SIRENOMELIA: A DETAILED FETAL AUTOPSY STUDY

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ABSTRACT

Sirenomelia also known as mermaid syndrome, characterized by fused lower limbs, is a lethal and rare congenital abnormality. This is an extreme example of caudal regression syndrome caused by vascular steal of single umbilical artery. Sirenomelia is found approximately one in 100,000 live births and is usually fatal because of complications associated with pulmonary hypoplasia, abnormal development of the kidneys and urinary bladder. Most of the cases are associated with maternal diabetes and single umbilical artery.

We report a case of sirenomelia terminated at 21 weeks of gestation due to multiple congenital abnormalities. Antenatal scan of a 25-year-old primi revealed a single live fetus of 21 weeks gestation with severe oligohydramnios, non-visualization of kidneys and bladder and lower part of the spine. This pregnancy was terminated and the specimen sent to the department of anatomy for fetal autopsy. On external examination, a tail like rudimentary single midline lower limb without foot was noted. There were no external genitalia and anal orifice. Internal examination revealed hypoplastic lungs, atrial septal and ventricular septal defects, aberrant right subclavian artery, hypoplastic abdominal aorta distal to the single umbilical artery, complete agenesis of urinary system, rectal agenesis and rudimentary indeterminate gonads.

We would like to discuss the clinical features, etio-pathogenesis and review of literature of sirenomelia. Early diagnosis and termination of this lethal congenital anomaly results in minimizing the trauma related to the termination of pregnancy at advanced gestation.

KEY WORDS: Sirenomelia, Caudal regression syndrome, Vascular steal, Maternal diabetes, Single umbilical artery.

INTRODUCTION

Sirenomelia or Mermaid syndrome is characterized by fusion of lower limbs also associated with flexion and inversion in external rotation of the lower limbs, anomalies of lumbar and sacral spine, imperforate anus, agenesis of kidneys and urinary tract & agenesis of internal genital organs [1]. As reported by Johnson,1966; Martinez Frias et al.1992; Murphy et al.,1992, incidence varies between 1.1 to 4.2 per 100,000 births [2,3,4]. Most of the cases are sporadic and have very less chance of recurring in a next pregnancy. Our aim is to present the features of a Sirenomelia foetus, with detailed autopsy findings, and discussion of etio-pathogenesis and a brief review of literature.

CASE REPORT

A 25-year-old primigravida at 21 weeks of gestation was admitted for termination of
pregnancy due to ultrasound diagnosis of multiple congenital anomalies in the fetus. Routine anomaly scan performed during this pregnancy at 21 weeks revealed a single live foetus corresponding to 20 weeks of gestation with severe oligohydramnios, non-visualization of kidneys and urinary bladder, & agenesis of caudal spine. Both lower limbs could not be clearly assessed due to severe oligohydramnios. In view of these findings, a repeat ultrasound scan was done which confirmed the same. There was no history of consanguinity, drugs or radiation exposure or any other illness during pregnancy. There were no medical or obstetric risk factors. There was no personal or family history for diabetes mellitus or congenital abnormality. As these anomalies indicate guarded prognosis, the couple opted for termination of pregnancy. The fetus obtained was sent for detailed autopsy.

External examination of the fetus revealed: Potters’ facies, hypertelorism, low set ears (right ear was rudimentary with no external acoustic meatus (EAM) and left ear was normal), flattened nasal bridge and tip of the nose, and micrognathia. The upper torso of the body was normal. There were no external genitalia, no urethral and anal openings. Lower limb ended in a single tapering midline structure (Fig. 1).

Post mortem radiograph (Baby gram) showed pelvic aplasia, single midline rudimentary femur & rudimentary tibia. Fibula, tarsals, metatarsals, phalanges were not seen. Vertebral column was normal till lumbar region, then agenesis of sacrum and coccyx. Upper limb bones on both sides were normally present and developed as per gestational age (Fig. 2).

Internal examination of the fetus showed: single umbilical artery which was arising from the abdominal aorta, which was hypoplastic distal to that origin (Fig. 3). The liver, stomach, small intestine, spleen and pancreas were unremarkable. There was no gallbladder. The large intestine ended as a blind pouch at sigmoid colon. There was complete agenesis of rectum and anal canal. There was bilateral renal agenesis & agenesis of ureters and urinary bladder. The adrenals were flat and discoid lying on posterior abdominal wall. There were no uterus and vagina. There was an indeterminate gonad-like structure, bilaterally present. Histology showed rudimentary primitive indeterminate gonad (Fig. 4).

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*Fig. 1:* Foetus with Sirenomelia.

*Fig. 2:* X-ray of the foetus showing with rudimentary femur and tibia.

*Fig. 3:* Hypoplastic Aorta and Single umbilical artery.

*Fig. 4:* Histology showing rudimentary primitive indeterminate gonad.
Parimala Sirikonda, Nalluri Himabindu. SIRENOMELIA: A DETAILED FETAL AUTOPSY STUDY.

DISCUSSION

Cardiovascular examination delineated atrial septal defect and ventricular septal defects. There was aberrant right subclavian artery arising as fourth branch of arch of aorta and it coursed from left to right behind esophagus and trachea. There was pulmonary hypoplasia. Brain was appropriate for the gestational age but there was partial agenesis of corpus callosum: splenium was not formed (Fig. 5). Spinal cord below the lumbar segments was deficient.

Spine was normal till the lumbar region, C1-L5 vertebrae were normal. The sacral and coccygeal vertebrae were absent. There was a rudimentary midline femur which had a rounded mass fused to a rudimentary pelvic bone and rudimentary tibia with condyles.

