

CONGENITAL ANOMALIES AMONG INFANTS OF DIABETIC MOTHERS

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SUMMARY

Congenital anomalies are the most common cause of perinatal mortality in infants of diabetic mothers. Late fetal loss and metabolic abnormalities also feature in increased perinatal mortality due to maternal diabetes. Maternal hyperglycemia during early gestation is associated with an increased frequency of structural defects.

Four infants who were admitted to the Neonatal Intensive Care Unit (NICU) of our institution are presented here in a discussion of rare congenital malformations in infants of diabetic mothers.

Key Words: *Infant Of Diabetic Mother, Congenital Malformation, Perinatal Mortality.*

ÖZET

Diabetik Anne Bebeklerinde Konjenital Anomaliler

G n m zde bir ok merkezde izlenen diabetik anne bebeklerinde perinatal mortalitenin en sk nedeni konjenital anomaliler, ge fetal kayplar ve metabolik sorunlard r. Erken gestasyon haftalar ndaki maternal hiperglisemi konjenital anomali s kl n artt rmaktadır.

Diabetik anne bebeklerinde gr len nadir konjenital anomalileri tart mak amac yla Yenido an Yo unbak m nitesi nde izlenen 4 olgu sunulmaktadır.

Anahtar Kelimeler: *Diabetik Anne Bebe i, Konjenital Malformasyon, Perinatal Mortalite*

The incidence of major congenital anomalies is two to five times greater in infants of diabetic mothers than in other infants. Poor glycemic control in the first trimester during organogenesis is thought to be the major reason for congenital malformations (1).

The most frequently seen types of malformations in infants of diabetic mothers involve the cardiovascular, skeletal, central nervous, gastrointestinal and genitourinary systems, with cardiac malformations being the most common (2).

Four infants who were admitted to the Neonatal Intensive Care Unit (NICU) of our institution are presented here in a discussion of rare congenital malformations in infants of diabetic mother.

CASE 1

A 4.0-kg male infant born at 36 weeks to a gestational diabetic mother was admitted to the NICU at the third postnatal day because of poor sucking and jaundice. Physical examination revealed dehydration, jaundice and macrosomia. The infant had hypoglycemia, indirect hyperbilirubinemia, renal failure (prerenal), hyponatremia and metabolic acidosis. Abdominal Doppler ultrasonography revealed situs inversus, and an adrenal hemorrhage was performed. The diagnosis of situs inversus totalis was confirmed with the finding of dextrocardia. The infant was treated for renal failure, hyperbilirubinemia and electrolyte imbalance and was discharged on the twelfth postnatal day.

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CASE 2

A 3.6-kg female infant born at 38 weeks to a gestational diabetic mother was admitted to the NICU on the second postnatal day because of vomiting. Physical examinations revealed jaundice, omfalitis and a first-degree systolic murmur at the second left intercostal space. Hypoglycemia and indirect hyperbilirubinemia were documented. Staph.aureus was obtained from umbilical cultures. A chest X-ray showed decreased pulmonary vascularity and a cardiac silhouette similar to a Coues en sabot. Although the electrocardiogram was normal, two-dimensional echocardiography established the diagnosis of pulmonary atresia, ventricular septal defect (VSD), patent ductus arteriosus (PDA) and the presence of main aortopulmonary collaterals (MAPCA). The patient was treated for indirect hyperbilirubinemia and omfalitis and was transferred to the Cardiology Department for follow-up.

CASE 3

A 2.5-kg male infant with proximal esophageal atresia and an atrioventricular channel defect was born to a diabetic mother at the 32nd week of gestation due to premature rupture of membranes. The mother had been receiving treatment for insulin-dependent diabetes mellitus for the previous 12 years. The infant had low APGAR scores and had been resuscitated at birth. Physical examination revealed hypotonia, tachypnea, cyanosis and a 2/6° systolic murmur. The patient was diagnosed with respiratory distress syndrome and congenital heart disease. A surfactant was administered, and the infant was ventilated mechanically. Gastric distension was observed at the postnatal 12th hour, and an abdominal X-ray revealed the presence of free air in the abdomen. The inability to introduce a nasogastric tube led to a suspicion of esophageal atresia. An emergency operation was performed, and gastric perforation, proximal esophageal atresia was diagnosed. A cervical esophageal cutanostomy and funduplication were performed. Echocardiography revealed an atrioventricular channel defect. The infant died at 12 days with symptoms of cardiogenic shock.

