit a tortuous appearance (Fig. 2c). The ventral pancreas rotates about 180° clockwise (Fig. 1d), and extends to the middle of the right lateral wall of the portal vein, which is its final position. Two pancreatic primordia are related closely but not fused.

Stage 17

The dorsal and ventral pancreas come in contact at the ventral aspect of the portal vein (Fig. 1e). The branching of the lumen of the dorsal panceas is apparant (Fig. 2d).

Stage 18~19

The connective tissues are differentiating between the branches of the pancreatic duct (Fig. 2e).

Stage 20~23

The fused pancreas resembles the adult pancreas, and the tail, body, head and uncinate process are discernable in tissue sections (Fig. 2f). The ventral pancreatic duct becomes more prominent than the dorsal. As the connective tissues advelops, the pancreas becomes a more discrete structure. However, the acini and islets are not observed.

DISCUSSION

The human dorsal and ventral pancreas were described firstly by His (Odgers, 1930) and Phisalix (1888), respectively.

The dorsal pancreas appears in stage 12, and there is no disagreement on the time of its appearance. However, there are some disagreements on the time of its apperance and the mode of initial development of the ventral pancreas. The time of appearance is different according to various authors, that is, Bremer (1906), Gasser (1975) said it appeared in stage 13, Blechsmidt (1973) in stage 14, and Streeter (1948), O'rahilly *et al.* (1987) in stage 15. In this study, the ventral pancreas appeared in some embryos of stage 13, and the embryo of stage 14 shows early indication of the primordium. So, it can be said that the ventral pancreas appears in stage 13~14.

Considering the fact that the ventral pancreas rotates clockwise and fuses with the dorsal pancreas to form a definite pancreas showing the mechanisms which results in the formation of the annular pancreas, it is apparant that the mode of initial development of the ventral pancreas is important. At present, it is generally believed that the ventral pancreas originates from one primordium. However, some authors described it from two(Felix, 1892; Piper, 1900; Ingalls, 1907; Siwe, 1927; Odgers, 1930) or even multiple primordia(Delman, 1939). According to these authors, there are two primordia of which the right one is dominant the left one is rudiment. In this study, we observed a case in which a ventral pancreas seemed to be multiple. It is uncertain whether this was a normal variation, as stated by the above mentioned authors, during the normal development of the ventral pancreas or a maldeveloped state from the start.

This finding can be related with an annular pancreas. The exact mechanism of embryogenesis of this anomaly is poorly understood, but a number of explanations have been proposed as follows: 1) hypertrophy of both dorsal and ventral primordia (Tieken, 1899~1901), 2) fixation of the tip of the ventral primordium to the duodenal wall and fusion with the dorsal primordium (Lecco, 1910), 3) per-

sistence of a hypothetical left ventral bud (Baldwin, 1910), and 4) formation of the pancreatic potential in this area of the duodenum (Erimoglu, 1952). The incidence of this anomaly is very low (Regan *et al.* 1962).

However, there are relatively more reports which favor the multiple primordia of the ventral pancreas than its practical incidence, and there is no evidence that this phenomena is more frequently observed in abortus. So, it can be concluded that the formation of multiple primordia is normal process though not a constant feature and that the left primordia degenerates precociously. It is apparant from our results that the rotation of the ventral pancreas, starting in stage 15 and occupying its final position in stage 16, is a rapid process, and in fact it is impossible for it to be influenced by external forces during such a short period.

From our results of tissue observations, we can propose a characteristic feature of the developing pancreas in some stages, which can be used in assumming a probable developmental stage from tissue observation of a given embryo. In stage 13, the lumen of the dorsal pancreas is separated from the duodenum in some sections, which is not observed in stage 12. In stage 15, the ventral pancreas rotates about 90° and never exends beyond the ventral wall of the portal vein. In stage 16, it occupies its final position, but does not fuse with the dorsal pancreas.

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