Case report

Sirenomelia with associated systemic anomalies – an autopsy report in a full term neonate

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The mermaid syndrome, also known as sirenomelia, is considered an extremely rare congenital developmental disorder characterized by anomalies of the lower spine and lower limbs. Affected babies are born with partial or total leg fusion. Sirenomelia is thought to affect one in every 60,000 to 100,000 infants.

We report a case of sirenomelia occurring in a 28-year-old multiparous woman, a heavy smoker with gestational diabetes. In the other 5 pregnancies, however, she gave birth to normal babies. The post mortem examination completed the diagnosis, revealing also multiple malformations of several systems: respiratory, gastro-intestinal, genito-urinary and cardiovascular.

In our full term neonate case with grade VI sirenomelia, the presence of a single umbilical artery plus the abdominal aorta with an aberrant trajectory that ends in the umbilical cord differentiates this condition from caudal regression syndrome and also explains the under-development of pelvic organs (secondary to vascular steal phenomena).

Key words: sirenomelia, autopsy, full term neonate.

Introduction

Sirenomelia is a peculiar congenital condition in which the most visible feature is the fusion of the lower limbs, which gives the impression of a mermaid's tail. Severe malformations of the gastrointestinal, genitourinary, cardiovascular and musculoskeletal systems are usually present and the existence of a single umbilical cord artery characterizes this syndrome [1, 2].

Sirenomelia is more frequently referred to as a "mermaid" in mythology, that is, as a female, than as a male counterpart "merman," or Triton type sirenomelia. This is likely due to the more attractive and aesthetic sensual attributes, such as bosom, eyes and hair in the female gender, when external genitalia were omitted [3].

Mermaid syndrome affects males more often than females with a ratio of 2.7 : 1. The exact frequency is still unknown, but sirenomelia is estimated to occur in approximately 1 in 60,000 to 90,000–100,000 births [4, 5]. In 2019, the number of cases of sirenomelia reported so far totalled 300 cases [6].

Stocker and Heifetz (1987) divided sirenomelia into seven kinds based on the number of skeletal ele-

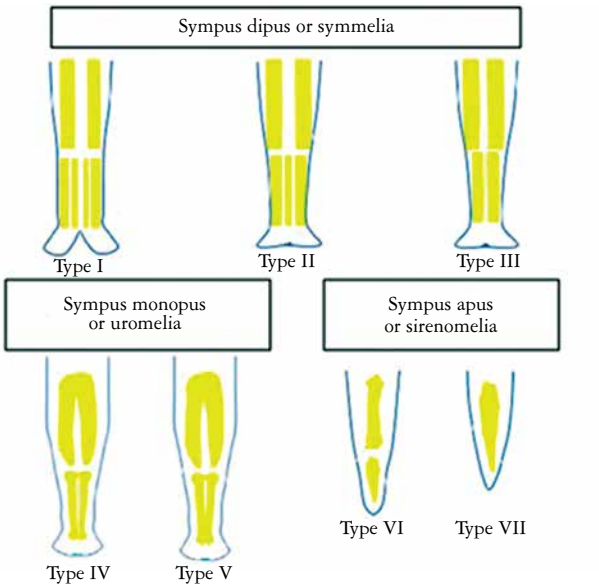

Fig. 1. Stocker and Heifetz classification of sirenomelia

ments present in the lower leg, and this classification is still used today [7]. This classification is presented in Figure 1 and Table I.

Material and methods

A 28-year-old grand multiparous woman, with gestational diabetes mellitus (left untreated) and a heavy smoker, with an unsupervised pregnancy, gave birth vaginally to a 2300 g fetus. Despite resuscitation manoeuvres he died after 40 minutes. On admission: cyanotic and cold skin, bradycardia 20 beats/minute, peripheral pulse absent, periodic gasping breathing, absent muscle tone, absent reflexes, plurimalformed appearance: absent external genitals, anal imperforation, fused lower limbs with the aspect of a mermaid, on palpation of the abdominal region a pseudotumour formation in the region of the left iliac fossa. Complementary and additional examinations were performed post mortem. (In our country, according to the law, autopsies are mandatory for patients under 1 year of age.)

External examination revealed a mature newborn, of 2316 g and 46 cm height (small for gestational age), with the signs of real death present (cadaveric rigidity, hypostasis). The lower part of the body was fused, represented by an extremity that ended with a single finger with two phalanges (18 cm length, 12 cm width) without an anal orifice (Fig. 2). Post-mortem radiological examination revealed the presence of a single femur, a single tibia without fibula, tarsus, metatarsus and one digit with 2 phalanges (Fig. 3).

