Case Report

Sirenomelia with vertebral, anal, cardiac defect, tracheo-esophageal fistula, renal anomalies, limb abnormalities association: a case report

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Received: 17 June 2020
Accepted: 08 July 2020

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ABSTRACT

Sirenomelia is a rare congenital malformation, characterised by abnormal development of caudal part of body with variable degree of fusion of lower limbs. VACTERL is an acronym used for a group of sporadic non-random birth defects involving multiple organ systems, namely vertebral (V), anal (A), cardiac (C), tracheoesophageal (TE), renal (R) and limb (L) defects. Combination of both the anomalies is very rarely reported in literature. Survival is extremely rare and early prenatal diagnosis may allow for termination of pregnancy. Here we present a case of sirenomelia phenotype, with a complete spectrum of autopsy findings, suggestive of VACTERL association.

Keywords: Caudal defect, Caudal dysgenesis, Mermaid baby, Sirenomelia, VACTERL

INTRODUCTION

Sirenomelia or sirenomelia sequence is a severe malformation of lower limbs characterised by complete or partial fusion of legs with a variable combination of visceral abnormalities. The incidence is 1.1-4.2 per 100,000 births with male to female ratio 3:1.1 The etiology of this devastating malformation, which share some common features with caudal dysgenesis (CD) and VACTERL association, is still an enigma.

Recently some animal studies point towards a genetic basis. VACTERL association is a mnemonically useful acronym for a condition characterised by the sporadic, non-random association of specific birth defects, namely vertebral anomalies (V), anal atresia (A), cardiovascular anomalies (C), tracheo-esophageal fistula (TE), renal anomalies (R) and limb defects (L).2

Sirenomelia has been described in literature as a part of VACTERL association, though rarely.3 Here we present a case of sirenomelia in a still born baby, which on autopsy revealed complete spectrum of VACTERL association.

CASE REPORT

A 26-year-old primigravida mother delivered a stillborn fetus weighing 1750 grams at 32 week of gestation. The mother was not a known case of diabetes mellitus and there was no history of consanguinity. Though the mother had antenatal check-up twice in a primary health care facility, no sonography was done.

Figure 1: Sirenomelia baby with fused lower limbs.
External examination of the fetus showed normal appearing upper part of the body but completely fused and axially rotated lower limbs (Figure 1). There were other features like potter facies, preaxial polydactyly involving right hand and right foot. Both the feet were directed dorso-medially with equinovarus deformity on left side (Figure 2). Both the knees were abnormally flexed and the hips seemed to be hypoplastic. There was no anal opening and a rudimentary phallus was seen (Figure 3). Post-mortem radiograph showed single femur, bilateral presence of tibia and fibula with sacral dysgenesis (Figure 4). It was diagnosed to be a case of sirenomelia phenotype. Fetal autopsy, carried out at a later date, revealed esophageal atresia, tracheoesophageal fistula (type A), hypoplastic kidneys and absence of urinary bladder. Examination of heart showed double superior vena cava and a large ventricular septal defect. Terminal part of the colon was dilated with a blind end, which was attached to the umbilicus posteriorly with a cord like structure (Figure 5). A single umbilical artery was present which was in direct continuity with abdominal aorta. All the features were consistent with sirenomelia and VACTERL association.

**DISCUSSION**

Sirenomelia is a rare congenital anomaly of unknown etiology. It is usually lethal and only five survivors till date, are described in literature. As per Stocker and Heifetz, sirenomelia is classified into seven types (type I to type VII). Type I is the mildest form in which the fusion only affects the superficial tissue and all bones in the fused limbs are present. Type VII is the most severe form, in which only a single bone is present without any leg or feet. According to another simplified classification, it is of three types, namely (a) Simpus Apus (Sirenomelus) - no feet, one femur, one tibia (b) Simpus Unipus (Uromelus) - one foot, 2 femur, 2 tibia, 2 fibula (c) Simpus Dipus (Simelus) - 2 feet, 2 fused legs (flipper...
like), popularly known as mermaid. This case belonged to Simus Dipus type. Sirenomelia phenotype is usually associated with other visceral anomalies.

