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BRIEF COMMUNICATION

Prenatal Diagnosis of Sirenomelia: Cluster of Three Cases

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Abstract Sirenomelia is an extremely rare anomaly characterised by varying degrees of fusion of lower limbs. Anomalies involving uro-genital tract, colo-rectal atresia and vertebral defects are often associated. Prognosis largely depends upon concomitant visceral malformations as well as the degree of fusion defect. Classical sirenomelia is incompatible with life although there are few report of survivors. Prenatal diagnosis, though possible, is difficult to make due to associated anhydramnios and anomalies. Ultrasound is the main diagnostic modality with fetal MRI playing a complementary role. We describe three cases of fetal sirenomelia that presented within a span of 1 year and propose possible vascular insult as the cause.

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Introduction

Sirenomelia (mermaid syndrome) is a rare congenital fetal anomaly characterised by complete or partial fusion of lower limbs. The incidence of the condition is estimated to be 0.01–0.16 per 10,000 live births and has a male to female ratio of 3:1 [1]. It is usually associated with malformations involving other organ systems like uro-genital, colo-rectal and spinal defects. Classical sirenomelia is incompatible with life and prognosis largely depends on concomitant visceral malformations. Etiology of the condition is still not established, although theories like vascular insult and genetic factors have been proposed [2]. There is also a considerable overlap of features between sirenomelia and VACTERL and caudal regression. A wide spectrum of fusion abnormalities can be seen as depicted in the classification system proposed by Stocker [3] (Table 1). We describe three cases of fetal Sirenomelia associated with renal and colo-rectal anomalies.

Case 1

A second gravida with no live issues and history of previous cesarean section for bicornuate uterus was referred in view of anhydramnios. Antenatal history was unremarkable with no significant drug intake or any maternal illness, including diabetes. Ultrasound showed a fetus of 17 weeks gestation, anhydramnios, two-vessel cord and non-

Table 1 Stocker and Heifetz classification of sirenomelia [2]

Type 1	All thigh and leg bones present		Sympus dipus or symmelia
Type 2	Single fibula		
Type 3	Absent fibulae		
Type 4	Partially fused femurs, fused fibulae		Sympus monopus or uromelia
Type 5	Partially fused femurs, absent fibulae		
Type 6	Single femur, single tibia		Sympus apus or sirenomelia
Type 7	Single femur absent tibiae		

visualised bladder and kidneys. Lower limbs were closely placed and femora appeared to be thick. As the visibility was very poor due to nil liquor and crowded appearance fetal MRI was done which confirmed sirenomelia. Parents opted for termination after counselling about the poor prognosis and postnatal autopsy was done. Fetus had fused lower limbs with the leg tapering to end without feet. Perineum was smooth with no identifiable external genitalia and urethral-ano-genital openings. Cord had single umbilical artery. On internal examination, there was right renal agenesis, left kidney was more medially located, small, cystic and dysplastic. Bladder was absent and there was agenesis of the bowel beyond ascending colon. There was severe pulmonary stenosis on cardiac dissection (Table 2 and Fig. 1). Abdominal aorta had a straight course and continued into the pelvis and fused limbs without branching into iliac vessels.

Case 2

A primigravida was referred at 19 weeks of gestation with oligohydramnios. She had conceived following ovulation induction with clomiphene citrate for infertility. There were no significant antenatal risk factors, no history of maternal drug intake or medical disorders and her blood sugars were normal. Ultrasound showed anhydramnios, single umbilical artery, bilateral dysplastic kidneys, non-visualised bladder and small stomach bubble. Lower limbs appeared to be very closely placed. Pregnancy was terminated in view of projected dismal prognosis. On autopsy, there was single fused lower limb which had a tapering end beyond knee joint. Perineum was smooth with no external genitalia and urethral-anal openings. Right kidney, ureter and adrenals were absent. Left kidney was more medially located and small with cystic surface. There was colo-rectal-anal atresia beyond the ascending colon (Table 2 and Fig. 2).

Case 3

A 28 year old multigravida was referred at 30 weeks of gestation as the fetus had multiple congenital defects on ultrasound. Her past medical records and family history were normal and there were no significant extrinsic risk factors. There was no history of exposure to radiation or drug intake. She was not a known diabetic and had no other medical disorders. The antenatal ultrasound done in our institute showed severe oligohydramnios, single umbilical artery, bilateral multicystic dysplastic kidneys, segmented vertebral bodies and fused femoral bones, raising the possibility of sirenomelia. There was ventricular septal defect and pulmonary stenosis on fetal ECHO. In view of multiple malformations, labor was induced after counseling the parents about the dismal outcome and a stillborn fetus weighing 1400 g was born. External examination revealed completely fused lower limbs, Potter's facies, left upper limb hypoplasia, absence of right thumb, rudimentary left upper limb no ano-genital openings. Postmortem skiagram