CASE 4

A 2.9-kg male infant was born by C/S at the 35th week of gestation to a 30-year-old gestational diabetic mother. The infant was large for his gestational age, and he was admitted to NICU following resuscitation. On physical examination, congenital anomalies including cleft palate, microphthalmia and glossoptosis and an obstructed airway were observed. The patient was intubated and administered continuous positive airway pressure. Echocardiography revealed intraventricular septal hypertrophy (IHSS). The patient died of airway obstruction on the second day of life.

DISCUSSION

Data from clinical series are consistent with the hypothesis that maternal hyperglycemia during early gestation is associated with an increased rate of structural defects in infants. Hyperglycemia, hypoglycemia and hyperketonemia during organogenesis have been shown to induce an increased incidence of major structural defects in animal models. Most human studies have used first-trimester glycosylated hemoglobin levels as an indicator of glycemic control during organogenesis. The incidence of major structural anomalies has been shown to increase with increased levels. Various other factors including somatomedin inhibitors, yolk sac failure, reduced intracellular myoinositol, arachidonic acid deficiency and maternal vasculopathy have been commonly associated with congenital anomalies in infants of diabetic mothers in experimental models (1-3).

When compared to the general population, no statistically significant increase in congenital malformations have been found among infants of mothers with gestational diabetes mellitus who do not require insulin during pregnancy (4,5). However, recent investigations indicate that gestational diabetes may be associated with an increased incidence of fetal malformations and perinatal mortality. Such a poor outcome is most likely confined to a subset of diabetes mellitus patients in whom diabetes was present but unrecognised before pregnancy (6,7).

Three of the presented cases are infants of gestational diabetic mothers, with Case 3 an infant of a Type I diabetic mother. This may support the observation that misdiagnosis of gestational diabetes in diabetic women in whom the diagnosis of diabetes mellitus was missed in the preconceptional period could be teratogenic.

There are no known diabetes-specific anomalies. A great diversity is seen among the types of malformations, with the most frequent involving the central nervous system (anencephaly, caudal regression syndrome, neural tube defects), the cardiovascular system (ventricular septal defect, transposition of main arteries), the gastrointestinal system (intestinal atresia) and the genitourinary system. Cardiac malformations are the most common (1-3).

Among the rare malformations seen in infants of diabetic mothers, the presented cases featured situs inversus totalis, pulmonary atresia, esophageal atresia and atrioventricular channel defect. The literature describes one infant with situs inversus and a neural tube defect (2). These two malformations are thought to be coincidental and a result of poor diabetic control during the lateralization period of organogenesis (2). Congenital anomalies such as glossoptosis are also among the rare abnormalities reported in infants of diabetic mothers.

Perinatal mortality rates of these infants decrease significantly with insulin treatment and better glycemic control of the mothers and with improvements in newborn intensive care management. However, perinatal mortality is still an important issue, with a reported 2.0-4.0% incidence of fetal demise. In many centers, congenital anomalies are the most common cause of perinatal mortality (40%) in infants of diabetic mothers. Late fetal loss and metabolic abnormalities also feature in increased perinatal mortality.

Cases 3 and 4 died of major congenital anomalies. The mother of Case 3 had a history of fetal loss during the last trimester. It is essential for the perinatologist to understand the mechanism of dysmorphogenesis in diabetic pregnancies and to apply specific strategies and practices that are effective in managing both mother and infant.

Screening programs should routinely be employed to identify those women most likely to develop gestational diabetes. Once identified, standard dietary management and insulin treatment should be introduced, if necessary, to maintain glycemic control within a narrow range.

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