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Sirenomelia: A case report and review of the literature

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Abstract:

Sirenomelia is a rare congenital anomaly characterized by the more or less complete fusion of the two lower limbs, consistently associated with significant urinary abnormalities. Its etiology is still very controversial.

We report a case of sirenomelia diagnosed early at 15 weeks of amenorrhea + 6 days in a 26-year-old woman during a follow-up obstetric ultrasound. The patient reported in her history an infection with COVID-19 at 11 weeks of amenorrhea which was pauci-symptomatic. Is there really a causal link between these two conditions? In this work we discuss the embryopathogenic and etiological factors of this anomaly, the interest of ultrasound diagnosis and the different malformative associations.

Keywords : case report, sirenomelia, malformations, diagnosis, associations.

Introduction :

Sirenomelia is a very rare congenital anomaly that affects 1 in 100,000 live births [1] characterized by a more or less complete fusion of the lower limbs giving the appearance of a mermaid tail. It can be partial or total, ranging from the absence of a bony structure (thus limited to a rudimentary extremity), to the simple fusion of soft tissues giving two complete lower limbs in the same integumentary sheath [1].

This condition is usually fatal due to associated anomalies such as renal agenesis. Other associated anomalies may be seen such as single umbilical artery, anal imperforation, internal or external genitalia anomalies [2], double inferior vena cava and angiomatous lumbosacral

myelocystocele [3]. Only a few cases with sirenomelia have survived beyond the neonatal period [4].

In this context we report the case of a fetus with this anomaly in order to identify the clinical, ultrasound and radiological picture and to discuss the possible etiologies.

Observation :

This is a case of Mrs BS. S, 26 years old, primigravida, who was referred to us at 15 weeks of amenorrhea (SA) + 6 days for an ultrasound examination in view of the discovery of anamnios.

The patient reports a history of COVID-19 infection at 11 weeks' gestation which was pauci-symptomatic. Moreover, she is not diabetic, has no other particular personal history and no consanguinity with her husband. No notion of diabetes or malformations were found in her family.

On ultrasound examination, there was an anamnios most probably related to bilateral renal agenesis, associated with the absence of the bladder and only one lower limb could be visualized with agenesis of one foot and longitudinal agenesis of one leg (Figure 1).

The decision was to terminate the pregnancy for fetal poly malformations characteristic of sirenomelia.

The patient expelled a 150gr polymalformed fetus. Indeed, we can note the absence of external genitalia, an anal imperforation, lower limbs fused from their base to the feet and their external palpations gave the impression of having probably two femurs. Both feet were limited to two thin buds. The two upper limbs and the thorax were integrated. The fetus had the appearance of a "mermaid" (Figure 2 and 3).

A fetal radiography was available which showed two superimposed femurs, absence of the bones of both legs and feet, existence of a single coxofemoral joint and the presence of only four lumbar vertebrae (Figure 4).

Discussion :

Sirenomelia has an estimated frequency of 1/60,000 to 1/100,000 pregnancies[5]. It affects all ethnic groups in the world [6], mainly males with a sex ratio of 2.7/1[7]. It is much more

important in the case of twin pregnancies, in fact 8 to 15% of sirenomelias are observed in the case of twin pregnancies, particularly monozygotic pregnancies where the risk is multiplied by more than 100 [5].

Positive diagnosis is based on ultrasound, which visualizes the malformation and specifies the various associated anomalies. It is usually done early, in the first trimester (12-13 SA) with the help of an endo-vaginal probe [8] and when the amniotic fluid, which is independent of the renal function, is still normally present favoring the visualization of the lower limbs and their movements. In the second trimester, the anomaly is suspected when the first sign of call is oligo-anamnios, a consequence of the renal agenesis [9], as in our case. Amnio-infusion may be necessary to recognize fused lower limbs, with little or no mobility. Color Doppler [10] is essential to overcome the difficulty of reading due to oligohydramnios. It studies the abdomino-pelvic vascularization, confirms the diagnosis of the single umbilical artery, specifies its level of implantation, the aspect of the abdominal aorta (complete or partial atresia), and may allow verification of the absence of renal vessels. Ultrasound can also be used to assess associated anomalies. Magnetic resonance imaging (MRI) may be useful in case of advanced pregnancy, in obese patients and in incomplete forms [11].

Stocker and Heifetz [12] propose a detailed classification based on the presence or absence of different bone elements of the lower limbs (Table I)

Our description corresponds to a type III form of the Stocker and Heifetz classification.

The etiology of sirenomelia remains poorly defined and very controversial. Several hypotheses have been put forward such as the theory of a defect in blastogenesis and a disorder of the gene control of gastrulation occurring before the 5th week of embryonic development and which may cause a major deficit in the differentiation of the whole caudal region of the embryo defining a malformative group known as the caudal regression syndrome [13].

