Agenesis of the Dorsal Pancreas in an Adult Diabetic Presenting with Duodenal Ileus

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THE EMBRYOGENESIS of the human pancreas is more complicated than that of most other tissues; nevertheless, congenital anomalies are uncommon. The most frequent development abnormality is ectopia,[2] followed by annular pancreas.[16] Other defects have been described occasionally.[3, 11, 12] Absence of the gland has been reported only in stillborn fetuses with multiple congenital malformations. One case of probable absence of the ventral pancreatic bud has been described.[20] Agenesis of the dorsal pancreas has been reported in two definite[6, 10] and two possible but poorly documented instances.[1, 15] Other cases[10] are probably partial congenital defects rather than failure of development of an entire anlage.

An instance of congenital atresia of the neck, body, tail and a major portion of the head of the pancreas was encountered recently in an adult diabetic patient who was operated upon for duodenal obstruction. The uncinate process was also absent. This is the *first reported case* in the English-language literature of atresia of the dorsal anlage of the pancreas discovered in a living patient.

Case Report

A 26-year-old man was admitted to Detroit Receiving Hospital on 3/4/64, complaining of periodic epigastric pain accompanied by nausea and vomiting. The pain was severe, came on approximately four times a day, mostly after meals, and was partially relieved by vomiting. Symptoms began about 18 months before and were associated with a loss of 20 pounds, for a present weight of 103 pounds. The vomitus was copious and bile-stained, and contained particles of food. He had no other gastrointestinal symptoms. He had been hospitalized seven times during the previous year for these complaints.

History. When he was 15 years old, diabetes mellitus was first diagnosed. He required 15 to 20 units of NPH insulin daily until 1 year before the present admission when his requirement rapidly increased to 80 units per day. Despite the increased insulin, he had glycosuria frequently and chronic skin ulcerations. Examinations and hospitalization failed to disclose the cause of epigastric pain and vomiting and it was assumed to be functional. After 6 weeks in a psychiatric hospital, he was diagnosed as immature personality with excessive preoccupation with physical symptoms, but no gross psychologic abnormalities. He had chronic asymptomatic pyuria following an acute urinary infection in childhood. During one recent hospitalization, evidence of bilateral, noncalcific, ureteropelvic stenosis without blunting of the calyces was found. Gastrointestinal x-rays showed duodenal ileus but this was not considered responsible for his symptoms. His mother and his maternal aunt had mild diabetes which began in middle age. One sister does not have diabetes and there is no history of diabetes on the paternal side.

Physical Examination. The patient was a poorly nourished, anxious man. Blood pressure was 125/100 mm. Hg, pulse 108/min., respirations 20/min., temperature 36.7° C. There was prominent parietal bossing of the skull and microaneurysmal dilatation of the retinal arteries. The abdomen was not distended and there were no palpable masses, but there was moderate tenderness over the epigastrium. There were numerous ulcerated areas on the lower legs and toes which were healing poorly but were not grossly infected. He had good pedal pulses. On neurologic examination there was some diminution of sensation over the lower legs and feet. The remainder of the physical examination was negative.

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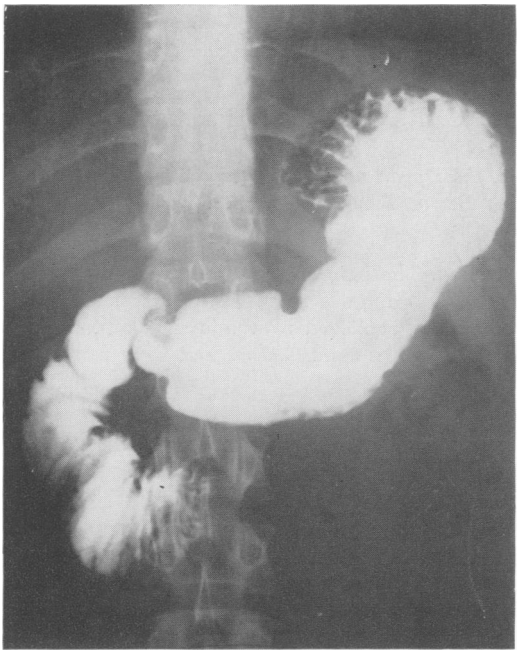

FIG. 1. Upper gastrointestinal x-ray demonstrating duodenomesenteric ileus.