Table 2 Salient clinical features

Parameter	Case 1	Case 2	Case 3
Liquor	Anhydramnios	Anhydramnios	Anhydramnios
Cord	2 vessels	2 vessels	2 vessels
Lower limbs	Completely fused lower limbs with single thigh and leg tapering to end without feet or toes	Completely fused lower limbs with single thigh and leg tapering to end without feet or toes	Almost completely fused thigh and legs with a groove in between. Fused feet with 6 toes
Upper limbs	Normal	Normal	Rudimentary left upper limb, absence of right thumb
Facies	Long philtrum	Long philtrum	Potter's facies
Perineum	Smooth with no ano-genital openings. Irregular bulge at lower back	Smooth with no ano-genital openings. Dimple at lower back	Smooth with no ano-genital openings Skin tags at lower back
GIT	Colo-rectal agenesis, blind ending ascending colon	Colo-rectal agenesis, blind ending ascending colon	Dilated colon ending blindly on the posterior aspect of persistent cloaca
Urinary tract	RK, ureters and bladder absent. Left cystic dysplastic kidney	Right side kidney, ureter and adrenal absent and left cystic dysplastic kidney	Bilateral multicystic dysplastic kidneys
Heart	Pulmonary stenosis	Normal	VSD + pulmonary stenosis
Aorta	Continuing straight into pelvis and down to the fused limbs without bifurcating into iliac arteries	Continuing straight into pelvis and down to the fused limbs without bifurcating into iliac arteries	Continuing straight into pelvis and down to the fused limbs without bifurcating into iliac arteries
Gestation at delivery	17 weeks	19 weeks	30 weeks
Fetogram/ X-ray	Single femur, single tibia and sacral dysgenesis	Single femur, single tibia and sacral dysgenesis	Absent right radius, femurs partially fused, joined fibulae and sacral dysgenesis
Stocker class	VI	VI	IV

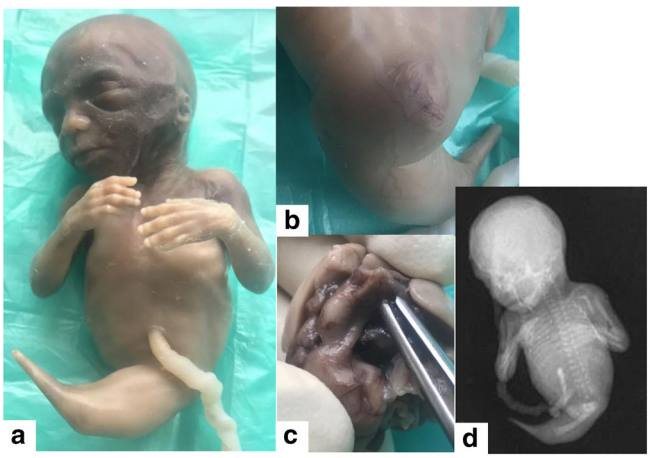

Fig. 1 Autopsy and radiological findings in Case 1

Case 1: Sirenomelia fetus with,

(a) Fused lower limbs with tapering end and smooth perineum with no ano-genital openings

(b) irregular bulge over lower back

(c) Pulmonary stenosis

(d) X-ray showing single femur and Tibia.

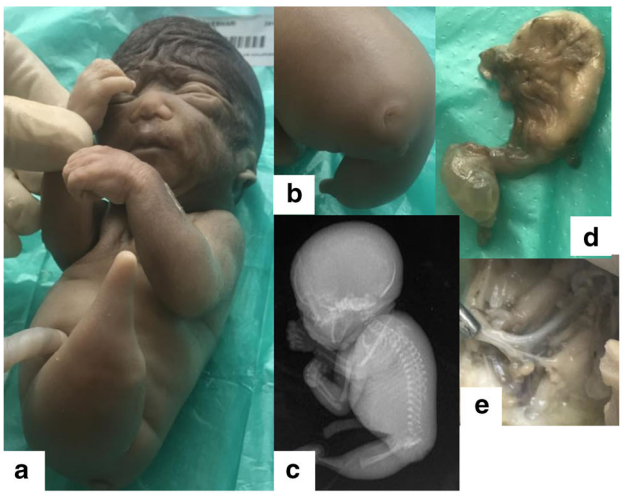

Fig. 2 Findings in Case 2

Case 2: Sirenomelia similar to case 1 with,

(a) fused lower limbs with a, (b)dimple over lower back

(c) X-ray showing single femur and Tibia.

(d) Large adrenal and small cystic dysplastic kidney.

