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## Case Report

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### Neonatal Diabetes Mellitus Due to Pancreatic Agenesis

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Neonatal diabetes mellitus, which is defined as hyperglycemia presenting within the first six weeks of life, is a rare disorder. It may result in transient or permanent disease. Pancreatic agenesis is a rare cause of neonatal diabetes.

We report a neonate who was small for gestational age and presented with diabetes mellitus and signs of malabsorption because of pancreatic agenesis.

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#### Introduction

A rare cause of hyperglycemia in early infancy is known as neonatal diabetes mellitus (DM), which presents during the initial six weeks of life.<sup>1,2</sup>

This condition occurs most often in those neonates who are small for gestational age and is characterized by hyperglycemia and pronounced glycosuria. It results in dehydration and sometimes metabolic acidosis, but minimal or no ketonemia or ketonuria.<sup>1-3</sup>

Neonatal diabetes can be transient or permanent. The former is mainly because of three genetic abnormalities on chromosome 6 and is spontaneously recovered within three to six months. The latter may result from a decrease in insulin production or resistance to its action.<sup>1-3</sup>

Pancreatic agenesis is a rare cause of neonatal DM, so there is not sufficient information to cover its clinical features. A survey, reviewing the literature on such a disorder, revealed that there were only 14 patients reported until March 2005.<sup>4-6</sup>

#### Case Report

A 10-day-old male neonate, the product of term pregnancy from consanguineous parents, was referred to the Neonatal Intensive Care Unit (NICU) of Ali Asghar Hospital, affiliated to Iran University of Medical Sciences, Tehran, Iran, because of lethargy and poor feeding. There was a history of oligohydramnios and intrauterine growth retardation (IUGR) in the prenatal period. He also had a history of passing frequent greasy stools since the sixth day of birth.

On physical examination, severe symmetrical IUGR (birth weight=1800 g, head circumference =30 cm, and length=41 cm), signs of dehydration, jaundice, and decreased neonatal reflexes were noted.

Laboratory evaluations revealed a severe hyperglycemia (blood sugar >400 mg/dL), and venous blood gas analysis showed a pH = 7.41, HCO<sub>3</sub> = 23 mEq/L, and PCO<sub>2</sub> = 35 mmHg.

Urinalysis showed a specific gravity of 1.023 and 3+ glucose, but no ketones.

Serum ketone was negative, serum insulin level was 0.7 mIU/mL (normal range: 2.1 – 22 mIU/mL), concomitant blood sugar was 470 mg/dL, and C-peptide was 0.06 ng/mL (normal range: 0.8 to 4.2 ng/mL).

The patient was treated for sepsis. Antibiotics and other supportive measures were given. After proper hydration, hyperglycemia was controlled by neutral protamine Hagedorn (NPH) insulin. He

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was very responsive to insulin and hyperglycemia was controlled with low doses of insulin (about 0.2 unit /kg/day NPH).

During the hospital course, he gradually developed signs of malabsorption including diarrhea, edema, abdominal distension, and hypoalbuminemia. Sudan III staining of stool showed more than 100 fat droplets/high power field (HPF), and stool pH was six.

Imaging study of the abdomen (ultrasonography and computed tomography with intravenous and oral contrast) showed no pancreatic tissue suggesting pancreatic aplasia.

After replacing the pancreatic enzymes, stool fat was reduced to less than 40 droplets/HPF, and edema and hypoalbuminemia improved gradually.

At the age of four months, his weight was 3900 g and his length was 52 cm. Although he had grown after pancreatic enzyme replacement therapy, the growth indices were still below that of the 3<sup>rd</sup> percentile.

## Discussion

The neonate who is reported here had clinical signs of exocrine and endocrine pancreatic insufficiency.

Pancreatic aplasia due to mutation in insulin promoter factor-1 (IPF-1) gene may be associated with other abnormalities such as cerebellar hypoplasia or absence of the gallbladder.<sup>7,8</sup> Investigation for presence of other abnormalities was negative in this case.

Two other conditions that can cause DM in early infancy, associated with signs of malabsorption, are the immunodysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome and the Wolcott-Rallison syndrome.<sup>3,6</sup>

In IPEX syndrome, the major clinical signs are association of a severe enteropathy with insulin-dependent diabetes mellitus (IDDM) along with eczema, hematologic abnormalities, and eventually other endocrinopathies. DM in this syndrome is due to insulin resistance. Our patient was not a case of IPEX syndrome because he was very sensitive to insulin, had low levels of insulin and C-peptide, and did not have any other clinical or paraclinical findings compatible with this syndrome.<sup>6</sup>

Wolcott-Rallison syndrome is characterized by the appearance of permanent DM within three months of life. It is also associated with multiple epiphyseal or spondyloepiphyseal dysplasia, cardiac anomaly, hepatic impairment, and ectodermal dysplasia.<sup>3</sup> Since there were no signs of the above-mentioned abnormalities in our patient, the presence of Wolcott-Rallison syndrome was not taken into account either.

## Conclusion

Pancreatic agenesis is a clinical entity characterized by severe IUGR, early onset permanent neonatal DM without ketoacidosis, and signs of malabsorption due to pancreatic exocrine dysfunction. Because of its high mortality rate, awareness of pancreatic agenesis is important for optimal management of growth-restricted neonates with DM and signs of exocrine pancreatic dysfunction.

## References

- 1 Metz C, Cavé H, Bertrand AM, Deffert C, Gueguen-Giroux B, Czernichow P, et al. Neonatal diabetes mellitus: chromosomal analysis in transient and permanent cases. *J Pediatr*. 2002; **141**: 483 – 492.
- 2 Wollew SL, Saranga S. Neonatal diabetes mellitus: a rare but important diagnosis in the critically ill infant. *Eur J Med*. 2006; **13**: 349 – 351.
- 3 Thornton CM, Carson DJ, Stewart FJ. Autopsy findings in the Wolcott-Rallison syndrome. *Pediatr Pathol Lab Med*. 1997; **17**: 487 – 496.
- 4 Baumeister FA, Engelsberger I, Schulze A. Pancreatic agenesis as cause for neonatal diabetes mellitus. *Klin Padiatr*. 2005; **217**: 76 – 81.
- 5 Ashraf A, Abdullatif H, Hardin W, Moates JM. Unusual case of neonatal diabetes mellitus due to congenital pancreatic agenesis. *Pediatr Diabetes*. 2005; **6**: 239 – 243.
- 6 Wildin RS, Smyk-Pearson S, Filipovich AH. Clinical and molecular features of the immunodysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome. *J Med Genet*. 2002; **39**: 537 – 545.
- 7 Stoffers DA, Stanojevic V, Habener JF. Insulin promoter factor-1 gene mutation linked to early onset type 2 diabetes mellitus directs expression of a dominant negative isoprotein. *J Clin Invest*. 1998; **102**: 232 – 241.
- 8 Stoffers DA, Zinkin NT, Stanojevic V, Clarke WL, Habener JF. Pancreatic agenesis attributable to a single nucleotide deletion in the human IPF-1 gene coding sequences. *Nat Genet*. 1997; **15**: 106 – 110.