Internal examination revealed multiple malformations of several systems and organs: single umbilical cord artery, abdominal aorta with aberrant trajectory which branched into a whitish fibrous main branch with a path in the umbilical cord (basically the abdominal aorta ended in the umbilical cord) (Fig. 4), pulmonary hypoplasia, the descending colon ended at the bottom with a dilated pouch with agenesis of sigma and rectum, bilateral renal agenesis, urinary tract agenesis, and agenesis of external genitalia. The testes were identified in the lower abdominal floor. The pathologist concluded that the baby had multiple and severe malformations of several systems (gastro-intestinal, renal, genital, pulmonary) and the final diagnosis of sirenomelia grade VI (Stocker and Heifetz classification) was established (based on the X-ray examination).

Histopathological examinations confirmed the presence of a single umbilical artery that arose from the abdominal aorta, pulmonary hypoplasia with pulmonary atelectasis, pulmonary hypertension, and cerebral oedema with acute neuronal distress.

Discussion

Decades of clinical, pathological, and epidemiological research, as well as the recent use of modern microarray and gene sequencing technologies, have led to a better knowledge of the aetiology and pathogenesis of the most common malformation patterns. Nevertheless, the pathophysiology of a number of malformation types has yet to be determined, for example in the case of sirenomelia [8].

Some authors view this syndrome as the extreme end of a spectrum of caudal regression syndrome, which includes conditions such as sirenomelia and ectopic anus [9]. The main anatomical differences

Table I. Stocker and Heifetz classification of sirenomelia

Stocker and Heifetz classification based on presence of ossified structures	
Type I	Presence of two separated femurs, two tibiae, and two fibulae
Type II	Presence of two separated femurs, two tibiae, and a medially fused fibula
Type III	Presence of two separated femurs, two tibiae and no fibula
Type IV	Presence of a partially fused femur, two tibiae, and a medially fused fibula
Type V	Presence of a partially fused femur, two tibiae, and no fibula
Type VI	Presence of a complete fused femur and a single fused tibia
Type VII	Presence of a complete fused femur

Fig. 2. External examination where fusion of the lower limbs is seen. Upper extremity normal aspect

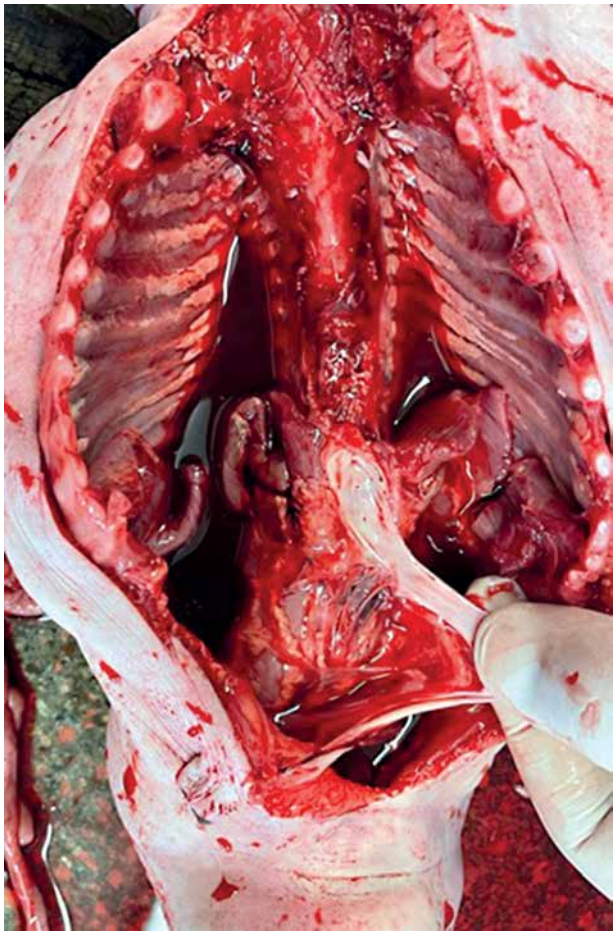

Fig.4. Aberrant branch of abdominal aorta (abdominal aorta ending in the umbilical cord)

between sirenomelia and caudal regression syndrome have been identified as a single midline lower limb and an abnormal abdominal umbilical artery. Otherwise, both conditions share other characteristics. The fact that sirenomelia is assumed to be the outcome of "vascular steal" is another distinguishing characteristic. Contrarily, it is believed that primary caudal mesoderm insufficiency is the cause of caudal regression syndrome [10, 11].

