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Sirenomelia – a case report

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Abstract

Sirenomelia is a rare congenital malformation affecting multiple organ systems. The phenotypic feature is fusion of the lower extremities. We hereby present a case of sirenomelia diagnosed at an ultrasound at 12 weeks gestation. The pregnant nulliparous woman had a history of bypass surgery and a BMI of 46. The father was treated with methotrexate at the time of conception due to psoriasis.. The pregnancy was by natural conception. The case study includes high quality ultrasound imaging and photos displaying the phenotype of the aborted fetus.

Keywords: Congenital malformation; teratogen; sirenomelia

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Introduction

Sirenomelia, also known as ”mermaid syndrome”, is a rare congenital malformation with an incidence of approximately 1:100.000 pregnancies (1). The most striking phenotypic feature is a partial or complete fusion of the lower limbs bearing resemblance to ancient greek mythology mermaid tales. In addition to the malformation of the lower extremities the syndrome displays a wide variety of anomalies involving practically all organ systems, most commonly malformations of the gastrointestinal-, urinary- and genital tract. Based on the morphology of skeletal abnormalities of the lower limbs sirenomelia can be classified into seven subtypes as described by Stocker and Heifetz in 1987 (2).

The syndrome is almost always lethal. Only a few cases of surviving infants have been reported (3).

The prenatal diagnosis is based on ultrasound diagnosis of the characteristic lower extremity malformations. Furthermore, single umbilical artery (SUA) as well as oligohydramnios resulting from urinary tract malformations often accompany the syndrome (4). Due to the development of severe oligohydramnios later in pregnancy the diagnosis is most feasible in the first trimester since the level of amniotic fluid by this point in pregnancy is not yet strictly reliant on fetal urine production. Therefore, in high resource countries most cases will be diagnosed early leading to termination of the pregnancy due to the poor prognosis.

Maternal diabetes and several teratogenic factors have been suggested but only reported in single case studies (5,6). To our knowledge only maternal exposures have been described.

We present a case of sirenomelia associated with paternal exposure to methotrexate (MTX).

Dividing conjoined twins by operation is a very complex surgery and is only offered by specialized centers with expert teams assigned (4,5).

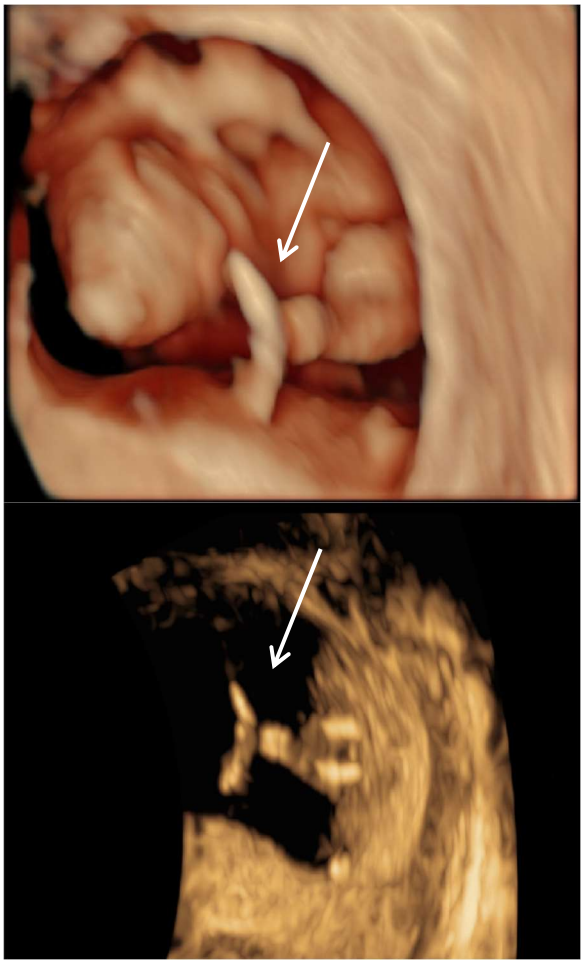

Figure 1: 3D ultrasound imaging of the fetus (upper frame) and 2D ultrasound imaging of the lower limbs of the fetus (lower frame). The arrows point to the described lower limb malformation in the fetus showing fused lower extremities resembling a mermaids tale.

