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AN INCIDENTAL POST AUTOPSY ASSOCIATION OF SIRENOMELIA WITH BILATERAL CONGENITAL ADRENAL AGENESIS: AN UNREPORTED ENTITY

Gynaecology

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ABSTRACT

Sirenomelia is a rare lethal congenital malformation and characterized by lower limb fusion, sacral and pelvic bony anomalies, absent external genitalia, imperforate anus, and renal agenesis or dysgenesis. Controversies on its etiopathogenesis persist and this developmental failure is supported by most recent theory of vascular pathogenesis resulting from a vitelline arterial steal which results in diversion of blood flow from caudal structures. Based on presence of skeletal elements in the thigh and leg, Stocker and Heifetz classified sirenomelia into seven different types.
A 26 years primigravida at 19 weeks gestation came with the report of multiple congenital anomalies in the fetus. She opted for termination of pregnancy. The fetus post expulsion was found to be Sirenomelia type VI. At post mortem examination, it was detected that the fetus had well-developed renal organs associated with bilateral adrenal agenesis. This variant in Sirenomelia has not been reported previously.
This case reinforces the role of the perinatal autopsy in stillborn anomalous fetuses, which could help us to verify the antenatal diagnosis, detect many more associated syndromic features, obtain tissue for histologic, molecular, or biochemical analysis and direct genetic testing and counseling sessions for parents.

KEYWORDS

Sirenomelia, Mermaid syndrome, Congenital malformations, Fetal autopsy

INTRODUCTION:

Sirenomelia is a rare developmental anomaly of the caudal region of the body with varying degrees of lower limb fusion, appears like a mermaid's tail. It is a rare congenital malformation and has an incidence of 0.8 to 1 case per 1,00,000 births and more common in males with male to female ratio being 3:1 (Källén et al., 1992; Nokeaingtong et al., 2015). The term "Sirenomelia" (Latin-Siren + Melia), here "Siren" means "a partly female creature of Greek legend" and "Melia" means "limb". The term Mermaid sequence is derived from word "Mermaid" (Mere-sea + maid-girl/young woman) which means imaginary aquatic creature with the head and upper body of a human female and the tail of a fish. It is seen to have resemblance to the mermaid of ancient Greek mythology (Kattel et al., 2018).

Sirenomelia has been reported with associated anomalies involving multiple systems like urogenital, respiratory and alimentary tract. We present a case of sirenomelia with well-developed renal organs and a rare association of adrenal agenesis which was detected incidentally at post-mortem examination.

CASE REPORT:

A 26 year primigravida at 19 weeks of gestation was admitted in the labor room for medical termination of pregnancy due to multiple fetal anomalies. The woman was married and had no history of any past illness, addictions or medications. Her family history was insignificant. Her antenatal Hb%, blood glucose, thyroid status was normal.

The first transvaginal sonographic examination at fifth week showed two intrauterine chorionic sacs with no embryonic details observed in one sac. Sonographic examination at 10 weeks revealed disappearance of a twin with single fetus inside uterus with crown rump length corresponding to 10 weeks and 5 days. The woman had not experienced any symptoms of vanishing twin syndrome. Nevertheless, no gross structural abnormalities were noticed on that sonographic examination.

The patient first attended our institution at 19 weeks gestation. On per abdomen examination, uterus was around 18 week size. A transabdominal sonography demonstrated a single live fetus with anhydraminos, malformed pelvis with abnormally positioned single femur with length appropriate to 19 weeks. The fetal urinary bladder, kidneys, lower lumbosacral spine could not be visualized. (Fig.1) The anatomic scan was limited because of severe oligohydramnios.

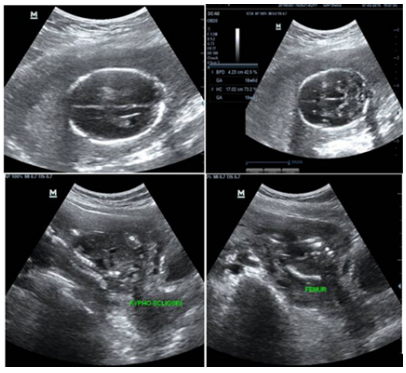

Fig. 1 The Ultrasonography Images Showing Normal CNS Structure, Anhydramnios, Defect In Development Of Spine And Lower Pelvic Bone with a single femur.