(e) Aorta continuing into pelvis and fused limb without branching into iliac vessels.

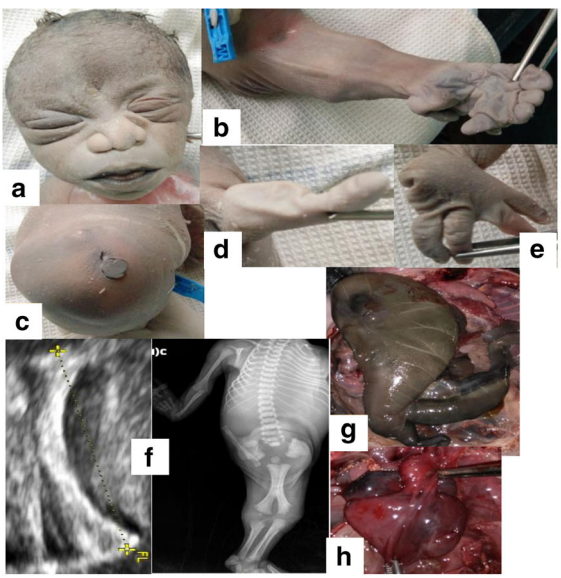

Fig. 3 Ultrasound, autopsy and radiological findings in Case 3

Case 3: (a) Potter facies, (b) fused lower limbs, (c) skin tags at lower back, (d) rudimentary left upper limb, (e) absent right thumb, (f) USG & X-ray: Fused femurs, 2 Tibiae, (g) Dilated colon and (h) Pulmonary stenosis.

showed partially fused femoral bones, sacral dysgenesis and absent right radius (Fig. 3). Autopsy revealed dilated and blind ending colon, bilateral cystic and enlarged kidneys, rudimentary tags as external genitalia, persistent cloaca and pulmonary atresia. Thus sirenomelia as part of VACTERL association was diagnosed.

Discussion

Sirenomelia is replacement of normally paired lower limbs by a single midline limb. This extremely rare anomaly has features that overlap with the caudal regression syndrome and VACTER malformation [4]. We encountered three such cases presenting in fetal life within a span of 1 year. Two of these were terminated in second trimester while one delivered preterm and expired immediately after birth. Sirenomelia can have varying degrees of lower limb fusion and prognosis varies with the extent of merger and associated anomalies. Seven types of fusion defects have been described by Stocker and Heifetz with Type 1 being the mildest and Type 7 the most severe form [3, 5]. Two of our cases (case no. 1 and 2) belonged to class 6 as they had single femur and tibia. Case 3 was grouped under Type 4 as the femurs were partially fused with joined fibulae. Associated anomalies involving uro-genital, colo-rectal and vertebral structures are common. Single umbilical artery and renal anomalies are almost invariably present. All our cases had single umbilical artery, renal and colo-rectal malformations. We have previously reported Case 3 which had multiple anomalies largely overlapping with that of VATER spectrum [6]. This fetus had upper limb defects, pulmonary stenosis, multicystic dysplastic kidneys and vertebral defects.

The underlying etiology is largely unknown while multiple hypotheses have been proposed. The most widely accepted ones are the vascular steal hypothesis which attributes the anomaly to single umbilical artery diverting the blood away from caudal mesoderm and defective blastogenesis involving retinoic acid (RA) or bone morphogenetic protein (Bmp) signaling [2, 7]. These cases are supportive of the vascular theory as the underlying cause for sirenomelia. All the cases described here had single umbilical artery and continuation of aorta into pelvis and fused limb without branching into common iliac arteries. Two cases also had severe pulmonary stenosis which could have further added to the state of hypo-perfusion predisposing the fetuses to multiple anomalies. Twin pregnancies and maternal diabetes are considered to be risk factors for sirenomelia but none of the mothers described here were diabetic.

Diagnosis of sirenomelia in fetal life is hampered by anhydramnios. Ultrasound is the main diagnostic modality aided by fetal MRI. Closely placed lower limbs which do not move independently and abnormally thick femur during biometry should raise the suspicion of fused limbs. There are a few case reports and series on prenatally diagnosed sirenomelia [8]. The condition is usually incompatible with life due to associated visceral anomalies although there are few reports of survivors. Thus a detailed scan for other associated malformations should always be done.

Conclusion

Sirenomelia is a rare and fatal congenital anomaly characterised by varying degrees of fusion of lower limbs. Antenatal diagnosis is possible despite the difficulty posed by anhydramnios and associated malformations. A though search for other anomalies should be done as the prognosis is largely dependent on them.

Compliance with Ethical Standards

Conflict of interest All the authors agree that there are no conflict of interest and there were no ethical issues involved. All the cases were part of project for which ethical clearance had been obtained from the institute.

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