Laboratory Studies. Hemoglobin 12.2 Gm./100 ml., white blood cell count 28,400/mm.^{3} with moderate neutrophilia; urine: trace of protein, 4–6 red blood cells and 24–26 white blood cells per low-power field in the uncentrifuged specimen, a trace of sugar. Blood glucose was 288 mg./100 ml. and the serum acetone was negative. CO_2 content was 29.9 and 31.2 mEq./L. on two occasions. Serum amylase and lipase levels were not elevated. Blood urea nitrogen was 16 mg./100 ml.; K 4.5 mEq./L., Cl 99 mEq./L. and Ca 4.7 mEq./L. and serum phosphate was 3.4 mg./100 ml. Overnight gastric acid secretion totaled 36 and 46 mEq./L. on two occasions. Gastrointestinal x-rays showed a dilated duodenum and obstruction in the region of the superior mesenteric artery (Fig. 1). This was confirmed by cinefluorography which also revealed abnormal duodenal retroperistalisis, without mucosal deformity.

Operation. The patient was operated upon with the diagnosis of duodenal ileus. Stomach and duodenal bulb appeared normal. The second and third portions of the duodenum were moderately dilated. On exposing the lesser omental bursa, the portal vein was immediately visible and there was no pancreas in front, behind or to the left of it. The only remnant of pancreas was a thin segment, approximately $2 \times 2\frac{1}{2} \times 1$ cm., within the duodenal sweep. The uncinate process was absent and the superior mesenteric artery passed directly, without interposition, across the transverse portion of the duodenum. The fourth portion of the duodenum appeared slightly diminished in caliber, and the change in size was at the level of the superior mesenteric vessels. There was no pancreatic tissue along the splenic artery and vein (Fig. 2). The spleen was brought onto the abdominal wall and removed. A side-to-side duodenojejunostomy was performed. The duodenum, bile ducts gallbladder, spleen and stomach, and residual pancreas and blood vessels were normal. The only abnormality other than slight duodenal dilatation was absence of the neck, body, tail uncinate process, and much of the head of the pancreas.

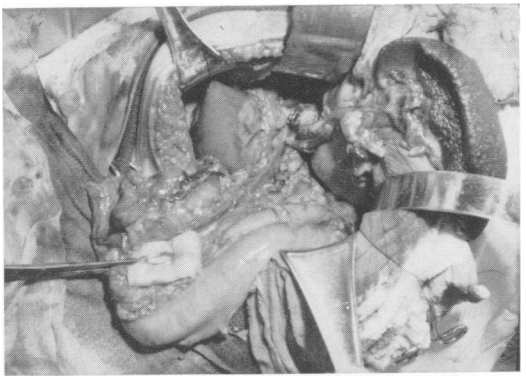

FIG. 2A. Photograph at operation, illustrating the pancreatic remnant and adjacent structures.

Postoperatively, the patient improved. He continued to have occasional spasmodic abdominal pain and vomited four or five times after operation. His insulin requirement diminished to 20 units per day and urine remained free of sugar. Gastrointestinal x-rays showed immediate empting of the duodenum into the jejunal loop without obstruction. Cinefluorography confirmed this finding but demonstrated delay in gastric emptying consistent with that seen in diabetic neuropathy of the stomach. Subsequent findings of neurogenic bladder dysfunction plus peripheral neuropathy supported the diagnosis of visceral diabetic neuropathy. It is believed that abdominal pain was a result of diabetic psuedotabetic crises. Despite the symptoms, the patient gained 30 pounds in the 3 months following operation and considered himself improved. Postoperative radioactive triolein absorption was low, but radioactive oleic acid uptake was normal, indicating an element of pancreatic exocrine insufficiency without mucosal block.

The patient was last seen on 12/9/64. He weighed 138 pounds and felt well. He had no abdominal complaints. Diabetes was well controlled with 20 units of NPH insulin daily and his leg ulcers had healed. He had, however, developed mild nocturnal fecal incontinence, presumably due to diabetic neuropathy.

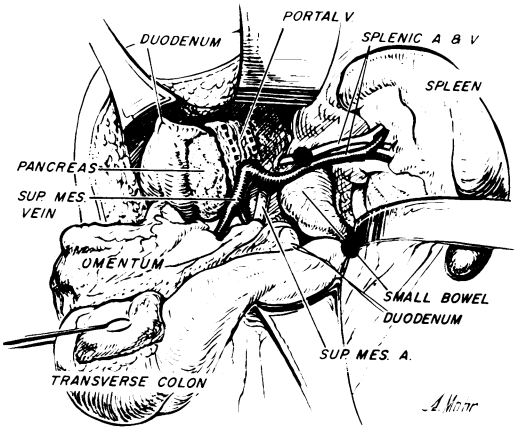

FIG. 2B. Artist's drawing to identify operative findings (the portal vein is located behind some loose areolar tissue to the left of the pancreas).

