Sirenomelia: Case Report and Review of the Literature

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Abstract

Sirenomelia birth or “mermaid syndrome” is very rare (about 4.2 to 1.2 per 100,000 births). These babies are born dead or die shortly after birth. The exact cause of sirenomelia is unknown. The aim of this study was to introduce a fetal anomaly of sirenomelia and to review the literature associated with it. In this paper, we introduce a baby with 20 weeks of gestational age whose abnormalities have not been diagnosed on ultrasound and the mother has been admitted to a hospital in Kermanshah for termination of pregnancy due to oligohydramnios. Sirenomelia was diagnosed after birth by observing the adherent lower extremities and prominent anomalies such as lack of genito-urinary system, external genitalia and anus. Sirenomelia is inconsistent with life and its early detection by appropriate diagnostic methods is important in reducing high-risk pregnancy complications, treatment planning and reducing stress in pregnant mothers.

Keywords: Mermaid syndrome; Oligohydramnios; Congenital abnormalities; Sirenomelia; Fetal anomaly

Abbreviations: RA: Retinoic Acid; BMP: Bone Morphogenetic Protein; V: Vertebral Defects; A: Anal Atresia; C: Cardiovascular Anomalies; TE: Tracheo-Esophageal; RL: Radial Limb; TSG: Twisted Gastrulation

Introduction

Mermaid syndrome (sirenomelia) was first described by Rocheus in 1542 and by Palfyn in 1553. Mermaid syndrome abnormality was described by Duhamal in 1961 as the most severe form of caudal regression syndrome [1,2]. Sirenomelia birth or mermaid syndrome is rare and its incidence is 1.2-4.2 per 100,000 births [3]. Some studies have reported its prevalence to be 1-8.0 per 100 thousand births with a male to female ratio 3:1. These babies are born dead or die shortly after birth [4]. The term “sirenomelia” is taken from Greek and Roman mythological stories [5]. Sirenomelia is involved in the lower extremities, which can vary from the soft tissue connection to connectivity of the entire lower limb and in only a femur bone [6]. Other abnormalities associated with sirenomelia include single umbilical artery, absence of bilateral kidney or renal dysfunction, lack of bladder, rectum or anus and absence of external genitalia, lumbarosacral and pelvic abnormalities, loss of sacrum, incomplete vertebrae and abnormalities related to the central nervous system [7]. The exact cause of sirenomelia is not known, but any damage to the mesoderm of the embryonic tail between days 13 and 22 may cause connection or lower limb disorders in newborns [8]. The aim of this study was to present a sirenomelia birth with a review of the cellular and molecular causes and to analyze the new findings associated with this disorder.

Case Report

Figure 1: Sirenomelia with normal upper half and lower limb abnormalities with a single and a bud of finger. Genitalia, anus and urethra do not exist.

The baby under study was born by an 18-year-old woman with gestational age of 20 weeks in her second pregnancy and her previous delivery leading to abortion in the first trimester. This woman was admitted to one of the hospitals of Kermanshah to terminate pregnancy due to severe oligohydramnios. She did not complain of any particular illness and had no history of...
In late gastrulation period, several BMP ligands along with their Cyp26a1. Bone morphogenetic protein (BMP) signaling has an incomplete retinoic acid signaling is a cause defects has not shown any evidence of human malformations Cyp26a1 gene mutation screening in the patients with tail the clear role of Cyp26a1 in the occurrence of sirenomelia, RA levels are associated with genetic factors, nutrition and iatrogenic consequences and can change [10]. Retinoic acid signaling in embryonic period has a vital role in fetal development, especially in the caudal region [11]. Many experiments have shown that the embryo is sensitive to changes in normal levels of RA in gastrulation period [12]. Cyp26a1 is an enzyme that lowers RA level and is expressed in the caudal area of the fetus and the growing vascular network [13]. Any disturbances or reduced expression of Cyp26a1 enzyme leads to increased levels of retinoic acid, which in turn causes growth defects in the tail area, including sirenomelia. Researchers have shown that excessive levels of RA in pregnant mice can lead to abnormalities in the caudal region of their fetuses [14,15].

In the studies conducted on rats, sirenomelia has been reported to be associated with increased RA signaling in the tail area of the fetus. Due to the effect of genetic and nutritional factors on RA levels, this metabolite has the potential to be a genetic/bioenvironmental cause of sirenomelia [10]. Cyp26a1 is expressed in the early stage of gastrulation in the stalk stem and its newly-formed mesoderm, and in late gastrulation stage changes its location into nephropore, hind gut endoderm and the tail bud mesoderm [16]. Cyp26a1 expression in the tail area plays a pivotal role in reducing retinoic acid and maintaining a proper balance between proliferation and differentiation. Despite the clear role of Cyp26a1 in the occurrence of sirenomelia, Cyp26a1 gene mutation screening in the patients with tail defects has not shown any evidence of human malformations [17]. However, incomplete retinoic acid signaling is a cause of sirenomelia because the role of retinoic acid in normal developmental stages has been proven in the mice with mutant Cyp26a1. Bone morphogenetic protein (BMP) signaling has an important role in the embryonic period, including gastrulation. In late gastrulation period, several BMP ligands along with their extracellular antagonists are expressed [18]. Because the natural formation of mesoderm and differentiation of hematopoietic cells is important to endothelial progenitor, BMP signaling can be a cause of sirenomelia. BMP7 is a member of BMP family and a member of large family of secreted proteins named transforming growth factor beta (TGFβ). TSG (Twisted gastrulation) is an activator or inhibitor of BMP signaling and can act as a moderator in the tail area of embryo [19]. Mermaid phenotype in double mutant BMP7/TSG is due to decreased BMP signaling in caudal-ventral mesoderm. This decline is more marked to be due to lack of BMP 7 alone because BMP7 mutation alone does not cause mermaid phenotype [20].

