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Sirenomelia: A case report

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Abstract

Sirenomelia also known as mermaid syndrome is a partial or complete fusion of lower extremities associated with visceral anomalies. It is a rare anomaly with a poor prognosis. Maternal age less than 20 years, maternal diabetes mellitus, and monozygotic twinning are some of the known risk factors. Diagnosis can be made via antenatal ultrasound or typical physical appearance after birth. A 2200 g baby was born from 18-year-old non-consanguineous mother via assisted breech delivery. The baby had fused lower limbs with 10 toes, absent external genitalia, and a single umbilical artery. It was small for gestational age. The baby was passed away after 30 min of birth. Young maternal age (18 years) was the identified risk factor for sirenomelia in this case. We recommend an early routine ultrasound anomaly scan in all pregnant women particularly for early detection and termination of pregnancy as the prognosis is poor. Avoiding teenager pregnancy and strict control of blood sugar in diabetic mothers can decrease this anomaly.

Keywords

Fused limbs, mermaid syndrome, sirenomelia

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Introduction

Sirenomelia also known as mermaid syndrome is a fusion of lower extremities.[1] It is a rare and fatal congenital anomaly with an incidence rate of 0.8–4 per 60,000 to 100,000 pregnancies.[2–4] The exact etiologies are unknown, but maternal diabetes mellitus, teratogenic drugs, genetic susceptibility, vascular hypoperfusion, cocaine, landfill water, and maternal age less than 20 years or greater than 40 years are known risk factors for this anomaly.[5–8] The possible mechanism for the failure of separation of extremity bud from the primordial cells is due to: a developmental anomaly in the veins feeding the lower extremities and an anomaly in mesodermal cell migration.[5,7] It can occur in any ethnic group. Sirenomelia is more common in monozygotic twins and males.[3,9]

Common features of mermaid syndrome are a partial or complete fusion of lower limbs characterized by a mermaid-like appearance.[3,10] Common associated anomalies with sirenomelia are absent external genitalia, ambiguous genitalia, imperforate anus, rectal atresia, absent urinary bladder, single umbilical artery, renal agenesis, esophageal atresia, omphalocele, pulmonary hypoplasia, cardiac defect, diaphragmatic hernia, lumbosacral/pelvic bone abnormities, and spina bifida.[2,6,9,11,12] Even though sirenomelia manifestation may overlap with caudal regression syndrome (CRS) and VACTERL association, they are different entities.[13–16] Sirenomelia is classified into seven types based on skeletal structures of the lower limb.[17]

More than half of sirenomelia cases end with stillbirth and those born alive usually die within a day or two of birth because of complications associated with a genitourinary, cardiac, respiratory, neurologic, or gastrointestinal associated malformation.[9,11,18] We report a singleton baby with sirenomelia syndrome born to a teenage mother from Bahir Dar, Ethiopia.

Case presentation

History

An 18-year-old primigravida mother was referred from the health center with a diagnosis of the latent first stage of labor and breech presentation. She had four antenatal care (ANC) follow-up at the local health center. Her blood group is B positive. Provider initiative counseling and testing for HIV (PICT), Venereal disease research laboratory (VDRL), and Hepatitis B surface antigen (HBSAg) test was negative.

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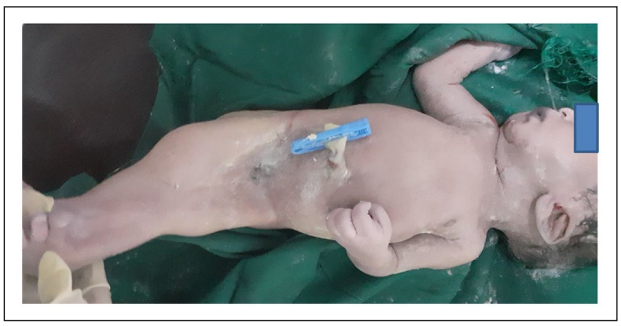

Figure 1. Fused lower limbs with visibly separated toes and absent external genitalia (mobile phone photograph).

No drug was taken during pregnancy other than iron and folic acid supplementation. An antenatal ultrasound study was not done. Otherwise, she had no history of excess alcohol intake or cigarette smoke exposure. She had no self or family history of diabetes. There was no antepartum complication. The onset of labor was spontaneously at the gestational of 40 weeks from Last normal menustrual period (LNMP). The duration of labor and rupture of the membrane were 12 and 4 h, respectively. The mother delivered a single baby with fused legs weighing 2200 g with APGAR score 4 and 6 at the 1st and 5th minute, respectively, via assisted breech delivery in Addis Alem Hospital, Bahir Dar.

Physical examination

The newborn was resuscitated for 20 min. The birth weight to gestational age was below the 10th centile (small for gestational age) on the Lubchenco curve. The baby had fused lower limbs and non-fused five toes at each side of distal feet which fused on the plantar surface. External genitalia were absent and cannot differentiate sex. It has also visible urethral meatus at the junction of the trunk and extremities. There was no anal opening or dimple. There was also a single umbilical artery. The upper part of the body was normal (Figure 1).