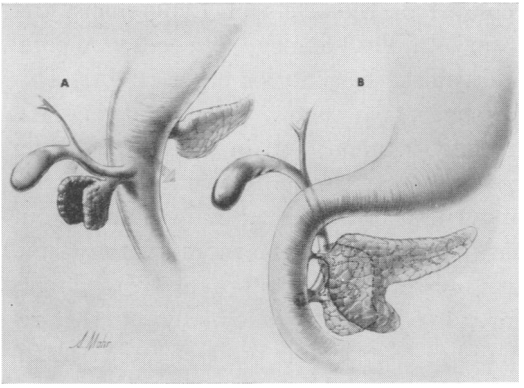

FIG. 3. Composite drawing indicating the early development of the pancreas. A. Initial rotation. B. Final position after ducts have fused.

Discussion

The first impression at operation was that the portal and superior mesenteric veins were displaced to a prepancreatic location, a rare phenomenon [9, 17] which may occur in association with situs inversus abdominus.[9] The only abnormality, however, was absence of the neck, body, tail and uncinate process of the pancreas. In addition the head was thinner than usual. This abnormality most likely resulted from congenital atresia since there was no evidence of inflammation, degeneration or fatty replacement of the gland.

Embryogenesis. The pancreas arises from two anlagen, emerging from opposite sides of the duodenal primordium. The paired ventral buds arise in conjunction with the hepatic diverticulum (Fig. 3A). As the gut elongates the buds rotate 90° from the midline to the right. The ventral bud rotates an additional 90°, bringing it and the bile duct behind the duodenum where the two portions fuse around the common duct. The superior duct of the small ventral bud then joins that of the larger dorsal anlage and most of the gland as the duct of Wirsung (Fig. 3B). Thus the ventral bud forms only a portion of the head of the pancreas, the dorsal gives rise to the remainder of the gland. It appears that our case is a rare instance of congenital absence of the dorsal bud of the pancreas.

Most studies of the mature ductal system, and embryologic data, suggest that the uncinate process arises from the ventral bud.[8] Gohn and Roman,[7] however, suggested that it might arise in part from the dorsal anlage. Russu and Vaida [18] indicate that both anlagen fuse and then form the uncinate process. Absence of the uncinate process indicates that this portion of the gland may arise entirely from the dorsal pancreatic anlage. That the uncinate process was absent in this patient may well have contributed to duodenal ileus by allowing the superior mesenteric vessels to fall across the third part of the duodenum. The contribution of the ventral bud to the head of the pancreas, although variable, is now considered to be less than was previously thought. The ventral anlage comes to lie mostly behind the dorsal bud but may extend above or below, behind the common bile duct which lies between the two anlagen (Fig. 3B). At times the ventral bud forms only a small portion of the posterior central region of the head in the vicinity of the ampulla of Vater.

The occurrence of *diabetes mellitus* in four of five [10] patients with pancreatic agenesis who survived until puberty also seems significant. It has been assumed that diabetes does not result from near-complete

removal of the islets of Langerhans, but from atrophy, damage to cells, humoral antagonists, heredity or other factors. This has been true following subtotal pancreatectomy in man [4] and in dogs after 90 per cent pancreatectomy. In two reported cases of agenesis of the dorsal bud [6, 10] and in our case, three fourths or more of the gland was missing. The history in two patients surviving beyond infancy suggests that remaining islets could produce sufficient insulin during childhood but not for the demands of puberty or of infection.

We are unable to account for improvement of the diabetes in our patient, especially since there was no evidence of pancreatitis. Obstruction of the duodenum may, through sphincter spasm or reflux, result in mild and reversible pancreatitis in afferent loop obstruction,[5, 13, 19] and in experimental pancreatitis produced by closed-loop duodenal obstruction.[14]

Summary

A 26-year-old diabetic man presented with epigastric pain, vomiting and weight loss for 18 months which appeared to be due to duodenomesenteric ileus. At operation the neck, body, uncinate process, tail and much of the head of the pancreas were absent. This agenesis of the dorsal pancreas is the first reported of a living patient in the English literature. Absence of the uncinate process suggests that this portion of the gland may arise from the dorsal bud alone rather than the ventral bud or a combination of ventral and dorsal analagen as others have suggested. The superior mesenteric artery lay across the duodenum without pancreatic interposition, and this anatomic abnormality was probably the cause of obstructive symptoms. Diabetes developed at the age of 15 years, perhaps because the pancreatic remnant derived only from the ventral bud was insufficient for long-term insulin production.

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