In 1986, Stevenson et al proposed a "vascular flight" theory in which caudal regression results from a detour of blood flow destined for the caudal part of the embryo through a large vessel derived from the yolk artery originating in the abdominal aorta [14]. This detour results in hypo-perfusion of the caudal mesoderm, from which there may be complete or incomplete agenesis of the caudal structures (lower limbs, kidneys, sacrum and lower parts of the gastrointestinal tract) except for the gonads which are intra-abdominal. However, it should be noted that this theory cannot explain the craniofacial and cardiac malformations that can be seen in sirenomelia. On the other hand, Jaiyessimi et al reported a case of sirenomelia without

this vascular flight through the vitelline artery, indicating that other factors may be responsible for sirenomelia in humans [14].

Maternal diabetes has also been incriminated and has been considered an important risk factor for caudal malformations [15]. Some authors have suggested that oxidative stress induced by the accumulation of free radicals could have a teratogenic effect in fetuses of diabetic mothers. However, only 0.5-3.7% of sirenomelia cases have been seen in diabetic mothers [16]. Therefore, the association between maternal diabetes and sirenomelia can be described as weak [14]. Our patient was not known to be diabetic which further confirms this weak association.

Recent experimental studies in mouse models suggest that there may be a genetic basis [15]. Indeed, the induction of loss-of-function mutations in the signaling sequences of the "Bone morphogenetic protein" (BMP-7) gene or gain-of-function mutations in the signaling sequences of the "retinoic acid" (RA) gene have allowed to observe the development of a phenotype similar to the one observed in humans, but this remains to be confirmed in humans [17].

In addition, heavy metal exposure has been shown to be associated with sirenomelia in humans [18]. Toxic substances are sometimes involved, such as cocaine for its vasoconstrictive effect, retinoic acid, and mifepristone [19].

The infectious etiology was not described in the literature. In our case an association with Covid-19 infection was observed, is there really a link between the two or is it just a coincidence ?

Another theory described in the literature considers sirenomelia as part of the VACTERL syndrome [14]. VACTERL syndrome is defined by a cluster of associated congenital malformations, characterized by the presence of at least three of the following malformations: vertebral anomalies, anal atresia, tracheoesophageal fistula, renal malformations and limb anomalies. There is significant overlap in the phenotypic manifestations of sirenomelia and VACTERL syndrome. In most cases, the distinction between the two diagnoses is made based on the degree of severity of the abnormalities and the presence of a single lower limb in sirenomelia [14].

Other theories exist, but given their controversies in the literature, they are not considered here.

Sirenomelia being a serious malformation, lethal if associated with bilateral renal agenesis, thus indicating medical termination of pregnancy.

Conclusion :

Sirenomelia is a rare and fatal poly-malformative syndrome, whose ultrasound diagnosis must be as early as possible because it results in an adapted obstetrical attitude. In Africa, it is associated with mystico-religious considerations and witchcraft and exposes the family to connotations and violent stigmatization.

Conflicts of Interest :

The authors declare no conflicts of interest.

Author Contributions :

All authors approved the final version of the manuscript.

Table and figures :

Table I : Classification of sirenomelia proposed by Stocker and Heifetz.

Figure 1 : Fetal ultrasound showing lower limb anomaly.

Figure 2 : Feto-pathological aspect of sirenomelia: anterior view.

Figure 3 : Fetopathological aspect of sirenomelia : posterior view showing the anal imperforation.

Figure 4 : Fetal radiograph showing two superimposed femurs and absence of bones in both legs.

Table I: Classification of sirenomelia proposed by Stocker and Heifetz [20].

Type	Characteristics
I	2 femurs, 2 tibias, 2 fibulae present
II	Only one fibula
III	No fibula
IV	Partially fused femurs, fibula fused
V	Partially fused femurs
VI	Single femur, single tibia
VII	Single femur, no tibia