Laboratory test and treatment

The newborn passed away after 30 min of birth due to cardiac and respiratory arrest. Internal abnormalities could not be evaluated as the baby died soon and lack of autopsy service in the hospital. The mother's oral glucose tolerance test result was normal. The mother was discharged with no postpartum complications. The mother was advised to have antenatal care at the hospital level where an ultrasound scan is available in the next pregnancy.

Discussion

Sirenomelia is an abnormal development of the caudal body of a fetus with partial or complete fusion of the lower extremity. It is also known as mermaid syndrome.[1,19] Sirenomelia was first described by Rocheus and Polfyr Way in the 16th century. Duhamel in 1961 defined the anomalies of mermaid syndrome and described it as the most severe form of CRS. Sirenomelia is a multisystem severe malformation usually involving the gastrointestinal, genitourinary, cardiovascular, and musculoskeletal systems.[19]

It is a rare and fatal congenital anomaly with an incidence rate of 0.8–4 per 60,000 to 100,000 pregnancies.[2–4] There are approximately 300 cases reported in the literature so far. About 10%–15% of cases occur in twin births, most often monozygotic twins.[7] Sirenomelia is more common in monozygotic twins and males. The risk of occurrence in one of two monozygotic twins is 100–150 times more than in singletons.[3,6,9] The male to female ratio is 2.7–3:1.[5,20] It can occur in any ethnic group.[6,9]

The exact cause of sirenomelia is unknown. Researchers believe that both environmental and genetic factors may play a role in the development of this disorder. Most cases appear to occur randomly for no apparent reason (sporadically), which suggests environmental factors or a new mutation. Most likely, sirenomelia is multifactorial, which means that several different factors may play a causative role.[20]

Poorly controlled maternal diabetes is a known maternal disease to be associated with sirenomelia. However, only ~0.5%–3.7% of sirenomelia cases have been reported in diabetic mothers.[2] It is thought that free oxygen radicals, whose production increases in maternal diabetes, exert a teratogenic effect in embryonic development leading to this anomaly.[2,3,6,21] But in our case, there was no maternal diabetes mellitus.

Maternal age below 20 years is strongly associated with sirenomelia as in our case (18 years old). This is the only identified risk for this anomaly in this case. Maternal age above 40 years is also a risk factor for this anomaly.[22]

Teratogens like retinoic acid, cadmium, and cyclophosphamide have been reported to cause sirenomelia in mice. Cocaine, landfill water, organic a solvent of fat, and appetite suppressors (diethylpropion) have been implicated in some cases of sirenomelia in humans.[5–8] So far, no chromosomal abnormalities have been reported causing sirenomelia in humans.[2] In animal models, several genes have been found to cause or be associated with sirenomelia. The *srn* (siren) gene is observed to cause hindlimb fusion in homozygous mice.[22] Mice with knockouts or mutations in both Tsg1 and Bmp7 can also have hindlimb fusion.[23–25] In the world literature, there are data for two cases of sirenomelia in one family. This report suggests a genetic basis for sirenomelia with a Mendelian inheritance pattern of 50% second generation incidence in offspring.[26]

There are two possible mechanisms for the failure of separation of extremity bud from the primordial cells. The first is due to a single large artery (vascular steal theory) arising from high in the abdominal cavity, which assumes the function of the umbilical arteries and diverts nutrients from the caudal end of the embryo distal to the level of its origin. The stolen vessel derives from the vitelline artery complex, an

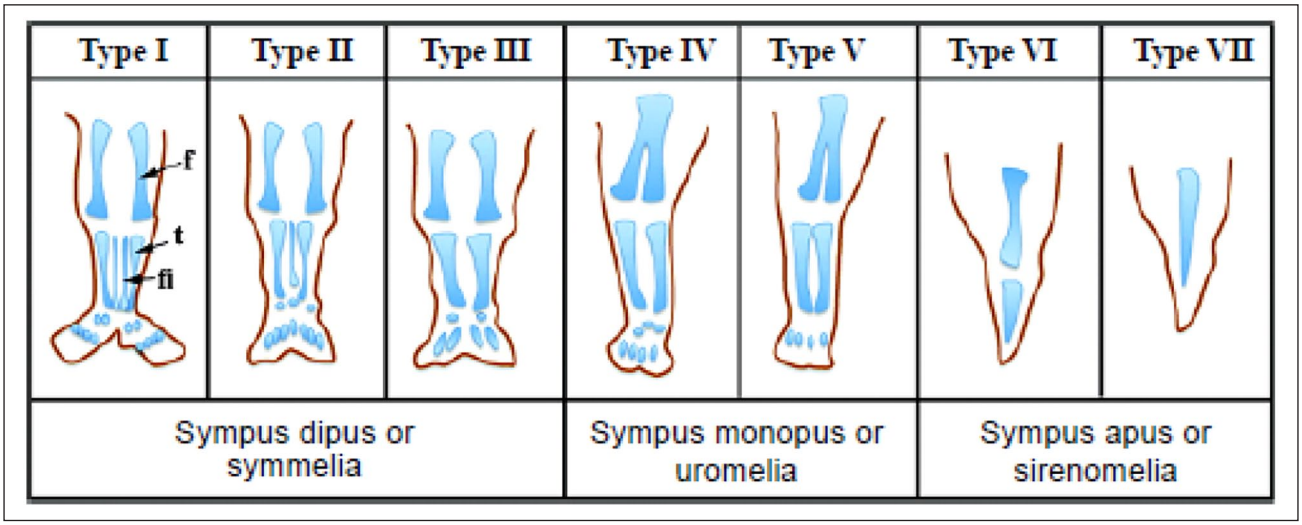

Figure 2. Classification of sirenomelia according to Stocker and Heifetz.

