VACTERL Association with Prune-Belly Syndrome

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We report a term, small for gestational age neonate having full spectrum of VACTERL association. In addition, the neonate also had triad of signs and symptoms associated with prune belly syndrome. The concurrence of these two syndromes could lie in their common etiology of defect in mesodermal differentiation. Such a combination is extremely rare and is generally incompatible with life.

Keywords: *Prune-belly syndrome, VACTERL association.*

The clinical manifestations of VACTERL association include vertebral anomalies, anal atresia, congenital heart disease, tracheo-esophageal fistula, renal dysplasia and limb abnormalities(1). Prune belly syndrome is the triad of deficiency of abdominal muscles, dilatation of urinary tract and crypt-orchidism(2). The association of these two syndromes in a child has been reported probably once in indexed literature(3). We report a case of VACTERL association who also had all the features of prune belly syndrome and discuss the possibility of a common etiology.

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Case Report

A small-for-gestational age male neonate was born vaginally at 37 weeks of gestation to a 20-year-old primigravida mother and a 26 year old father. The family history was unremarkable and the couples were non-consanguineous. The mother had no antenatal check up. There was no obvious antenatal teratogen exposure, fever, rash or any drug intake. There was no polyhydramnios or oligohydramnios and the placenta was normal. The neonate had Apgar scores of 8, 9, 9 at 1, 5 and 10 minutes, respectively and a birth weight of 2.3 kg. The length of the baby was 48 cm with an upper to lower segment ratio of 1.67: 1, chest circumference of 28.5 cm and head circumference of 34 cm.

Multiple malformations were recognized at birth. The anomalies identified on physical examination included esophageal atresia with tracheo-esophageal fistula, anal atresia, a short and malformed right upper limb with valgus deformity, absent right thumb and rudimentary left thumb. The abdomen was distended with lax abdominal wall, a high placed umbilicus and single umbilical artery. The phallus was large (megalopenis) with bilateral cryptorchidism (*Fig. 1*). Urinary bladder was palpable and the overlying skin of the penis had rugosities. There was a corneal opacity in left eye. Cardiovascular system examination revealed a pansystolic murmur.

X-ray of chest showed coiling of the nasogastric tube in dilated upper esophageal pouch with presence of gas in stomach suggesting a diagnosis of esophageal atresia with tracheo-esophageal fistula. Skiagrams of upper limbs showed absent radius and short ulna on right side with absent first metacarpal in both hands. *X*-ray of the lumbosacral spine showed fusion of L4-L5 vertebra.

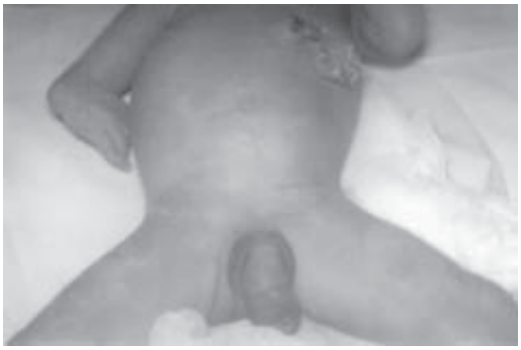

Fig. 1. Prune Belly with high placed umbilicus, large phallus, bilateral cryptorchidism and deformed right upper limb.

Ultrasonography of the abdomen revealed a normal right kidney with non-visualization of left kidney. Bladder was enlarged and thick walled with rest of the viscera being normal.

On the basis of above anomalies, a diagnosis of VACTERL association with Prune-Belly syndrome was made. The child had severe respiratory distress since birth and was oxygen dependent. In view of multiple major malformations, parents did not agree for a surgical intervention and the child died on 3rd day of life. Autopsy findings revealed bilateral intra-abdominal testes, which were found normal for age on histopathological examination. Additional anomalies found in autopsy were pulmonary hypoplasia, hypoplastic abdominal musculature, bladder diverticula and megalourethra. The right kidney showed glomerular cysts, a sign of early obstruction. In place of left kidney, a tiny cystic structure was identified which on microscopy was confirmed to be a cystic dysplastic kidney. Fusion of L4-L5 vertebrae was also detected. The heart was normal except for the presence of a patent ductus arteriosus.

Discussion

Our patient had vertebral body defects, anal atresia, single umbilical artery, esophageal atresia with tracheo-esophageal fistula, dysplastic kidney and radial defects; all classical features of a full spectrum VACTERL association(4). The patient also had hypoplastic abdominal wall musculature and urinary tract abnormalities suggesting the additional diagnosis of a complete Prune Belly syndrome. The complete form of Prune Belly syndrome consists of an abdominal wall deficient in muscular tissue, dilated urinary tract, and bilateral cryptorchidism and thus seen only in males(5).

Urogenital anomalies like unilateral or bilateral cryptorchidism, hypospadius and micropenis in males and ambiguous genitalia and bladder exostrophy in females have been frequently described in VACTERL association(4,6). In the largest such series of 286 patients, 81 (28%) had severe genital defects(7). Abdominal wall abnormalities like omphalocele and gastroschisis are also occasionally reported(7) but concurrence of a full-fledged Prune-Belly syndrome is extremely rare. Lukusa, *et al*.(8) described incomplete Prune Belly anomaly in a female child with additional features of the VACTERL association. Ozturk, *et al*.(3) for the first time reported concordance of complete Prune Belly syndrome and VACTERL association in a premature male child. Both the above cases did not have esophageal atresia or tracheo-esophageal fistula. Full spectrum of VACTERL (all six components) with a complete Prune Belly syndrome in our case reflects a severe disruption of both cranial and caudal mesoderm.

Associations are derivatives of causally nonspecific disruptive events acting on the developmental field which could be the entire embryo during first four weeks of life(9). This pattern of malformation generally has a sporadic occurrence in an otherwise normal

family. A disruption in differentiating mesoderm in first 4-5 weeks has been suggested to be the basis for such a non-random association(7). Other defects of mesodermal origin such as neural tube defects, orofacial clefts, bladder extrophy and diaphragmatic defects are occasionally seen in cases with VACTERL association. The overlapping of defects of VACTERL association with CHARGE association and Goldenhar's syndrome have also been described(4). This overlap implies an etiologic commonality which has been described as the axial mesodermal dysplasia spectrum(10).

Early disturbance of mesodermal development in both the abdominal wall and the urinary tract has also been suggested to be responsible for Prune Belly syndrome(11). The timing of the insult appears to be around third week of gestation which would account for all three parts of the triad. Presence of single umbilical artery also suggests the insult around the fourth week of intrauterine life(12). As both VACTERL association and Prune-Belly syndrome have a common etiology of a defect in the differentiating mesoderm in early first trimester, we believe that concurrence of these two syndromes is another addition to the axial mesodermal dysplasia spectrum.

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