Case

The pregnant woman, a nullipara, (aged 33) presented with her partner (aged 48) at the first routine pregnancy scan in gestational week 11+5. The woman had a history of gastric bypass surgery, weight loss of 40 kg and a current prepregnant BMI of 46. She was otherwise healthy without any prescription drug use. The male partner had a history of psoriasis for which he had received treatment with methotrexate (MTX) 20 mg/week. The pregnancy was by natural conception. None of the two had a family history of congenital malformations or of recurring miscarriages.

The ultrasound scan detected lower limb malformations and SUA. The lower extremities were fused, the feet pointing in opposite directions. The femur, as well as some bone structure of the lower leg were visible. It was not possible to determine, if both the tibia and fibula were present. Evaluation of the kidneys and the urinary tract was not possible (Fig. 1).

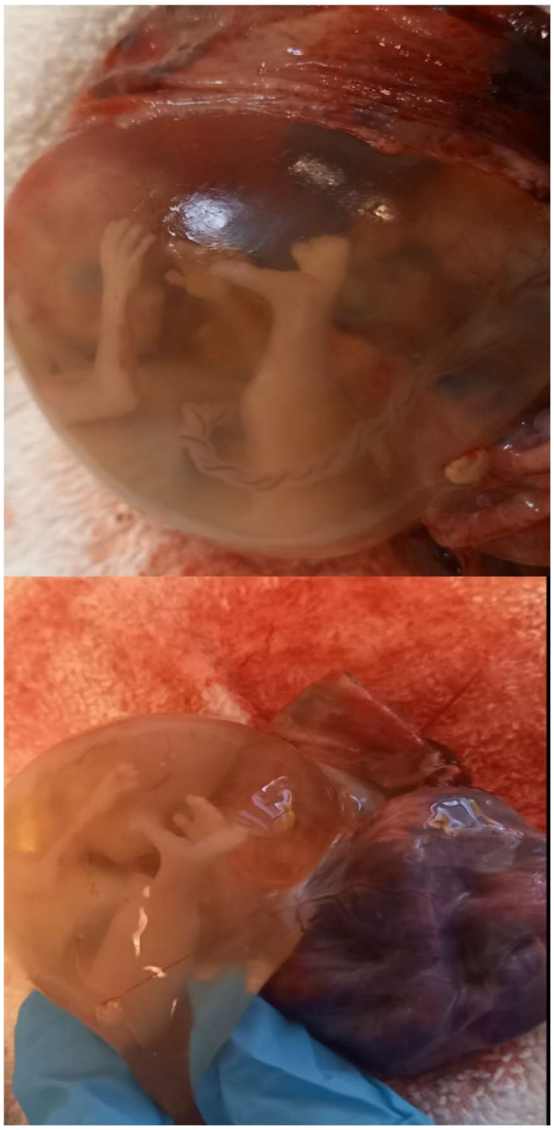

Figure 2: Phenotype of the aborted foetus

The couple decided on termination of the pregnancy. The phenotype of the aborted fetus matched the ultrasound description (Fig 2). Placental examination and array CGH were normal. Informed consent for publication was obtained.

Discussion

Several case reports addressing possible maternal exposure to teratogens resulting in sirenomelia have been described including first trimester exposure to medications such as trimethoprim and antiepileptics as well as illicit drug use. To our knowledge our case report is the first to present a link to preconceptional paternal exposure to a teratogenic agent.

The aetiology and pathogenesis have been debated. Two theories include firstly a defect in the migration of mesodermal cells in early embryogenesis and secondly the "vascular steal"-hypothesis, which is based on a supposed abnormal development of the blood supply to the caudal structures of the embryo resulting in an underdevelopment of these structures. Both theories have been rejected as a valid single explanatory model due to conflicting findings (7).

Methotrexate is a folate analog with known teratogenic effects in early pregnancy (8). In terms of paternal exposure to methotrexate prior to pregnancy knowledge is sparse. In contrast to maternal exposure to methotrexate with direct effects on the developing embryo paternal exposure would only result in a risk of birth defects if methotrexate affected spermatogenesis.

In a review by Grosen et al the question of paternal methotrexate exposure was addressed (9). The authors noted that methotrexate has been found to affect spermatogenesis in animal models but not in humans. However, with regard to pregnancy outcome only a few small studies were eligible for review. Comparing exposed individuals to controls showed no increased risk of major malformations. Establishing a causal relation would require very large cohorts due to the relatively high general background incidence of congenital malformations.

While our case may be a chance finding, studies are needed to add to knowledge about preconceptional paternal teratogenic effects.

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