Because BMP and RA are both involved in the development of the tail area, it is logical to think they can adjust each other. Recently, it has been shown that RA can reduce BMP signals through declining the phosphorylation of Smad1, which is an intracellular component of BMP signaling pathway [21]. If this interaction, which is specified in the neural tube development, acts in the embryonic tail area, RA level rise due to decreased BMP signaling levels will affect the BMP signaling and negative regulation of RA signaling during cartilage generation [22].

**Discussion**

Mermaid is a rare syndrome that, due to severe abnormalities, leads to intrauterine death or immediately after birth. Therefore, its early diagnosis and planning for therapeutic abortion of great significance. Sirenomelia is classified according to the number of bones in the lower extremities, with a reported male/female ratio of 3-to-1. Sirenomelia, due to lack of bilateral kidneys, results in severe oligohydraminos and fatal pulmonary hypoplasia, and most babies are born dead or die within hours of birth [23]. Several hypotheses have been proposed for sirenomelia. Duhamel suggested that this syndrome is part of the degeneration of the embryonic tail region (caudal regression). One of the most common assumptions is vascular steal. It occurs as a result of the presence a single umbilical artery, increased pressure of abdominal aorta and the subsequent reversal of blood flow in the opposite direction to the tail area of embryo, and is followed by decreased blood supply to the tail area [24]. According to this hypothesis, umbilical artery is originated immediately below the celiac branch of the fetal abdominal aorta and leads to inadequate blood supply and mesoderm developmental defects of tail area, kidney, colon and reproductive organs [25]. Another theory is damage to the tail area mesoderm in gastrulation of the third week of pregnancy that interferes with the formation of the notochord, causes the death of cells in the tail mesoderm and hide gut endoderm and leads to abnormal structures [126.-28]. The third theory mentions sirenomelia as a part of caudal regression syndrome. This theory was formulated after observation of a rare congenital anomaly, including the sacrum abnormalities, defects in the spinal cord, urinary system disorders, misplaced lower extremity and ectopic anus.

The fourth theory states sirenomelia can be a part of VACTERL association. Sirenomelia and VACTERL have similar...
phenotypic features, including vertebral defects (V), anal atresia (A), cardiovascular anomalies (C), Tracheo-Esophageal fistula with esophageal atresia (TE), Radial limb and renal dysplasia (RL) [29]. The fifth theory is the theory of pressure in which embryo tail is afflicted with hypoplasia and body growth disorder under pressure from outside the area, which has not been accepted [30]. Sirenomelia prognosis is fatal. Diagnosis may often be delayed until the end of the second and third trimesters because it is difficult to detect abnormalities by ultrasound due to severe oligohydramnios or lack of amniotic fluid. The cause of sirenomelia is unknown and different causes have been proposed for its incidence. However, maternal diabetes [31,32], genetic predisposition, environmental factors and lack of artery and umbilical artery, blocking blood flow and nutrient supply to the lower half of the body and the limbs [24], have been proposed as possible factors. Abnormalities seen in sirenomelia include degrees of the lower limb connection along with multiple abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems. Oligohydramnios is caused by renal abnormalities of gastrointestinal, urogenital, cardiovascular and muscular-skeletal systems.

In general, there are three different types of abnormalities of the lower extremities in sirenomelia:

a. Symelia apus: There are no feet and toes, legs are fully conjoined and just a femur and a tibia are seen.

b. Unipus symelia: There is a foot (incomplete combination of both legs), but there are two femur, and two tibial and two fibular bones.

c. Symelia dipus: There are two leg-like fins and lower limb connection after knee can be seen [35].

Stocker and Heifetz divided sirenomelia into seven categories:

i. Femur and tibia bones are formed.

ii. Only a fibula bone can be seen.

iii. There is no fibula bone.

iv. The two femur and two fibula bones are conjoined imperfectly.

v. The two femur bones are conjoined imperfectly.

vi. Only a femur and a tibia can be seen.

vii. Only a femur can be seen and there is no tibia.

Currently, diagnosis of sirenomelia is possible by prenatal ultrasound. According to the literature, ultrasound diagnostic keys comprise of oligohydramnios, agenesia of kidney and existence of a fibular bone between two tibial bones. However, sirenomelia is a severe form of unknown caudal regression. Severe oligohydramnios can sometimes prevent correct diagnosis of fetal abnormalities and decision for miscarriage. Because this abnormality is fatal, prenatal ultrasound for early detection and timely medical termination of pregnancy seems necessary to reduce the high-risk pregnancy and maternal stress.

References


