A rare disorder characterized by a phenotypic female with an XY karyotype.

**Diagnosis**

- Male & Female

### Related Diagnoses:
- Undescended testes
- Gonadal dysgenesis

### About Swyer syndrome

Swyer syndrome is characterized by a 46 XY karyotype (Pic. 1), a female phenotype with normal female external genitalia, and a hypoplastic to normal uterus, streak gonads and primary amenorrhea (missing menstruation cycles). A person diagnosed with Swyer syndrome is a female with altered genetic information containing male sex chromosomes. It belongs to the category of sexual abnormality. Gonads have no hormonal or reproductive potential. This leads to hormonal imbalance characterized by elevated gonadotropins, normal female levels of androgens and low levels of oestrogens. Streak gonads display fibrous tissue that vaguely resembles ovarian stroma but no follicles can be found. Majority of patients suffering from Swyer syndrome show minimal breast development. Minimal breast enlargement reflects peripheral aromatization of androgens (the chemical transformation of androgens into female sex hormones happening in peripheral tissues of the body).

Swyer syndrome is hard to detect as before puberty (even in normal females) the ovaries play little or no role in bodily changes. The problem manifests itself at puberty as a result of an inability of the streak gonads to produce sex hormones (both oestrogens and androgens). The incidence of Swyer syndrome reported in literature is 1: 100 000.

The etiology of 46XY, gonadal dysgenesis is believed to be deletion (missing part
of genetic information) of short arm of Y chromosome involving the sex determining region of Y (SRY) gene, mutation in other genes leading to inhibition of SRY function, or mutation of SRY itself. In another words, there are some parts of chromosomal DNA (deoxyribonucleic acid) responsible for gonadal development, such as SRY gene. If such part of DNA is missing, changed or dysfunctional, the development of gonads goes wrong.

DNA genetic information basically represent a “recite” for protein production. SRY gene encodes a specific protein called TFD (testis-determining factor). TDF initiates male sex determination. Mutations in this gene give rise to XY females with gonadal dysgenesis (Swyer syndrome). Some studies revealed that SRY gene is not missing in Swyer syndrome patients so the most probable cause is its mutation.

Swyer syndrome affects early development of an embryo through mutated SRY gene. In embryonic stage the bipotential gonads can differentiate either into the male or female direction, depending on the correct and timely expression of specific genes. With the expression of SRY male sex differentiation is initiated, resulting in the full masculinization of internal and external genital structures. Thus testicular Anti-Mullerian Hormone (AMH) causes regression of the mullerian duct structures (uterus and fallopian tube) whereas androgens cause stabilization and development of the Wolfian duct structures (epididymis, vas deferens and seminal vesicles) and the formation of the prostate and the male external genitalia. In Swyer syndrome patient’s mesonephric ducts (Wolffian ducts) are in atrophy, paramesonephric ducts (Müllerian ducts) develops to uterus, fallopian tubes and part of the vagina as a result of lacking testosterone and inhibitor of Müllerian ducts.

The diagnosis of Swyer syndrome is based upon general examination (sex characteristics of the body, weight, height, ect.) combined with hormonal blood tests (sex hormone concentrations and closely related gonadotropin concentrations; the hormones directing the function of gonads), genetic analysis and monitoring of genital development within the body.

There’s no way to cure Swyer syndrome in affected persons. That means that the therapy consists of systematic treatment of symptoms related to Swyer syndrome. Early diagnosis is essential, not only because of the need to be aware of the risk of gonadal malignancy, but also because hormonal therapy is vital for the induction of puberty. Hormone replacement is also necessary to prevent osteoporosis. Bilateral gonadectomy (surgical removal of both gonads) is often recommended due to the high risk (20-30 % chance) of tumour development (Pic. 2).

**Associated diseases**

- gonadoblastoma
- dysgerminoma
- embryonal carcinoma
Complications

- infertility
- osteoporosis
- gonadoblastoma (benign tumour of germ cells and sex cord stroma)
- dysgerminoma (germ cell tumour)

Risk factors

- genetic predispositions

Impact on fertility

Swyer syndrome causes complete infertility. A woman suffering from XY gonadal dysgenesis develops all reproductive organs (vagina, uterus, fallopian tubes) except the ovaries. Instead of ovaries, dysfunctional streak gonads develop that are unable to produce reproductive cells – oocytes. As there are no functional gonads, no sex hormones (necessary for proper function of other reproductive organs) are produced. Nevertheless, after proper hormonal treatment, which restores functionality of uterus, there is a possibility for a woman suffering from Swyer syndrome to become pregnant using donated oocytes.

