Occurrence of an aortic arch anomaly in two siblings born to a diabetic mother

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A patient with interruption of aortic arch type A, born to a diabetic mother, is described. The patient, a male infant, was the fourth child of a 29-year-old mother, and had a sibling with coarctation of the aorta. The mother had been treated for insulin-dependent diabetes mellitus for the previous 10 years. The infant died on the 3rd day of life after symptoms of cardiogenic shock. To our knowledge, interruption of aortic arch type A has not been previously described in infants of diabetic mothers. The relevance of the case is discussed and the literature reviewed.

Key words: infants of diabetic mothers, interruption of the aortic arch type A, aortic arch anomalies.

The incidence of congenital heart disease in infants of diabetic mothers is about four to five times higher than that observed in the normal population[1,2]. Conotruncal anomalies (tetralogy of Fallot, truncus arteriosus, double outlet right ventricle) and ventricular septal defects are among the most common cardiac defects found in infants of these women[3-6]. Interruption of the aortic arch (IAA), especially type B, has been discussed within the realm of conotruncal anomalies. The literature lacks any reports of IAA type A and B in infants of diabetic mothers.

We report a patient with IAA type A born to a diabetic mother. Interestingly, one of the patient's siblings had coarctation of the aorta.

Case Report

A male infant, the fourth child of a 29-year-old mother, was delivered by cesarean section at the 37th week of gestation, and weighed 3740 g (Apgar score 8) at birth. The mother had been treated for insulin-dependent diabetes mellitus for the past 10 years.

The family's first child, who is presently 10 years old, was afflicted with meningomyelocele at the lumbosacral region. The second child is healthy at eight years of age. The third child, born with coarctation of the aorta, ventricular septal defect, and atrial septal defect, died at one month of age after an attempt at resection and end-to-end anastomosis at another hospital.

At the 20th week of gestation in the fourth pregnancy, fetal echocardiography revealed muscular ventricular septal defect. Because of the mother's extreme obesity, the fetal aortic arch could not be demonstrated.

At birth, the physical examination revealed a pale tachypneic neonate weighing 3740 g and measuring 52 cm in length. His facial appearance was normal. His heart rate was 130 beats per minute, and respiratory rate was 56 breaths per minute. There was evidence of peripheral, but not central, cyanosis. No murmur was detected on auscultation and both femoral pulses were palpable. Other physical findings were within normal limits.

The chest X-ray revealed enlargement of the heart and prominent pulmonary vasculature (cardiothoracic index was 0.67). Thymus shadow was apparent. An electrocardiogram showed sinus rhythm and hypertrophy of the right ventricle.

Laboratory findings showed normal levels of serum Na^+ and K^+, and transient hypoglycemia and hypocalcemia. Pulse-oxymeter of the upper extremities showed O_2 saturation of 96-98

percent, while umbilical arterial blood gas analysis indicated PO_2 = 46 mmHg, O_2 saturation 70 percent, and PCO_2 = 47 mmHg.

Two dimensional echocardiographic examination demonstrated the presence of muscular, trabecular ventricular septal defect, thick interventricular septum and aortic interruption. Angiography, which was performed after PGE_1 treatment, indicated the presence of ventricular septal defect, patent ductus arteriosus, aortic interruption (distal to the left subclavian artery) and pulmonary hypertension (pulmonary artery pressure was 42/25 mmHg) (Fig. 1).

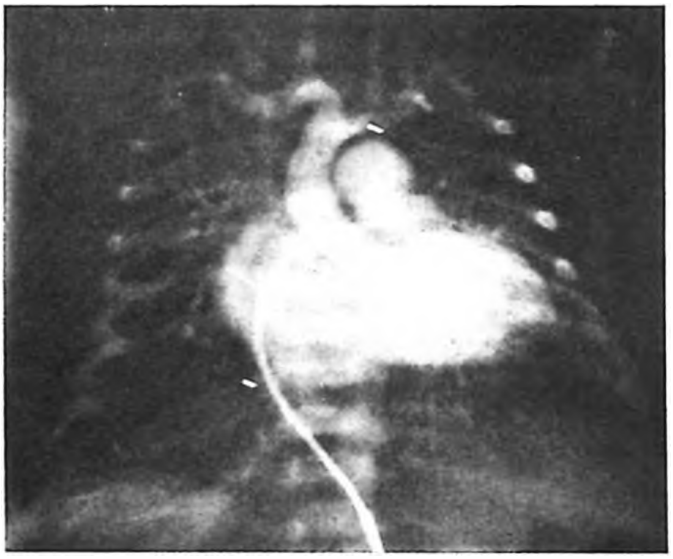

Fig. 1. Contrast injection of the left ventricle demonstrating the interruption of the aortic arch after the left subclavian artery.

During follow-up his general condition gradually worsened, and progressive acidosis developed. Despite therapy for heart failure, he developed severe bradycardia and symptoms of cardiogenic shock. The infant died on the 3rd day after birth. Permission for autopsy could not be obtained. No chromosomal abnormality could be demonstrated.

The fifth child of this family had a small muscular ventricular septal defect on echocardiography and his arcus aorta was normal.

Discussion

The teratogenicity of diabetes mellitus is complex, and arises due to a combination of various genetic, environmental and toxic factors. Diabetes dictates a fetal genetic susceptibility to abnormal development and may induce a maternal factor which can alter neural crest ectomesenchymal cell migration and growth in the fetus or directly cause fetal cardiomyopathy[4].

In itself, insulin or insulin analogue therapy for diabetes neither decreases nor increases the risk of malformation in the fetus, but a longer duration of diabetes has been shown to be significantly associated with higher risk for such abnormalities. Chung et al.[7] suggest that mothers who have had the disease longer have a higher incidence of fetal malformations. Because the mother's diabetes was under control, the prolonged duration of disease might have been a factor in our case.

Interruption of the aortic arch is estimated to occur in three of 100,000 live births, accounting for approximately one percent of congenital heart disease cases in infancy[8]. Since IAA type B is closely related to neural crest abnormality, it can be expected to occur more frequently in infants of diabetic mothers than type A. However, we could find no reports of either abnormality in infants of diabetic mothers.

Coarctation of the aorta, as seen in our patient's sibling, has been listed as one of the common cardiac defects seen in fetuses of diabetic women[8]. Furthermore, the coexistence of IAA type A and coarctation of the aorta in two children of a diabetic mother is particularly interesting, since Pierpont et al.[10] found no congenital cardiac malformations in siblings of children with IAA type A.

Interruption of the aortic arch is clearly not due to an involution or atresia of any of the aortic arches, because the interruption is located between the origin of the left subclavian artery and the ductus arteriosus, i.e. at the aortic isthmus. In preductal coarctation of the aorta, the obstruction also involves the isthmus. Both IAA type A and coarctation of the aorta therefore must manifest themselves relatively late in development, after the seventh cervical intersegmental artery has completed its proximal migration[11].

The similarity between the pathogenesis of IAA type A and coarctation of the aorta may partially explain their existence in the siblings in our case.

In conclusion, despite the well controlled maternal diabetes mellitus in the case presented, the presence of IAA type A and coarctation of the aorta in two siblings and the meningomyelocele in another sibling suggest diabetes mellitus as a common etiologic factor in these disorders.

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