



## Rare successful pregnancy in a patient with Swyer Syndrome



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### ARTICLE INFO

#### Article history:

Received 26 September 2016

Accepted 17 October 2016

Available online 18 October 2016

#### Keywords:

Swyer syndrome

XY female

Gonadal dysgenesis

Primary amenorrhoea and HRT

Pregnancy in Swyer syndrome

### ABSTRACT

**Objective:** To report a rare successful pregnancy after fertility treatment in a patient with Swyer syndrome.

**Design:** Case report.

**Setting:** Herts & Essex Fertility Centre, Cheshunt, UK.

**Patient(s):** A 36-year-old patient with 46, XY gonadal dysgenesis. 31 year old husband with normal sperm analysis.

**Intervention(s):** Chromosomal analysis, Saline infusion sonography, Pipelle endometrial scratch, ICSI using donor eggs, Embryo Transfer, and Caesarean delivery.

**Main Outcome Measure(s):** Successful pregnancy and live birth.

**Result(s):** Successful treatment with donor eggs, pregnancy, and delivery.

**Conclusion(s):** A patient with 46, XY gonadal dysgenesis in a specially tailored fertility program, can maintain a normal pregnancy and delivery.

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## 1. Background

Swyer syndrome is a rare disorder of sex development (DSD) which encompasses any disorders in which chromosomal, gonadal or anatomical sex development is abnormal. It is characterized by the failure of the sex glands (i.e. testicles or ovaries) to develop. The National Organization for Rare Disorders (NORD) classifies Swyer syndrome as 46 gonadal dysgenesis, expressed either in complete or incomplete form: 46, XY complete gonadal dysgenesis; 46, XY pure gonadal dysgenesis; gonadal dysgenesis, XY female type.

Characteristics of fully expressed Swyer syndrome are as follows: female phenotype, either normal or tall stature, bilateral gonadal dysgenesis, sexual infantilism with primary amenorrhoea and eunuchoid habitus. The phenotype is completely female, with existing tubes, vagina, and various grades of uterus hypoplasia ranging from severe to mild underdevelopment. Dysgenesis-related streak gonads appear in 30%–40% cases of patients with primary amenorrhoea. The prevalence of ovarian insufficiency in women with primary amenorrhoea varies between 10% and 28% [1]. Mutations in several different genes are known to cause Swyer syndrome. This condition can occur as the result of a new gene mutation or can be inherited in an autosomal dominant, autosomal recessive, X-linked or Y-linked manner.

## 2. Case Report

This patient presented to Herts and Essex Fertility Centre in 2014 at 37 years of age for consultation regarding her options of having a pregnancy with donor eggs. She and her husband worked as security officers.

She was diagnosed with Swyer syndrome at 15 years of age following investigations for primary amenorrhoea. Following the diagnosis by karyotype and imaging, she had laparoscopic removal of streak gonads in 2009 to reduce the risk of malignancy. She had a female phenotype, tall stature and minimal breast development (she subsequently had breast augmentation in 1998).

She had female external genitalia and female body hair (grades II–III), grade 2 axillary hair and no evidence of clitoromegaly. Pelvic ultrasound revealed a hypoplastic uterus with uterine longitudinal diameter 60 mm, anteroposterior diameter 25 mm, and transversal diameter 35 mm.

She was hypothyroid and was on levothyroxine 50 mcg OD orally. She was a non-smoker, non-alcoholic, with no history of recreational drug use.

The patient had been on hormone replacement therapy since the age of 19 and had regular cycles on HRT. She was on Levest 150 mg orally once a day. She was managed in a specialist multidisciplinary clinic which also had a support group for individuals with Swyer syndrome. They had counselling about future fertility and were aware of the need for donor eggs for future conception. She was compliant with HRT to prevent further uterine hypoplasia in order to carry a pregnancy when ready. They had further supportive counselling and assessment.