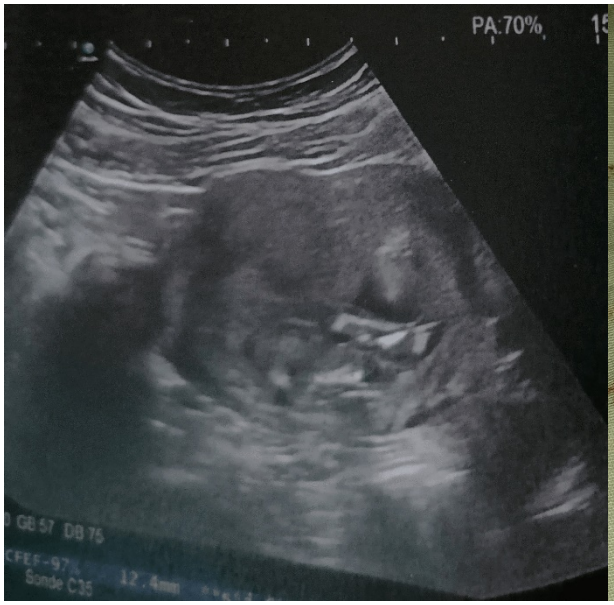

Figure 1

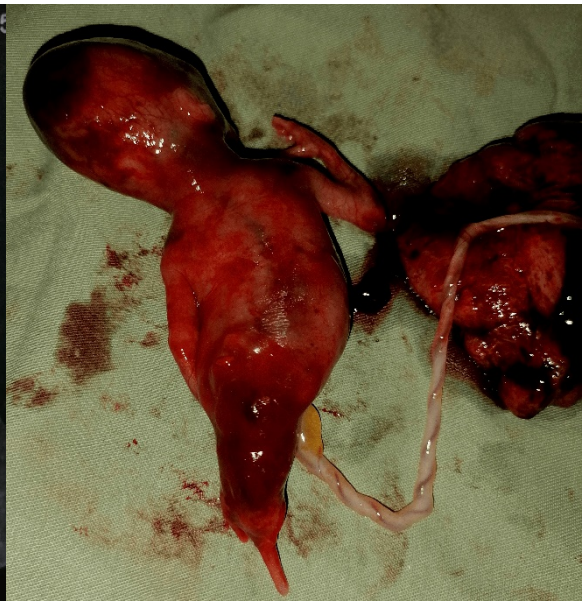

Figure 2

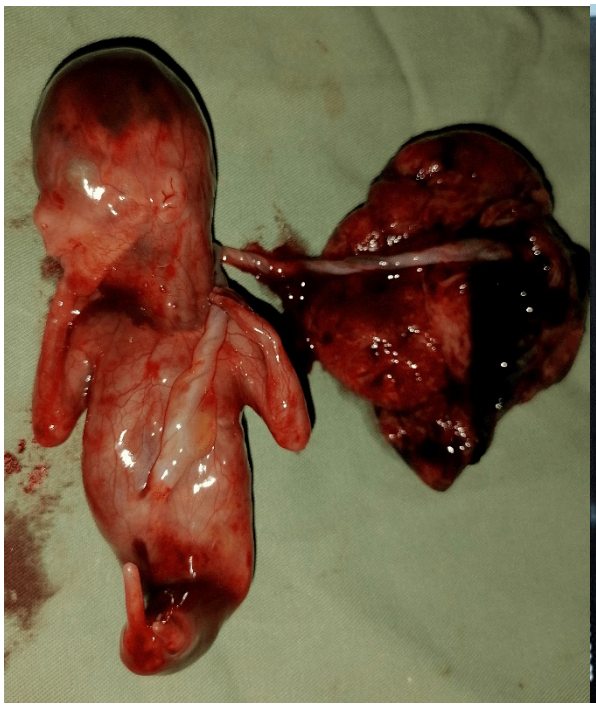

Figure 3

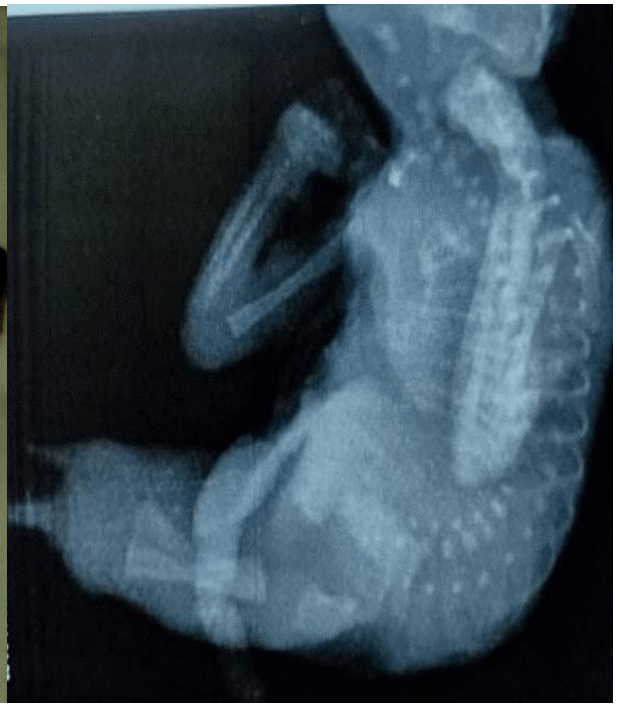

Figure 4

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