Prevention

As mentioned above, Swyer syndrome is related with genetic information alterations. Nowadays there are procedures focusing on genetic analysis that can reveal such alteration in in gametes or embryos. Specifically, the PGS (pre-implantation genetic screening)/PGD (pre-implantation genetic diagnosis) allows studying the DNA of eggs or embryos to select those that carry certain damaging characteristics. This assisted reproduction technique may help to reveal the abnormalities of sex determining regions of DNA in time.

Symptoms

- delayed puberty
- primary amenorrhea
- increased level of FSH (follicle-stimulating hormone) and LH (luteinizing hormone)
- low oestrogen concentrations
- minimal breast enlargement
- minimal development of pubic hair (sparse pubic hair)
Therapies

Self therapy

None available.

Conventional medicine

Psychological therapy

Due to altered physical aspects some psychic problems may appear so the counselling with psychologist or psychiatrist may be recommended.

Pharmacotherapy

Hormonal replacement therapy (HRT)

Hormonal replacement therapy is applied to induce puberty (in child patients), to prevent osteoporosis and restore hormonal balance within the body. This includes oestrogen administration and a progesterone administration, in case of women who wish to become mothers. The oestrogen administration not only helps to prevent complications related with this syndrome, but also prepares the uterus for implementation of fertilized oocyte. Consequential progesterone administration is necessary to maintain the pregnancy.

Surgical therapy

Gonadectomy

Gonadectomy is strongly recommended to prevent gonadal tumour development.

Assisted reproduction

The assisted reproduction clinics offer to a patient suffering from Swyer syndrome a solution to infertility problem. Thanks to donation
programme the patient may use donated oocytes for in vitro fertilization (IVF) or intra-cytoplasmic injection (ICSI). Before the IVF or ICSI cycle can begin, the HRT must take place in order, to prepare the uterus for embryo implementation.

Donated oocytes are stored using cryopreservation (storage of oocytes within extremely low temperatures). After thawing procedure they may be used for fertilization of an oocyte under laboratory conditions. The IVF procedure involves the fertilization of an oocyte with sperm sample containing up to 100,000 sperm cells. ICSI procedure involves a single sperm carefully injected into the centre of donated egg using a microneedle. After fertilization of an oocyte, its implementation within the functional uterus follows. This is called as embryo transfer procedure.

Find more about related issues

**Diagnoses**

**Undescended testes**
In the case of cryptorchidism one or both testes are absent from the scrotum. It is the most common etiologic factor of azoospermy in the adult.
Learn more at: [www.fertilitypedia.org/therapy/diag/undescended-testes](http://www.fertilitypedia.org/therapy/diag/undescended-testes)

**Gonadal dysgenesis**
Any congenital developmental disorder of the reproductive system characterized by a progressive loss of germ cells on the developing gonads.
Learn more at: [www.fertilitypedia.org/therapy/diag/gonadal-dysgenesis](http://www.fertilitypedia.org/therapy/diag/gonadal-dysgenesis)

**Risk factors**

**High level of FSH**
FSH levels above what an expected levels for one’s age and is indicator of proper ovarian function.
Learn more at: [www.fertilitypedia.org/therapy/rf/high-level-of-fsh](http://www.fertilitypedia.org/therapy/rf/high-level-of-fsh)

**High level of LH**
A condition with high blood luteinizing hormone (LH) leading to irregular periods and reduced fertility in both females and males.
Learn more at: [www.fertilitypedia.org/therapy/rf/high-level-of-lh](http://www.fertilitypedia.org/therapy/rf/high-level-of-lh)
**Symptoms**

**Increased level of FSH**
A condition with high serum follicle–stimulating hormone (FSH) concentration.
Learn more at: [www.fertilitypedia.org/edu/symptoms/increased-level-of-fsh](http://www.fertilitypedia.org/edu/symptoms/increased-level-of-fsh)

**Therapies**

**Egg donation**
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: [www.fertilitypedia.org/edu/therapies/egg-donation](http://www.fertilitypedia.org/edu/therapies/egg-donation)

**ICSI**
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: [www.fertilitypedia.org/edu/therapies/icsi](http://www.fertilitypedia.org/edu/therapies/icsi)

**Sperm donation**
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: [www.fertilitypedia.org/edu/therapies/sperm-donation](http://www.fertilitypedia.org/edu/therapies/sperm-donation)

**Standard IVF**
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: [www.fertilitypedia.org/edu/therapies/standard-ivf](http://www.fertilitypedia.org/edu/therapies/standard-ivf)

**Gallery**
The male karyotype (chromosomal analysis) is characterized by the presence of chromosome Y in the last (23th) pair of chromosomes (sex chromosomes called as gonosomes).

The left gonad is anaplastic classified as strek gonad (B). Encapsulated right gonad was affected by malignant tumour (A).

**Sources**

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