4 Pathology of the Pancreas

G. Klöppel and E. Schlüter

CONTENTS
4.1 Congenital Anomalies 69
4.1.1 Agenesis and Hypoplasia 69
4.1.2 Annular Pancreas 69
4.1.3 Pancreas Divisum 70
4.1.4 Abnormalities of the Pancreaticobiliary Junction 70
4.1.5 Ectopic (Heterotopic) Pancreas 70
4.1.6 Congenital Cysts and Dysplastic Changes 70
4.2 Vascular and Traumatic Lesions 71
4.2.1 Vascular Lesions 71
4.2.2 Traumata 71
4.3 Hereditary Diseases of the Pancreas 72
4.3.1 Cystic Fibrosis 72
4.3.2 Lipomatous Atrophy (Shwachman-Diamond Syndrome) 72
4.3.3 Hemochromatosis 73
4.3.4 Hereditary Pancreatitis 73
4.4 Pancreatitis 73
4.4.1 Classification 73
4.4.2 Acute Pancreatitis 73
4.4.3 Chronic Pancreatitis 77
4.4.4 Special Types of Chronic Pancreatitis 80
4.4.5 Pancreatic Lobular Fibrosis in Elderly Persons 81
4.4.6 Pancreatic Pathology in Diabetes Mellitus 81
4.5 Exocrine Pancreatic Tumors 82
4.6 Intraductal Papillary-Mucinous Tumor 83
4.7 Endocrine Tumors 91
4.7.1 General Considerations 91
4.7.2 Epidemiology 91
4.7.3 Macroscopy 92
4.7.4 Microscopy 92
4.7.5 Criteria of Malignancy 92
4.7.6 Individual Types of Endocrine Tumors 93
4.7.7 Multiple Endocrine Neoplasia 94

4.1 Congenital Anomalies

4.1.1 Agenesis and Hypoplasia

Complete absence of the pancreas is extremely rare and is usually associated with other malformations such as cardiac defects, diaphragmatic hernia, or gallbladder aplasia (Wöckel and Scheibner 1977). Clinically, these patients present with diabetes mellitus, malabsorption, and severe fetal growth retardation. In partial agenesis, i.e., hypoplasia, which is likewise rare, either the body and tail or the head of the pancreas is absent, suggesting that the dorsal or the ventral anlage has failed to develop. Recently, it has been suggested that a mutation of the developmental protein IPF1 may be responsible for pancreatic agenesis, since a patient with complete absence of the pancreas was found to be homozygous for a point deletion in the IPF1 gene (Stoffers et al. 1997).

4.1.2 Annular Pancreas

In annular pancreas, pancreatic tissue encircles and sometimes obstructs the descending part of the duodenum (Fig. 4.1). A total of 10% of the cases of duodenal stenosis in childhood are due to annular pancreas. The annulus represents the ventral part of the duodenal pancreas, which has remained fixed to the duodenum (MacLean 1979; Starck 1965) as a result of retardation of rotation. A distinction is made between an extramural and an intramural type. In the extramural type, the annulus is drained by ducts running around the duodenum to join the main pancreatic duct. In the intramural type, pancreatic tissue is intermingled with muscle fibers in the duodenal wall and small ducts drain directly into the duodenum.
Fig. 4.1. Annular pancreas in a newborn: the duodenum is encircled by pancreatic tissue

4.1.3 Pancreas Divisum

Pancreas divisum is caused by an insufficient or incomplete fusion of the ventral and dorsal primordia of the pancreas. As a result, the dorsal duct of Santorini drains the majority of the gland (dorsal head, body, and tail), passing through the minor papilla, while the ventral duct of Wirsung drains the smaller ventral remnant. In unselected autopsy specimens, the incidence of pancreas divisum ranges from 4% to 10% (DELHAYE et al. 1985). In children, this malformation is usually silent. Adults may present with pancreatitis in the dorsal pancreas, probably because of intermittent relative obstruction at the minor papilla (GREGG 1977).

4.1.4 Abnormalities of the Pancreaticobiliary Junction

Marked variations in the anatomy of the ducts are seen at the pancreaticobiliary junction within the ampulla of Vater, with a complete separation of the orifices of the common bile duct and the major pancreatic duct at one end of the spectrum, and a long common channel at the other end.

4.1.5 Ectopic (Heterotopic) Pancreas

Ectopic pancreatic tissue has been noted in up to 15% of autopsy specimens (Feldman and Weinberg 1952). Most commonly, it is found in the stomach (25%-30%) and the duodenum (30%) (Fig. 4.2), followed by the jejunum, ileum, and Meckel's diverticulum (DOLAN et al. 1974). Uncommon localizations are the gallbladder (HORANYI and FÜST 1963), liver (GADRAT et al. 1965), mesentery (KUBOTA 1955), spleen, and omentum. In trisomy 18, ectopic pancreatic tissue seems to be a frequent change (WARKANY et al. 1966).

In the bowel, ectopic pancreas presents as a small submucosal lump with a granular or ulcerated surface. Its diameter varies from some millimeters to several centimeters (2–4 cm). In more than 50% of cases it is located in the submucosa, in 25% in the muscular layer, and in 10% in the subserosal region (ELFRING and HÄSTBACKA 1965; Nicolesco and Velciu 1968). In at least one third of patients, the ectopic pancreas shows normal pancreatic tissue, while in the other cases it consists mainly of ducts intermingled with endocrine elements. Usually, one duct connects to the overlying mucosa through a nipple-like projection. Ectopic pancreas usually remains asymptomatic, but occasionally it may result in stenosis, ulceration, bleeding, or invagination (JANSEN and ROTHEMUND 1965; MACKINNON and NASH 1957).

Pancreatic tissue with a normal exocrine and endocrine composition may be noted especially in mediastinal teratomas (HONICKY and de PAPP 1973; SCHLUMBERGER 1946; SUDA et al. 1984).

4.1.6 Congenital Cysts and Dysplastic Changes

Congenital cysts of the pancreas can be either single or multiple. Both types are uncommon, but, unlike solitary cysts (Fig. 4.3a), multiple cysts are usually associated with other congenital anomalies such as von Hippel-Lindau disease (CHENG et al. 1997; FISHMAN and BARTHOLOMEW 1979; NICOLESCO and VELCIU 1968; SEIFERT 1984) (Fig. 4.3b), or polycystic kidney disease. In these conditions, the cysts are of