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DISCUSSION

Sirenomelia is a lethal congenital anomaly with abnormal development of the caudal region of the body involving varying degrees of fusion of the lowerlimbs with or without bony defects. In addition to the leg fusion phenotypes, Sirenomelia presents with abnormal pelvic or uro-genital organ development affecting the kidney, ureter, bladder, rectum and external genitalia. Owing to the visceral abnormalities, sirenomelia is incompatible with life.

Hind limb fusion types: Stocker and Heifetez (1987) classified Sirenomelia into 7 types - Type I to Type VII mainly according to the presence of skeletal elements in the thigh and leg. In type I, the mildest form, all bones in the two fused limbs are present and the fusion only affects superficial tissues. In type VII, the most severe form, only a single bone is present, with no indication of legs or feet [5]. Our case falls in Type VII.

Visceral malformations: Kallen et al., 1992 stated that all the human cases of Sirenomelia analysed showed a variable degree of renal and urethral dysplasia, with total renal agenesis being very frequently reported [6]. Goodlow et al., 1998, Kallen et al., 1992 stated that malformation of the urinary tract is consistently associated with genital malformations. These affect mainly the external genitalia, which were either absent or represented by an indistinct tag of tissue, whereas the gonads were usually unaffected [7,6].

In our case there were no external genitalia and even the gonads were indistinct. On microscopic examination of the gonads, a picture of primitive indeterminate gonad was observed.

Kallen et al., 1992 reported the presence of gastrointestinal anomalies in Sirenomelia as a common feature, the most frequent being a blind ending colon, rectal atresia and imperforate anus [6].

Our case had a blind ending sigmoid colon, with agenesis of rectum and anal canal.

Vascular malformations: Heifetezet al.1984 & Stevenson et al.1986, reported that the vascular abnormalities in Sirenomelia deserve special mention owing to their possible relevance to pathogenesis. The human umbilical cord normally contains two umbilical arteries (returning deoxygenated blood from the fetus to the placenta) and a single umbilical vein (supplying oxygenated blood to the fetus).

However, fetuses with Sirenomelia almost invariably exhibit a single umbilical artery (SUA) [8,9]. Martinez – Frias et al.2008, reported that
Parimala Sirikonda, Nalluri Himabindu. SIRENOMELIA: A DETAILED FETAL AUTOPSY STUDY.

Our case showed pulmonary hypoplasia and cardiac defects viz. Atrial Septal Defect (ASD) and Ventricular Septal Defect (VSD) and aberrant right subclavian artery. According to the defective blastogenesis hypothesis, sirenomelia is a primary defect of blastogenesis that occurs during the final stages of gastrulation at the tailbud stage, corresponding to the third gestational week in humans as reported by Opitz et al. 2002, Duesterhoeft et al. 2007, & Davidson 1993 [11,14,20]. Although the vascular steal hypothesis and the deficient blastogenesis hypothesis do not exclude one other, it is reasonable to assume that deficient blastogenesis would concomitantly affect organ and vessel development.

Genetic aspects of Sirenomelia in animal models: A Sirenomelia-like phenotype has been observed in several genetically modified mouse strains with either gain of function of Retinoic acid (RA) signaling or loss of function of bone morphogenic protein (BMP) signalling [21]. RA, maternal diabetes, and heavy metals, have been described as important environmental risk factors for caudal malformations. The involvement of RA signalling in the genesis of sirenomelia is well established in experimental models and represents a potentially interesting connection to the environment, because RA levels can be modified by genetic, nutritional and iatrogenic causes. However, to date, sirenomelia has not been reported among the malformations of RA-exposed human fetuses.

Maternal diabetes is considered as a causative environmental factor for Caudal Dysgenesis (CD) because 10–15% of affected children have diabetic mothers according to Passarge and Lenz, 1966, Kalter 1993, Twickler et al. 1993, Lynch and Wright 1997, Assimakopoulos et al. 2004 & Castori et al. 2010 [22-27]. However, this association remains controversial for sirenomelia because only 0.5%–3.7% of reported cases have diabetic mothers according to Stocker and Heifetz 1987, Duncan and Shapiro 1993, Lynch.
association with CD and sirenomelia in both experimental models according to Ferm and Carpenter 1968, Hilbelink and Kaplan 1986; and in humans as reported by Castilla et al. 2008, &Orioli et al. 2009 [29-32].

Association of Sirenomelia with new reproductive technologies, namely Intra Cytoplasmic Sperm Injection (ICSI) was also described [33].

Karyotyping of the specimens was normal as reported by other researchers. This was not done in our case.

CONCLUSION

Sirenomelia is a rare and fatal congenital anomaly. Early prenatal diagnosis by first trimester scan should be the aim to minimize the trauma related to the termination of pregnancy at advanced gestation. Colour Doppler imaging can be helpful in identifying the single large vitelline artery and the absence of renal arteries. 3D sonography and MRI may complement the 2D-sonographic findings. Post-mortem pathologic examinations and experimental animal studies will remain necessary to determine the exact patho-genetic mechanisms involved in the congenital malformations. Unless one searches carefully and systematically for these anomalies, they may remain unnoticed. Often, they play an important part in the gravity of the total disorder, because functional disturbances resulting from these associated malformations may in themselves lead to death. Although in our case the mother did not have evidence of the risk factors, the couple should be counselled about early screening in the subsequent pregnancy. We hope the detailed report of our case may help in the wider understanding of the many possible features & perhaps also the patho-genetic mechanisms of sirenomelia; which would indirectly contribute toward better medicare in the world.

ABBREVIATIONS

SUA - Single Umbilical Artery
RA - Retinoic Acid
CD - Caudal Dysgenesis

Conflicts of Interests: None

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