The couple was informed about the presence of multiple lethal anomalies and its prognosis, they opted for second trimester medical termination of pregnancy. She expelled a grossly anomalous fetus weighing 315 grams, measuring 23 cm in length with chest circumference of 16 cm. Placenta appeared normal, central insertion of cord and no retroplacental clot.

The appearance of the foetus was normal above the level of umbilicus except potter facies. Umbilical cord was short (30 cm) and had a single umbilical artery. There was a single fused lower tapering extremity with absence of external genitalia, anal orifice and meningocele at lumbo sacral region. (Fig.2)

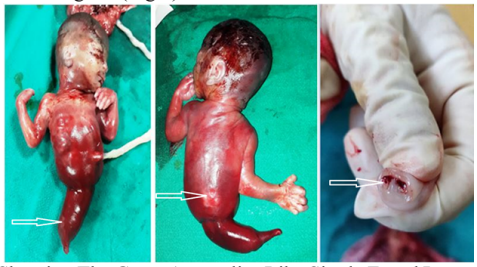

Fig.2 Showing The Gross Anomalies Like Single Fused Lower Limb, Absent External Genitalia And Imperforate Anus

The sex could not be determined as the external genitalia were absent. The infantogram showed lower lumbosacral agenesis and absent pelvic bones. A single large lower limb (thigh) with a single femur was seen in the middle resulting from fusion of both the lower extremities. The lower leg was rudimentary with partially formed tibia and fibula. (Fig.3)

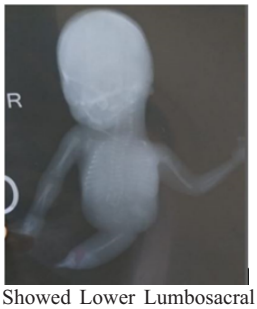

Fig. 3 Infantogram Showed Lower Lumbosacral Agenesis, Absent Pelvic Bones, A Single Femur, Rudimentary Fused Lower Limb Bones

Autopsy report showed the fetus to have normal brain and heart, bilateral hypoplastic lungs, bilateral normal renal cortex as well as cortico-medullary junction, bilateral adrenal agenesis, abdominal aorta supplying all organs upto the large intestine, undefined external genitalia, bilateral gonad seen intraabdominally, absence of ureters and urinary bladder, bilateral pelvic bones, lumbosacral vertebral agenesis and single umbilical artery in the umbilical cord. (Fig.4)

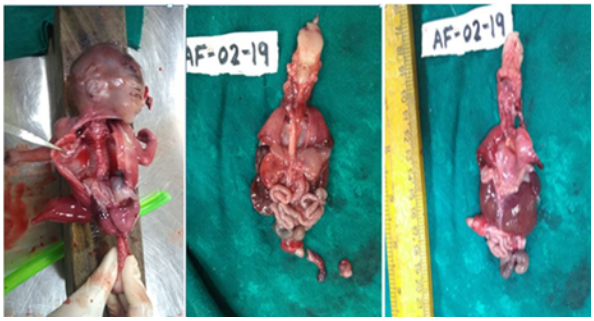

Fig.4 Autopsy showed the fetus to have bilateral hypoplastic lungs, bilateral adrenal agenesis, abdominal aorta supplying all organs upto the large intestine, undefined external genitalia, bilateral gonad seen intraabdominally, absence of ureters and urinary bladder

On histopathological evaluation umbilical cord showed single umbilical artery and vein. Gonad like tissue on autopsy confirmed it to be testis. Membrane cultures showed to have no microbial growth. Karyotype of the fetus showed 44 autosomes and two X chromosomes.