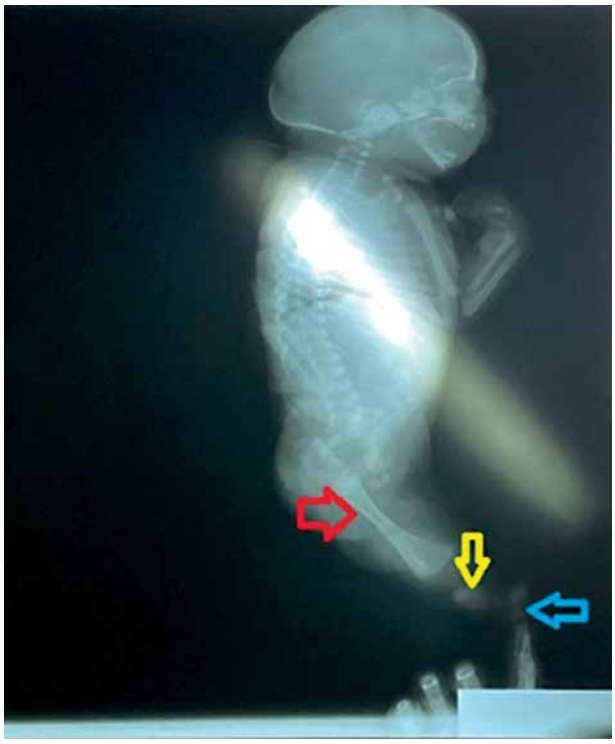

Fig. 3. X-ray examination: red arrow – femur (single); yellow arrow – tibia (single); blue arrow – one digit with 2 phalanges

Several aetiological theories have been postulated, the most widely known of which include vascular steal, defective blastogenesis, and mechanical compression of the embryonic caudal body [12].

In humans and animal models, environmental and teratogenic variables including cocaine, retinoic acid, heavy metals, cyclophosphamide, and some antibiotics have been related to the mermaid syndrome. Also, nicotine, alcohol, radionuclides, diethylpropion, appetite suppressants, organic solvents of lipids, and even air pollution have been linked to the pathogenesis of sirenomelia. Other studies have suggested that fetal exposure to cadmium, lithium, phenytoin, sodium valproate, carbamazepine, warfarin, methylergonovine, diethylpropion, or trimethoprim could be the cause of this abnormality. Diabetes mellitus, hyperthermia during the first trimester of pregnancy, amniotic bands, and maternal age of less than 20 years or more than 40 years at conception are all examples of maternal risk factors [13].

Sirenomelia and maternal diabetes have a substantial correlation and the relative risk ratio is 1/200–250, and it was reported to be 22% among fetuses with anomalies. The ratio of boys to girls is 2.7 : 1 [5, 14]. In the case presented by us, we were able to detect as risk factors the sex of the fetus (male), maternal gestational diabetes and mother's smoking status. Due to the autopsy that we performed, we also identified another important risk factor, the vascular steal phenomenon with the single umbilical artery and lack

of a major artery supply in the lower extremity due to the aberrant trajectory of the abdominal aorta.

In humans, the genetic abnormalities that cause sirenomelia have yet to be discovered. All human fetuses with sirenomelia are known to have normal karyotypes, with the exception of a few newly described cases. An article by Gabriele *et al*. described a fetus with mermaid syndrome who had a triploid mosaic (69, XXX/46, XX), while another case had a de novo balanced reciprocal translocation 46X, t(X; 16) (p11.23; p12.3) [15, 16] .

Because the amniotic fluid content is relatively normal during the first trimester, a diagnosis of sirenomelia may be easier to make. Diagnosis made based on ultrasound may be delayed later due to severe oligohydramnios caused by renal agenesis or dysgenesis [17].

During the first-trimester scan, ultrasound detection of lower limb abnormalities or presence of an intra-abdominal cyst positioned laterally may be a warning indicator of sirenomelia. This should elicit a thorough inspection of the fetal lower body and intra-abdominal anatomy, including the main abdominal vessels, for further confirmation [18].

The management of sirenomelia is challenging and unpredictable due to the poor prognosis. In order to select the cases with the best prognosis, it seems more than justified to emphasize antenatal diagnostics [19]. These fetuses with sirenomelia typically die either during pregnancy or immediately after delivery [20].

Conclusions

Although the diagnosis of sirenomelia is made based on ultrasound (beginning in the first trimester), it is imperative to perform neonatal fetal autopsy in order to document and complete the diagnosis. In our full term neonate case with grade VI sirenomelia, the presence of a single umbilical artery plus the abdominal aorta that ends in the umbilical cord differentiates this condition from caudal regression syndrome and also explains the under-development of the lower extremity, secondary to the vascular steal phenomena, thus lacking a major artery supply in this area.

The authors declare no conflicts of interest.

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