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Before starting the donor egg treatment programme, she had saline infusion sonography to assess the endometrial cavity. This revealed a normal cavity, and pipelle endometrial scratch was performed. The uterine cavity measured 7 cm from external cervical os to fundus. From the day 3 of the subsequent withdrawal bleed, she commenced Progynova orally 2 mg three times daily and enteric coated Aspirin 75 mg orally once a day for endometrial preparation.

The anonymous egg donor had controlled ovarian stimulation in a short antagonist protocol with recombinant FSH. Five mature eggs were received and all were microinjected by intracytoplasmic sperm injection (ICSI) using her husband's sperm. On the same day she commenced luteal support with 800 mg of Cyclogest suppositories twice daily. Five days after egg collection, two blastocysts (two embryos transferred due to average to poor embryo quality of grades 4CB and 3CB) were transferred with 1 µL of Embryoglu transfer media and under ultrasound guidance. Pregnancy test 9 days later was positive, with a serum b-hCG level of 256 mIU/mL. Transvaginal ultrasound scan at six weeks gestation confirmed the presence of two intrauterine gestational sacs, but fetal heart action noted only in one fetal pole. At 8 weeks there was a singleton ongoing pregnancy noted. The pregnancy was monitored with fetal medicine unit scans and a plan for elective caesarean section was made after review in consultation with her Obstetrics team in hospital. A healthy baby girl weighing 8 lb. 5 oz. with an Apgar score of 9 was delivered by caesarean section at the 39 weeks of gestation. The baby was tested for chromosomes and was confirmed 46 XX girl.

### 3. Discussion

Swyer syndrome was first described by Dr. Swyer in 1955 in two women with primary amenorrhea, with normal appearance of external genitalia and normal vagina but with hypoplastic uterus and gonads localized at the place where ovaries are commonly positioned. These women were of tall stature, minimally developed breasts, normal pubic and axillary hair, normal vagina and cervix, small uterus, and no palpable adnexal structures. Swyer syndrome implies no match between genotype phenotype correlations. Phenotype is female and genotype is male [2]. The mean age of diagnosis is 18–23 years, with the commonest presentation being primary amenorrhea [3]. These patients have an increased risk of developing cancer of the underdeveloped gonadal tissue. Gonadal tumours can develop at any age including during childhood before a diagnosis of Swyer syndrome is even suspected. Approximately 30% of women with Swyer syndrome develop a tumour that arises from the cells that forms the testes or ovaries (gonadal tumour). The most common gonadal tumour in women with Swyer syndrome is a gonadoblastoma, a benign (non-cancerous) tumour that occurs exclusively in people with defective development of the gonads. However, gonadoblastomas may be precursors to the development of a malignant (cancerous) tumour such as a dysgerminoma, which has also been reported to have a higher incidence in women with Swyer syndrome than in the general population. Prophylactic removal of the dysgenetic gonads is therefore recommended.

Other risks of gonadal dysgenesis include prolonged hypoeestrogenemia with osteoporosis and virilisation. Hormone replacement therapy (HRT) is therefore essential. HRT enables breast development, regular menstrual cycles. It also prevents further uterine hypoplasia, enabling the women carry a pregnancy to term.

The presence of the XY genotype And H-Y antigen does not affect normal uterine and endometrial response, and the possibility of maintaining a normal pregnancy and delivery confirms the physiological ability of the uterus to accommodate and maintain a successful pregnancy in patients with XY dysgenesis [4]. However, in the published literature there are fewer than 13 live births reported in patients with Swyer syndrome [5–13]. It is quite clear that we need reports on pregnancy and outcomes in this rare and unique patient population.

As in our patient's case, most reported pregnancies in patients with Swyer syndrome were delivered by caesarean section for different indications, including unstable lie of the baby, androgenic shape of the pelvis, and the hypoplastic uterus. We postulate that the hypoplastic uterus, although able to respond well to exogenous and endogenous hormones and maintain a full term pregnancy, may lack the intrinsic capability to respond in labour. On the other hand, there is the possibility of caesarean deliveries without obstetric indications due to patient and physician anxieties due to the rarity of this condition.

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