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Sirenomelia with upper limb malformation: a case report and review of the literature

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Summary

Sirenomelia sequence is a rare lethal pattern of congenital anomalies characterized by fusion of the legs and a variable combination of visceral abnormalities. Some cases accompanied with rare malformations have been reported. In this article, the authors report a case of sirenomelia with upper limb malformations and a review of the literature.

Key words: Sirenomelia; Upper limb malformation; Prenatal diagnosis.

Introduction

Sirenomelia is a rare congenital malformation characterized by different degrees of fusion of the lower extremities in association with sacral agenesis, imperforate anus, colonic or rectal atresia, renal agenesis, absent bladder, absent internal genitalia, and a single umbilical artery, with a reported incidence ranging between 1 /24,000 and 1/67,000 births [1]. Survival is extremely rare. Prenatal diagnosis of this condition can be accomplished by ultrasound and relies on the inability to demonstrate separate lower limbs or the identification of a single femur. All human cases of sirenomelia analyzed thus far show a variable degree of renal and urethral dysplasia and gastrointestinal anomalies. There are a few documented cases in which sirenomelia have upper extremities defects. In this article, the authors describe and discuss the association of upper limbs malformations along with craniofacial defects in a sirenomelia, rarely reported in mainland China.

Case Report

A 30-year-old woman, gravida 3, para 0, was referred to the present hospital for nuchal translucency screening at 12 weeks' gestation. She reported two spontaneous miscarriages during the first trimester, and the karyotype of the abortus tissue in the second miscarriage identified no chromosomal anomalies. She and her husband were non-consanguineous and healthy. She had no history of drugs and alcoholism. There was no history of maternal diabetes or exposure to teratogens. One of her husband's cousins has sexual deformity. A detailed ultrasound examination was performed. The CRL was 54.5 mm and the NT measurement was 2.1 mm. However, the image of the fetal lower limbs was obscure. She underwent another ultrasound examination at 15 weeks' gestation. A singleton fetus was revealed with the lower extremity completely fused and no foot. Only one femur about 14 mm was found. Single umbilical artery was showed, and a great intra-abdominal vessel continued in the umbilical cord without branching into the normal left and right common iliac arteries (Figure 1-Aa). The amniotic fluid volume was normal. Owing to the gestational age, the assessment of the fetal organs was difficult. These sonographic findings favored the diagnosis of sirenomelia. In addition, there was a cleft lip and palate, as well as lumbosacral kyphoscoliosis with a cyst about 9 x 9 x 9 mm. Most importantly, the ultrasound demonstrated the presence of the abnormal upper limbs with only the ulna in left forearm, and only the humerus in the right upper limb, both hands were fixed with ulnar deviation (Figure 1-Ab).

The patient and her husband were informed of the findings and received genetic counseling and testing. Fetal karyotyping was performed by cordocentesis, which revealed a female karyotype (46, XX, 9qh+). The parents opted for termination of pregnancy. The abortus was delivered weighing 89 g and measuring 17 cm length.

The diagnosis of sirenomelia was confirmed by X-ray at postmortem examination. The ribs, scapulae, and clavicles were normal. Lower limbs were fused and only one femur was noted. It was also found that only the ulna in left forearm and only the humerus in right upper limb with both hypoplastic hands having ulnar deviation (Figure 1-B).

Postmortem studies revealed hemipelvis, single femur, no foot, and single umbilical artery in the umbilical cord originated high from the abdominal aorta (Figure 1-Ca). The external genitalia were absent and the anus was imperforate. The lumbosacral neural tube was defected with myelomeningocele (Figure 1-Cb). Other malformations included absent bladder, and cleft lip and palate (Figure 1-Cc). The upper limbs were hypoplastic and contracted (Figure 1-Cd).