early embryonic vascular network that supplies the yolk sac. Arteries below the level of this stolen vessel are underdeveloped and tissues dependent upon them for nutrient supply fail to develop, are malformed, or arrest in some incomplete stage. The other possible mechanism is an anomaly in mesodermal cell migration.[5,7,11,18]

Common features of mermaid syndrome are a partial or complete fusion of lower limbs characterized by a mermaid-like appearance.[3,10] Our case had fused lower extremities, imperforate anus, absent external genitalia, single umbilical artery, and was small for gestational age. Our case had typical physical features of the sirenomelia syndrome. Other associated anomalies of this syndrome are ambiguous genitalia, rectal atresia, absent urinary bladder, renal agenesis, esophageal atresia, omphalocele, pulmonary hypoplasia, cardiac defect, diaphragmatic hernia, lumbosacral/pelvic bone abnormities, and spina bifida.[2,6,9,11,12] Sirenomelia can be classified into seven types based on skeletal structures of the lower limb as shown in Figure 2.[17] In our case, the type of sirenomelia is likely to be type II based on the morphological appearance of the hindlimb. But to X-ray or CT scan imaging is needed to classify the type of sirenomelia perfectly.

The diagnosis can be made with antenatal ultrasound before birth as early as 14 weeks of gestational age.[21] Patients with caudal regression may have similar findings of sirenomelia on an antenatal sonogram.[13] Previously, sirenomelia was thought to be a severe form of sacral agenesis/CRS, but more recent research confirms that these two conditions are separate anomalies. The presence of two umbilical arteries, non-lethal renal anomalies, non-fused lower limbs, abdominal wall defects, and abnormalities of tracheoesophageal tree, neural tube, and heart differentiate CRS from sirenomelia. Sirenomelia causes bilateral lethal renal anomalies and severe oligohydramnios associated with severe pulmonary hypoplasia, whereas fetuses with caudal regression demonstrate normal or increased amniotic fluid with non-lethal renal anomalies and two umbilical arteries. The etiopathogenetic mechanisms are also different in CRS and sirenomelia. CRS represents abnormalities in blastogenesis and is due to disturbances of a primary embryonic field. The entire embryo during blastogenesis (days 1–28) represents the primary field.[14] The defects of the primary field lead to failure of axis formation, midline, primitive node and streak, gastrulation, segmentation of the paraxial mesoderm, laterality determination, and cardiac formation. The pattern of single or multiple malformations occurring in association with lower vertebral column maldevelopment is governed by perturbations in the morphogenic signaling pathways, which are involved in late blastogenesis and the development of secondary fields. Sirenomelia may be caused by abnormalities in blastogenesis that affect the distribution of blood to the caudal region of the fetus. The "vascular steal theory" indicates that a single large artery assumes the function of the umbilical arteries, thus diverting blood flow from the caudal portion of the embryo to the placenta.[13–15]

Even though many of the concomitant abnormalities in sirenomelia fetuses are identical to those of the VACTERL association, which is associated with certain genetic factors such as mitochondrial dysfunction, chromosomal deletions or duplications, and mutations in *HOXD13, ZIC3, PTEN, FANCB*, and *FOXF1* genes, lower extremities are not fused in isolated VACTERL association.[16] In our case, the diagnosis of sirenomelia was made after birth based on the typical feature of sirenomelia syndrome on physical examination.

The prognosis of sirenomelia is poor with an average survival of less than 1 week. More than half of sirenomelia cases end with stillbirth and those born alive usually die within a day or two of birth because of complications associated with a genitourinary, cardiac, respiratory, neurologic, or

gastrointestinal associated malformation.[9,11,18] Our case died soon after birth due to cardiorespiratory arrest. We report a singleton baby with sirenomelia syndrome born to a teenage mother from Bahir Dar, Ethiopia. We recommend an early routine anomaly scan in pregnant women in general and mothers with related history in particular, as the recurrence risk is 3%–5%.[27,28]

Conclusion

Sirenomelia/mermaid syndrome is a rare but fatal anomaly. Typical manifestations are a partial or complete fusion of lower limbs, genitourinary anomaly, and pulmonary malformations. Young maternal age is risk factors of this anomaly. A routine early second-trimester ultrasound examination is recommended to make the diagnosis of sirenomelia.

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Informed consent

Informed written consent was taken from the mother for possible publication without listing her name or revealing her identity.

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