There are two other congenital defects, namely VACTERL association and caudal dysgenesis (formerly caudal regression syndrome), who had many overlapping features with sirenomelia and may be due to a common pathogenic process.

VACTERL association is typically defined by the presence of at least three of the following congenital anomalies: vertebral defects, anal atresia, cardiac defects, tracheoesophageal fistula, renal anomalies and limb defects. The estimated incidence is 1/10,000 to 1/40,000 infants. But this may be an overestimation as many other pathological conditions e.g. Fanconi anemia, 22q11.2 deletion syndrome, CHARGE syndrome, Townes-Brocks syndrome etc. share some of their features with VACTERL. This case had sacral agenesis, anal atresia, cardiac defects in the form of VSD and double superior vena cava, tracheoesophageal fistula, hypoplasia and limb defects in the form of bifid thumb, polydactyly and sirenomelia. Caudal dysgenesis (CD) is characterised by some form of sacral agenesis, lowerlimb defects along with other defects in variable proportion like lumbosacral, vertebral, cardiac, anorectal and genito-urinary malformations. It is mostly associated with infants of diabetic mother and rarely associated with single umbilical artery (SUA). In our case the mother had no history of diabetes mellitus.

Although the primary molecular defect causing sirenomelia is still unknown, several hypotheses had been put forward to explain the etiology. Two most important pathogenic hypotheses are the vascular steal hypothesis and defective blastogenesis hypothesis. According to vascular steal hypothesis, there is usually a single umbilical artery of vitelline origin which diverts blood from the lower part of the body to placenta. As a result, fusion of the lower limbs occur due to the deficient blood flow and nutrient supply to the caudal mesoderm. In this case abdominal aorta was seen to be narrowed down after giving rise to renal arteries and continued as a single umbilical artery, which may be derived from the vitelline artery. But this does not explain the other defects in the upper half of the body in sirenomelia, as in our case.

According to the second theory, there is a primary defect of blastogenesis that occurs during the final stage of gastrulation at the tailbud stage, corresponding to third gestational week in humans. A single ‘hit’ during this period may produce defects in different progenitor fields, causing polytopic manifestations. Sirenomelia has been associated with other congenital malformations, namely alobar holoprosencephaly, cleft lip and palate, anencephaly, agenesis of corpus callosum, meningomyelocele, omphalocele, pentalogy of cantrell, vestigial tail etc. Environmental risk factors associated with sirenomelia are retinoic acid, heavy metals like cadmium, drugs like misoprostol, radiation and cocaine exposure. In humans a genetic etiology for sirenomelia is still not confirmed. Experimental studies in mice have shown that sirenomelia has a genetic basis resulting from either a gain- of- function of retinoic acid (RA) signalling or loss-of-function of bone morphogenetic protein (Bmp) signalling. Bmp signalling pathway is important in normal formation of mesoderm as well as establishment and remodelling of the vasculature. Likewise, several key signalling pathways have been implicated in pathogenesis of VACTERL association. These include classic Sonic hedgehog signalling and disruption of pathways involving SHOX and retinoic acid signalling. So there is an overlapping of genetic factors associated with the etiopathogenesis of both the condition.

CONCLUSION

The index case had features of sirenomelia with complete spectrum of VACTERL association, which supports the defective blastogenesis theory and may be due to some unknown insult in the early phase of gastrulation. There is no serological marker for diagnosis of this condition. Early antenatal sonographic diagnosis before 24 weeks of gestation is very important in view of dismal prognosis and allows for termination of pregnancy.

ACKNOWLEDGEMENTS

Authors would like to thank Department of Anatomy, KIMS for providing assistance in conducting the fetal autopsy.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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