Discussion

Sirenomelia derives its name from the physical resemblance to the mythic mermaid (siren), with lower extremity fusion and abnormal or absent foot structures [1]. ICD-10 lacks a specific code for sirenomelia, which may be coded as

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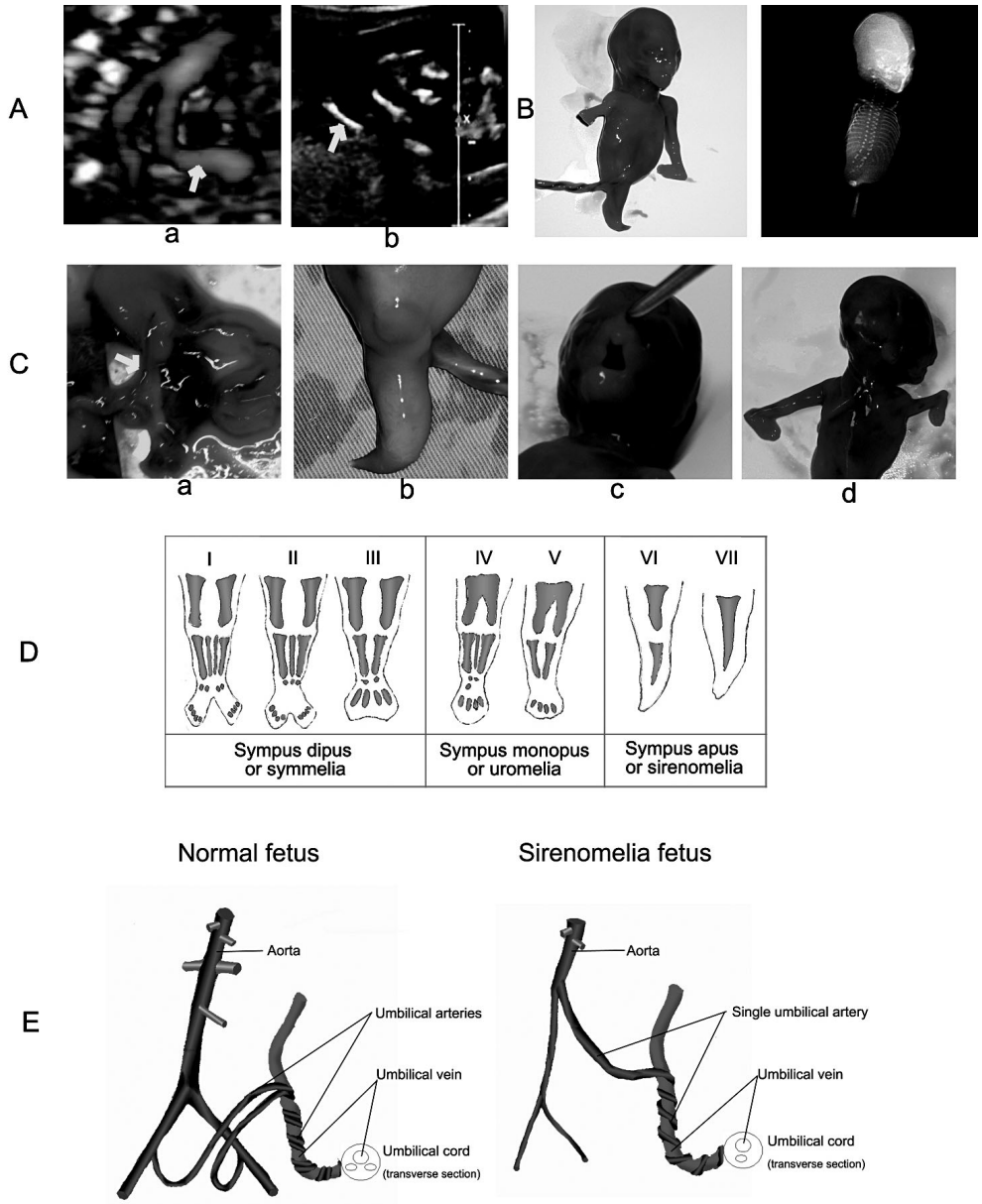

Figure 1. — A. (a): a great intra-abdominal vessel; (b): only one femur in the lower extremity. B. Photograph and corresponding radiography. C. (a) single umbilical artery originating high from the abdominal aorta. (b) myelomeningocele. (c) a cleft lip and palate. (d) hypoplastic and contracted upper limbs. D. Types of sirenomelia (Stocker *et al.* [7] and alternative nomenclatures). E. Vascular pattern in a normal versus sirenomelia fetus.