DISCUSSION

Sirenomelia was first described by Rocheus and Polfyr in sixteenth century, Duhamel defined all the associated anomalies of mermaid syndrome and described it as the most severe form of caudal regression syndrome (Duhamel et al., 1961). It had been reported with various anomalies like vertebral and central nervous system, anal atresia, cardiac defects, tracheo-esophageal fistula, esophageal atresia, absent kidneys and bladder, hypoplastic lungs, single umbilical artery.

The associated risk factors for sirenomelia are decreased maternal age (< 20 years) at pregnancy, maternal diabetes, maternal drug abuse such as cocaine, exposure to cyclophosphamide, lead (Kattel et al., 2018), artificial reproductive methods like ICSI and in twin gestation, the incidence in monozygotic twin is 100 -150 times higher than dizygotic twin (Bakhtar et al., 2006; Zakin et al., 2005). However, in our case there was no history of diabetes or drugs, moreover, she had twin gestation which underwent single fetal demise in early at 10 weeks.

The precise etiology of sirenomelia is not known but many theories have been proposed like vascular steal hypothesis, defective blastogenesis theory or the most severe form of Caudal Regression Syndrome. Presently the most accepted theory is the theory of primary developmental defect during blastogenesis.

In our case, the possible pathogenetic mechanism is vascular steal theory, this was supported by the autopsy reports of partial lower limb agenesis, lower lumbosacral agenesis, absence of urinary bladder, presence of intraabdominal gonads, presence of single umbilical artery.

Stocker and Heifetz classified sirenomelia into type I to type VII, according to the presence of skeletal elements in the thigh and leg. We found our case to be Type VI. (Stocker et al., 1987). (Table.1) Antenatal diagnosis of this universally lethal condition is desirable so that possible termination of pregnancy can be offered at the earliest.

Table 1. Classification Of The Sirenomelic Sequence Adapted From Stocker And Heifetz

Type	Characteristic
I	All thigh and leg bones are present
II	Single fibula
III	Absent fibula
IV	Partially fused femurs, fused fibulae
V	Partially fused femurs
VI	Single femur, single tibia
VII	Single femur, absent tibia

Congenital adrenal agenesis is an extremely rare condition wherein the adrenal glands fail to develop. The true incidence and pathogenesis of congenital adrenal agenesis is unknown. Majority of the reported cases of adrenal agenesis were undiagnosed on antenatal imaging, as in our case and were detected incidentally at postmortem examination.

The reasons for the difficulty achieving a prenatal diagnosis of adrenal agenesis may include anatomic variation, the retroperitoneal suprarenal location of the adrenal glands, a lack of knowledge of the condition or poor visualization in the context of oligohydramnios (D'Arcy et al., 2014).

Among the heterogenous presentations of adrenal agenesis, our case is a rare presentation of sirenomelia with well-developed renal organs and bilateral adrenal agenesis. Literature search did not reveal any case of bilateral adrenal agenesis with sirenomelia making this case a rare entity. Even though the common developmental pathway is shared between adrenal cortex, kidney, adrenal glands and gonads but there are case reports of bilateral adrenal agenesis with normal development of kidneys and gonads (Biason-Lauber et al., 2000). Similar finding was observed in our case, which could be due to complexity in adrenal development that involves at least 69 genes encoding for multiple transcription factors, signaling molecules, steroidogenic hormones, it is likely that more than one gene is involved in the pathogenesis of adrenal agenesis (Else et al., 2005). One of our shortcomings was our failure to conduct any further genetic testing in adrenal agenesis due to lack of facility.

In conclusion, we are reporting a case of sirenomelia with well-developed renal organs and a rare association of congenital adrenal agenesis which was detected incidentally during postmortem examination. Thereby, we mentioned the importance of doing postpartum autopsy in stillborn anomalous fetuses, which could help us to verify the antenatal diagnosis, detect many more associated syndromic features, obtain tissue for histologic, molecular, or biochemical analysis and direct genetic testing and counseling sessions for parents.

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No competing financial interests exist.

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