

# A Rare Case Report of Sirenomelia Following Intracytoplasmic Sperm Injection Embryo Transfer

Kamala Selvaraj, Priya Selvaraj, S. Sivapriya, Vijaya Annigeri, Suganthi V

GG Hospital, Fertility  
Research and Women's  
Speciality Centre, Chennai,  
Tamil Nadu, India

### ABSTRACT

Sirenomelia is a very rare developmental abnormality which is characterized by fusion of lower limb to form a single limb. This condition is often associated with internal organ abnormality and is considered incompatible with life. Sirenomelia is sporadically reported from across the world, but no case associated with artificial reproductive technology (ART) has not been reported. We report a case of sirenomelia in a 29-year old woman who conceived by ART, which to our knowledge is the first reported case in ART. The defect was detected early during first trimester and the pregnancy was terminated.

**KEYWORDS:** *Diabetes mellitus, intracytoplasmic sperm injection embryo transfer, mermaid syndrome, sirenomelia*

## INTRODUCTION

Sirenomelia, also known as mermaid syndrome, is a rare fetal malformation involving the caudal part of the embryo. It is characterized by complete or partial fusion of legs to form a single lower limb. The other abnormalities include anomalous kidneys and large intestines, genital abnormality, and single umbilical artery and vein. The upper body defects are rare and include abnormalities of heart, lungs, arms, spine, and brain.

Sirenomelia malformation is generally incompatible with life, and perinatal deaths are common. Recently, few exceptional cases have been reported, wherein children with preserved renal function with sirenomelia have survived after undergoing reconstruction surgery to restore pelvic organs and leg separation.<sup>[1]</sup> The abnormalities found in such cases are single umbilical artery, unossified nasal bone, dilated loops of bowel, cystic area seen in the lower abdomen, obstructed bowel, bilateral empty renal fossa, absent bladder, and fused lower limbs with single abnormal foot. The diagnosis is obvious at birth and from perinatal ultrasonography (USG). Antenatal USG findings include oligohydramnios, renal agenesis, absent urinary tract, and external genitalia.

The incidence of sirenomelia varies between 1.1% and 4.2%/100,000 births. The male-to-female ratio was 3:1.<sup>[2]</sup> The exact cause of sirenomelia abnormality is not known. However, several associations have been noted. It is an autosomal dominant genetic condition, caused by a new spontaneous mutation, that has a combined genetic and environmental component.<sup>[3]</sup> Maternal diabetes is strongly associated with sirenomelia, with an increased incidence of 1:200–250, and up to 22% of such infants have maternal diabetes mellitus. We report a case of sirenomelia in a patient after *in vitro* fertilization (IVF) by intracytoplasmic sperm injection (ICSI) and IVF and embryo transfer (IVF-ET).

## CASE REPORT

Mrs. A, 29 years, known case of polycystic ovarian syndrome in a nonconsanguineous marriage of 6 years came to us for primary infertility on May 23, 2018. The sperm analysis of her husband, aged 31 years, was normal. There was no significant family history of fetal abnormalities or malformations on either side of the family. She had irregular menstrual cycles and no other specific history.

**Address for correspondence:** Dr. Kamala Selvaraj,  
GG Fertility and Women's Speciality Centre, Chennai,  
Tamil Nadu, India.  
E-mail: drkamala@gghospital.in

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She had a normal body mass index of 28 kg/m<sup>2</sup> and had pregestational diabetes. She had a diagnostic laparoscopy along with ovarian drilling done elsewhere in the year 2013, with two unsuccessful intrauterine insemination (IUI) cycles. At our center, all the routine investigations done were within the normal limits. Her previous obstetric history revealed two chemical pregnancies at 40 days, with initial positive beta-human chorionic gonadotropin (HCG), which then declined in both instances.

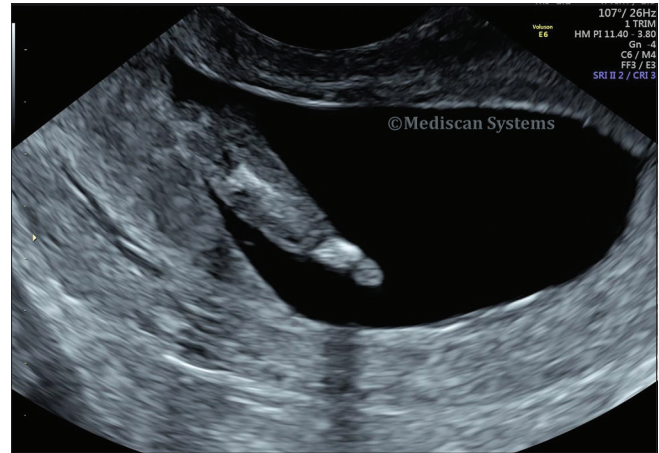
The karyotype of couple was normal. She underwent a diagnostic hysterolaparoscopy at our center on June 8, 2018, which was normal, and the histopathology report revealed a proliferative endometrium. She underwent two more cycles of IUI which failed.

The couple then opted for IVF in November 2018 after a detailed counseling session for the same. She underwent the long protocol with oral contraceptives administered from day 5 of her menstrual cycle, followed by downregulation on day 20 with injection Zoladex 3.6 mg on November 5, 2018. Controlled ovarian hyperstimulation was commenced on day 3 of the following cycle with a combination of recombinant follicular-stimulating hormone and highly purified human menopausal gonadotropins for a total period of 6 days. She was triggered with recombinant HCG when four or more mature follicles were detected by ultrasound, measuring 1.8 cm × 1.8 cm. The transvaginal aspiration was performed on December 3, 2018. We retrieved 20 oocytes and 15 oocytes underwent conventional ICSI, of which 13 were fertilized. On day 3, four 8 cells Grade I-II and on day 5, two expanded blastocysts and two compact blastocysts were vitrified, and the procedure of ET was canceled due to ovarian hyperstimulation syndrome. Four embryos (day 3) and four blastocysts (day 5) were vitrified.

