Primary amenorrhoea: Swyer syndrome in a woman with pure 46,XY gonadal dysgenesis and late presentation

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Simple 46,XY gonadal dwysgenesis, also called Swyer syndrome, is a very rare condition, estimated to occur in approximately 1/100 000 people. The condition first becomes apparent in adolescence, with delayed puberty and primary amenorrhoea. This is a case study of a patient who presented with primary amenorrhoea and primary infertility. She was a 24-year-old phenotypically female patient with a delayed diagnosis of Swyer syndrome.

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Case report

A 24-year-old nulliparous woman consulted for investigation of primary amenorrhoea and infertility at the gynaecological outpatient department of our tertiary academic hospital. The initial referral diagnosis was testicular feminisation syndrome. On physical examination, the patient was phenotypically female, height 178 cm, weight 72 kg, with normal secondary sexual characteristics (pubic and axillary hair present, breast development Tanner stage IV). Normal external genitalia were present with a normal clitoris. On speculum examination vaginal length was normal, and the cervix appeared normal.

On bimanual examination the uterus was found to be of normal size and no adnexal masses were palpable. Investigations revealed the presence of elevated gonadotropins (follicle-stimulating hormone, luteinising hormone) and a low level of oestrogen. A karyotype study revealed a chromosome complement of 46,XY.

A vaginal ultrasound scan confirmed the clinical findings of a normal-sized uterus; the ovaries could not be visualised.

The patient underwent diagnostic and operative laparoscopy, where streak ovaries were evident (Fig. 1). Bilateral gonadectomy was performed and histological examination confirmed that both gonads had features consistent with streak ovaries. There was no neoplasia. Postoperatively the patient was started on combined oestrogen/progestin treatment in the form of oral contraception (COC).

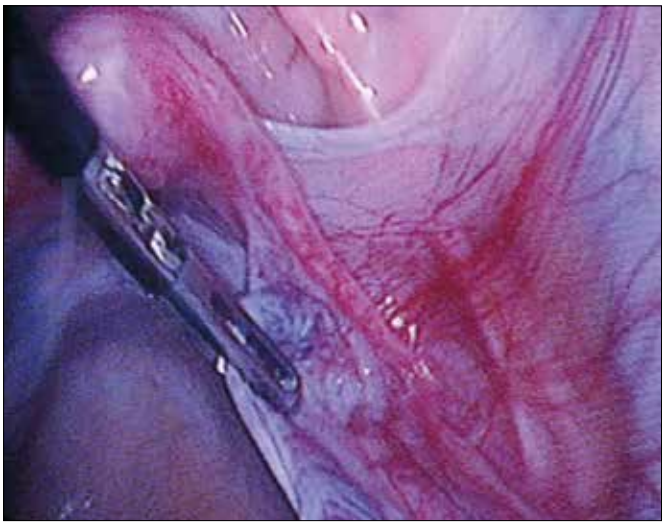

Fig. 1. Laparoscopic findings of the uterus, tube and a streak gonad.

Discussion

Simple 46,XY gonadal dysgenesis, also called Swyer syndrome, is a very rare condition, and has been estimated to occur in approximately 1/100 000 people.[1,2] The condition first becomes apparent in adolescence, with delayed puberty and primary amenorrhoea. Pure gonadal dysgenesis (or Swyer syndrome) is characterised by a 46,XY karyotype in a female phenotypic patient. Despite having XY chromosomes, the patient with Swyer syndrome appears female and has functional female genitalia and structures, including a vagina, uterus and fallopian tubes.

Embryogenesis is thought to be a likely cause; the indifferent gonads fail to differentiate into testes in an XY (genetically male) fetus. Several different gene loci, both on the Y chromosome and other chromosomes, have been identified where a defect may occur.

So-called 'pure gonadal dysgenesis' may be of the XX or XY type, or mixed, in which XX and XY cell lines appear. The other form of gonadal dysgenesis occurs in which an entire chromosome is missing; the most common is Turner's syndrome.

In the absence of testes, no testosterone or anti-Müllerian hormone (AMH) is produced. Without testosterone, the external genitalia fail to virilise, resulting in normal female genitalia. The upper Wolffian ducts fail to develop, so no internal male organs are present. Without AMH, the Müllerian ducts develop into normal internal female organs (uterus, fallopian tubes, cervix and upper vagina).

As in this case, delay in diagnosis is often due to a normal phenotypic appearance, despite the fact that non-functional gonads result in amenorrhoea. 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). Most of the secondary sexual characteristics do not develop, and menses are absent in the majority of phenotypically female patients with pure gonadal dysgenesis.

In this case, the secondary sexual characteristics did develop, as pubic and axillary hair was present. The breasts were not fully developed, although Tanner stage IV had been attained. The main source of oestrogens would be the peripheral aromatisation of androgens into oestrone, which is a weak oestrogen compared with ovarian-derived oestradiol.

The main complaints of this patient were primary amenorrhoea and primary infertility.

The gonads of XY pure gonadal dysgenesis have a high risk of gonadoblastoma and germ cell tumour, particularly dysgerminoma.[2,3]

In this case, as typically occurs, the diagnosis was delayed and made at the age of 24 years. A study by Michala *et al.*[4] from the UK in 2008 showed that particularly in patients over the age of 30 years when data were collected, accurate diagnosis was delayed, and the mean age was 23 years; in those under 30 years at data collection, the age of diagnosis was 16 years. In the older cohort, medical practitioner delay contributed to late diagnosis. Early diagnosis is important, 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. Breast development was close to normal in this patient, but failure of development has been reported. Hormone replacement is also necessary to prevent osteoporosis. In Michala *et al.*'s study[4] 60% of the 29 patients had evidence of osteopenia on dual-emission X-ray absorptiometry.

Following removal of the gonads, COC therapy was promptly initiated. The oestrogen-progestin sequential therapy supports female secondary sexual characteristics. The COC can usually induce menstruation and also increases the uterine size and improves its shape. Pregnancy can be achieved or fertility can be optimised by using donor oocytes, and successful pregnancies in patients with pure gonadal dysgenesis have been described.[4,5]

Conclusion

This a case of pure gonadal dysgenesis in a 46,XY phenotypically female patient, who presented with primary amenorrhoea and infertility. The primary care physician needs to be aware of this condition, as early referral to tertiary centres is necessary for appropriate management. Delay in presentation may be also be affected by patient delay in seeking help.

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