Q87.2 "congenital malformation syndromes predominantly affecting limbs"[2]. There are variable associated anomalies of the lower body, including sacral agenesis, imperforate anus, colonic or rectal atresia, renal agenesis, absent bladder, and absent internal genitalia (but not the gonads). Sometimes it also accompanies some rare malformations such as facial dysmorphism, agenesis of corpus callosum, costo-vertebral segmentation defects, anal atresia/stenosis, cardiac malformation, tracheo-esophageal fistula and/or esophageal atresia, renal, and limb anomalies (VACTERL) [3]. Albeit at a much lower frequency, sirenomelia is also associated with malformations of the upper part of the body, including cleft palate, upper thoracic and cervical vertebral abnormalities, pulmonary hypoplasia, and cardiac defects [4]. Till now there are few detailed cases of sirenomelia with upper limbs malformations reported in mainland China. Here the authors found a sirenomelia fetus accompanied with upper limbs malformations with only the ulna in left forearm and only the humerus in right upper limb with both hypoplastic hands. Lynch and Wright once reported a sirenomelia with limb reduction defects, cardiovascular malformation, and renal agenesis in an infant [5]; the present case overlapped with other malformations, such as a cleft lip and palate, myelomeningocele, et al.

Two separate systems of classifications of sirenomelia have been proposed. One is classified into three types according to the number of feet: sympus dipus, both feet present; sympus unipus, only one foot present; sympus apus,

both feet absent [6]. The other is based on the presence of skeletal elements in the thigh and leg proposed by Stocker and Heifetz [7]: classification I, paired femora, tibiae and fibulae; II, a single fused fibula; III, absent fibula; IV, partially fused femora and single fibula; V, partially fused femora and absent fibulae; VI, single femur and tibia; VII, single femur, and absent tibiae and fibulae (Figure 1-D). The present case belonged to type VII according to Stocker's classification.

The present authors also found single umbilical artery in the umbilical cord arising from the high abdominal aorta which was one of the pathogenic hypotheses of sirenomelia. Stevenson *et al.* proposed the vascular steal theory [8]. Fetuses with sirenomelia almost invariably exhibit single umbilical artery instead of the normal two. Moreover, this artery has an abnormal origin, arising from the high abdominal aorta, usually immediately below the celiac branch, where it always branches into the common iliac artery. Blood is shunted to the placenta by the single umbilical artery, and the vessels distal to this aberrant umbilical artery were underdeveloped and malformed [9] (Figure 1-E). The single umbilical artery has also been referred to as the persistent vitelline artery. In the present case color Doppler was used to prenatal diagnosis of the vitelline artery. Postmortem examination also confirmed its existence.

Another major hypothesis for sirenomelia is direct damage to the caudal mesoderm of the embryo. This damage may occur from extrinsic pressure or overdistension of the neural tube. Other theories propose an influence of teratogenic agents like cocaine or retinoic acid abuse during the first trimester of pregnancy. Genetic factors, such as *HLXB9, sonic hedgehog, patched, brachyury,* receptor of retinoic acid, *CYP26A1, BMP7,* and *twisted gastrulation (tsg)*, appear to play another role [9].

In the karyotyping test the abortus showed a female karyotype (46, XX, 9qh+). It was reported that the sex ratio of male to female was 2.7:1 in sirenomelia [1]. X-linked oligogenes and X-linked mutations are suggested to explain the excess of males. Moreover, 7% of cases are associated with monozygotic twinning, higher than in dizygotic twins or singletons [10].

Since sirenomelia is uniformly lethal, early prenatal diagnosis is required in order to allow termination of pregnancy at an early stage. Both color and power Doppler have been reported as useful to diagnosis this malformation. However, there is only a narrow window, between weeks 8 and 16 of gestation, when the amniotic fluid still depends mainly from maternal production, when visualization of sirenomelia to ultrasound is possible. During the late second trimester, severe oligohydramnios, secondary to renal agenesis or dysgenesis, may hamper a proper evaluation of fetal lower extremities. In those situations, magnetic resonance imaging provides a substitute [10].

In conclusion, sirenomelia is a multisystemic human malformation without explicit etiology. The early diagnosis of this lethal malformation during suitable gestation week is crucial to the treatment plan and termination of pregnancy. Although sporadic case reports and animal models have provided some important insights into the problem and given rise to the pathogenesis, much more work should be done to explore the mechanism and the prevention of sirenomelia in the future.

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