

Pancreatic Agenesis with Congenital Diaphragmatic Hernia and Congenital Heart Disease: A Case Report

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Abstract

Keywords

- ▶ pancreatic agenesis
- ▶ congenital diaphragmatic hernia
- ▶ congenital heart disease
- ▶ therapy

Pancreatic agenesis is a rare disease that causes neonatal diabetes mellitus and exocrine pancreatic insufficiency. We report the case of a very low birth weight infant with congenital diaphragmatic hernia, and congenital heart disease (ventricular septal defect and patent ductus arteriosus). Failure to gain weight, despite well-managed respiratory and heart failure, was improved by infusion of subcutaneous insulin, administration of pancreatic enzyme, and nutrition of medium-chain-triglyceride -enriched formula. This is the first case of pancreatic agenesis with both malformations where the patient is discharged from the hospital. Early diagnosis and adequate treatments to compensate pancreatic function may prevent mortality and improve growth.

Pancreatic agenesis is a rare disease that causes endocrine and exocrine insufficiency. Its main features are neonatal diabetes mellitus and malabsorption of lipids and proteins. In addition, many kinds of malformations in other organs have been reported. We describe the case of an infant with severe additional malformation, congenital diaphragmatic hernia, and large ventricular septal defect.

Case Report

A female infant was born at 37-week gestation to a 45-year-old gravida 1, para 1 mother via cesarean section because of fetal growth restriction. Birth weight was 1,353 g (less than third percentile), body length was 39.5 cm (less than third percentile), and head circumference was 30 cm (less than third percentile). The placenta was examined, but no abnormality of placenta without relatively small size, 15.5 × 15 × 1.5 cm, and no abnormality of umbilical cord were detected. Apgar scores were 8 and 8 (at 1 and 5 minute). She was admitted to our neonatal intensive care unit because of threatened respiratory distress. Chest X-ray showed left

diaphragmatic hernia and echocardiography showed large (4-mm diameter) ventricular septal defect (VSD) that was located in the anterior and superior portion of the septum, called doubly committed subarterial defect, type 1 defect in Kirklin classification. She received mechanical ventilation through endotracheal tube, and surgical correction of the hernia was undertaken on day 2. At surgery, the stomach, spleen, and small intestines were reduced from the left chest cavity. After the operation, respiratory failure and cyanosis were improved. Then, she underwent pulmonary artery banding and ductus arteriosus ligation for heart failure because of VSD and patent ductus arteriosus on day 24. Pulmonary blood flow was well managed and heart failure was improved after the operation.

However, she had no weight gain despite improving respiratory and heart failure. Moreover, blood sugar was unstable and elevated as feeding increased. Blood tests on day 58 revealed hyperglycemia (19.4 mmol/L), low levels of insulin (< 1 μU/mL), and C-peptide (< 0.03 ng/mL). Ketonuria was not presented. Although subcutaneous insulin therapy was started and blood glucose levels were

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Fig. 1 Enhanced computed tomographic scans of the patient's abdomen. Axial section (A), coronal section (B), and sagittal section (C) show no pancreatic parenchyma.

decreased, poor weight gain was continued, and she presented a protuberant abdomen and shiny yellow greasy stools. In addition, tests revealed large amount of fat droplets in her stools, low levels of plasma pancreatic enzyme (trypsin < 38 ng/mL, pancreatic phospholipase A2 < 100 ng/dL, and pancreatic amylase 2 IU/L), and bleeding tendency (prothrombin time international normalized ration 2.12, partial thromboplastin time 67.1). Both endocrine and exocrine pancreatic insufficiencies were present. A magnetic resonance image of her abdomen showed absence of pancreas (→Fig. 1). The diagnosis of pancreatic agenesis was made. In addition to subcutaneous insulin therapy, administration of pancreatic enzymes, medium-chain-triglyceride (MCT)-enriched formula, and fat-soluble vitamins subsequently induced weight gain, and bleeding tendency was improved. She was discharged at the age of 9 months. At the age of 18 months, she had psychomotor retardation. Her developmental quotient score was 68, assessed by the Kyoto Scale of Psychological Development.

Discussion

Pancreatic agenesis is a rare disease and its incidence is unclear. Endocrine insufficiency is secretion defects of insulin, and the patients present permanent neonatal diabetes mellitus (PNDM). Exocrine insufficiency is secretion defects of digestive enzymes for lipids and proteins, and the patients' present malabsorption for them.

One of the most frequent symptoms is intrauterine growth restriction (IUGR) because insulin and C-peptide are major intrauterine growth factor.¹ Baumeister et al reported that 93% of patients presented IUGR.² In our case, severe IUGR existed and common causes for IUGR (e.g., congenital infection, abnormality of placenta, and umbilical cord) were all negative.

It is difficult to notice the absence of pancreas in neonatal period because hyperglycemia and IUGR can be caused by PNDM alone. The key symptom that suggests the pancreatic agenesis was lipid-rich stool. This symptom is caused by defect of pancreatic enzymes.

Pancreatic agenesis sometimes accompanies malformations in other organs such as biliary system, heart, and

cerebellum. Congenital heart diseases have been reported at relatively high frequency.²⁻⁵ Baumeister et al demonstrated that 36% of the infants with pancreatic agenesis have heart malformation. On contrary, congenital diaphragmatic hernia is rare combination to pancreatic agenesis, and to our best knowledge, two cases have been reported.^{6,7} Moreover, only one case has reported diaphragmatic hernia and heart diseases,⁶ who died at 24 hours after birth. Therefore, our patient is the first case of pancreas agenesis with both malformations who was successfully discharged.

The etiology for most instances of pancreatic agenesis is unknown. Mutations in *PDX1* and *PTF1A* were reported in some patient's families.^{8,9} Recently, *GATA6* mutations have been reported to the patients with pancreatic agenesis and heart malformation.^{10,11} There was no family history of diabetes mellitus, diaphragmatic hernia, or congenital heart defects in our case.

Pancreatic agenesis has been reported as the disease with high mortality, and almost all patients present extrauterine growth restriction because of lack of protein anabolic effect of insulin, malabsorption of lipid, and hyperglycemia. Our patient could gain weight by infusion of subcutaneous insulin, administration of pancreatic enzyme, and nutrition of MCT formula, and could discharge. Early diagnosis and adequate treatments to compensate pancreatic function may prevent mortality and improve growth.

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