A month later, two (day 3) embryos and one expanded blastocyst (day 5) were transferred following conventional hormone replacement therapy. She tested positive for pregnancy on January 14, 2019, with beta-HCG value of 184.7 mIU/ml, and the second test 2 days later was 352.2 mIU/ml. Her 38<sup>th</sup>-day scan revealed a single regular intrauterine gestational sac. Fetal heart pulsation was confirmed on the 45<sup>th</sup> day. Her subsequent antenatal scans showed normal growth.

USG done during 12<sup>th</sup> week of pregnancy revealed the following findings: single umbilical artery, unossified nasal bone, dilated loops of bowel, cystic area seen in the lower abdomen, suspected obstructed bowel, bilateral empty renal fossae, absent bladder, and fusion of both lower limbs with single abnormal foot with features suggestive of sirenomelia [Figures 1 and 2].

After counseling, the couple opted for termination of pregnancy with misoprostol induction on March 19, 2019, and the anomalous fetus was expelled. On external examination, fused lower limbs with single abnormal foot were noted [Figures 3 and 4].



**Figure 1:** Fused both lower limbs with single abnormal foot



**Figure 2:** Dilated loops of bowel with absent bladder



**Figure 3:** Single abnormal foot



**Figure 4:** Single abnormal foot

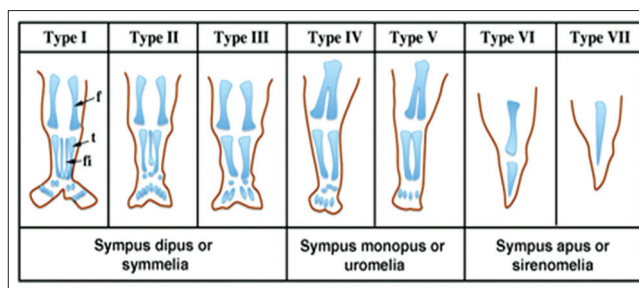
After the termination, she was suggested an option of preimplantation genetic testing for aneuploidy/monogenetic disorders (PGTA/M) along with endometrial receptivity array (ERA). The remaining five blastocysts were vitrified, of which four vitrified blastocysts were from day 5 and day 6, and 2-day 3 embryos which were grown into blastocyst was suggested for embryo biopsy. The remaining one nonbiopsied blastocyst of day 6 was vitrified.

The four vitrified blastocysts were biopsied which revealed two normal and the rest abnormal embryos. The patient was put on HRT cycle, and the blastocysts with normal biopsy findings were transferred, but the result turned out to be negative. Now, the patient is under our treatment.

## DISCUSSION

Many infertile couples have benefitted from IVT transfer. At the same time, it has been found that more congenital malformations occur in infants born from assisted reproductive technology (ART) in the form of neural tube defects and transposition of great arteries and so on.<sup>[4]</sup> The controversy of increased abnormalities in infants born out of ART exist for a long time since the inception of the technique, but the conclusive evidence remains elusive. In a study of a large cohort of children born after standard IVF and ICSI ( $n = 2840$  and  $2955$ , respectively), the rate of major congenital malformations was approximately 4%,<sup>[5]</sup> and another large prospective study comparing children born after ICSI with controls conceived spontaneously reported a relative risk of 1.24 of fetal abnormalities (95% confidence interval: 1.02–1.50).<sup>[6]</sup> A retrospective analysis in Western Australia showed that infants conceived with the use of ICSI or IVF have twice as high a risk of a major birth defect as naturally conceived infants.<sup>[7]</sup>

The advantage today is that due to advanced technology, these cases can be diagnosed as early as possible and



**Figure 5:** Sirenomelia Classification- Type I – VII<sup>[11]</sup>

terminated. In case, sirenomelia is diagnosed early at 10 weeks when the limb buds are clearly seen, termination of pregnancy can be done as was the case in our patient.

The cause of sirenomelia is unknown. However, two hypotheses have been proposed to explain the abnormality: (1) vascular steal hypothesis and (2) defective blastogenesis hypothesis. The vascular steal hypothesis involves aberrant vasculature pattern of the caudal body present in most individuals with sirenomelia.<sup>[8-10]</sup> In such cases, the fusion of the limbs occurs due to deficient nutrition resulting from abnormal blood flow to the caudal mesoderm, which results in agenesis of midline structures and abnormal approximation of both lower limbs. The defective blastogenesis proposes that the malformation sometimes originates due to the defective development of the caudal and tail bud [Figure 5].<sup>[11]</sup> This condition is found more in diabetic women. Sirenomelia is easy to diagnose early, and termination is possible within the first trimester, as it is not compatible with life. A caution to bear in mind is to treat women with diabetes periconceptionally and also treat meticulously till term.

## CONCLUSION

We report a case of sirenomelia in a 29-year-old diabetic woman who conceived after ICSI-ET. Ours is a tertiary care center for the treatment of infertility, mainly pertaining to ART. In our experiences, this is one of the rare anomalies following ICSI-ET. The abnormality was detected early in the pregnancy by USG, and the pregnancy was terminated.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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## Conflicts of interest

There are no conflicts of interest.

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