CASE REPORT

Swyer syndrome in a woman with pure 46, XY gonadal dysgenesis and a hypoplastic uterus

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Abstract

Swyer syndrome or pure 46, XY gonadal dysgenesis is a condition in which the individuals have female appearance. They classically present as sexually infantile phenotypic females with primary amenorrhoea. People with this disorder have female external genitalia but the uterus and fallopian tubes are underdeveloped. However, they do not have functional gonads (ovaries or testes). Instead, they have streak gonads. We are reporting a case of Swyer syndrome with partially developed breasts, hypoplastic uterus, and absent streak gonads. The patient was treated with hormonal therapy and few years after her presentation, breast and uterine development were noted. In view that the patient is already married, the option of fertility was discussed with her. This case illustrates a rare case of gonadal dysgenesis and demonstrates the importance of counseling on the options of treatment, especially regarding fertility.

Introduction

The condition known as Swyer syndrome or pure 46, XY gonadal dysgenesis is described classically as female phenotype with unambiguous female genital appearance. The patients have normal but underdeveloped uterus and fallopian tubes, and bilateral rudimentary streak gonads. The condition usually presents as primary amenorrhoea due to the fact that the gonads have no hormonal or reproductive potential.[1] A high incidence of tumour such as gonadoblastoma and germ cell malignancies have been reported; therefore, the current practice is to proceed to gonadectomy once diagnosis is made.[2]

A small number of successful pregnancies achieved with oocyte donation have been reported in patients with Swyer syndrome.[3] We are now reporting a case that had successful development of the uterus after hormonal treatment, and also the importance of discussion on pregnancy possibilities with the patient and her husband.

Case Report

A 27-year old, single, Chinese female presented with primary amenorrhoea and sexual infantilism to the outpatient clinic in 2005. Physical examination revealed a phenotypic female with eunuchoid habitus measuring 166.5 cm in height. She had a Tanner Stage I right breast, a Tanner Stage II left breast, and normal female external genitalia. Blood examination revealed that she had a very high level of follicle-stimulating hormone (FSH) and luteinizing hormone (LH) and a low level of oestrogen. Her testosterone level was in the normal range for females. A karyotype study revealed that she had 46, XY chromosome with the SRY gene, which confirmed the diagnosis of Swyer syndrome. Initially the patient was shocked and could not accept the diagnosis, but after few consultations and reassurance, she was able to accept it.

She was then referred to the Obstetrics & Gynaecology Clinic and has been followed up for the past 8 years. Magnetic resonance imaging (MRI) of the abdomen revealed that

the uterus and gonads were absent. Only a small tubular soft tissue was seen posterior to the urinary bladder suggestive of underdeveloped Mullerian duct.

There was a discussion in the clinico-pathologic conference and majority of specialists, including a consultant endocrinologist, agreed that laparoscopy was not necessary in view of the MRI findings. The collective expert opinion was explained to the patient and she decided not to go for laparoscopy.

She was started on a daily 1.25-mg Equine oestrogen dose for 6 months to stimulate the growth of the uterus. Then, she was administered with Provera (medroxyprogesterone acetate) 5 mg daily for 10 days a month and Premarin (conjugated equine oestradiol) 0.6 mg daily cyclically for 3 months. She experienced menses while on cyclical hormone replacement therapy (HRT; Premarin and Provera). As the patient was concerned about her undeveloped breasts, later the therapy was changed to Yasmin®, a low-dose combined oral contraceptive pill (COCP) cyclically. The patient was very satisfied to be on Yasmin, as not only her breasts developed but also her uterine size increased. However, there was no weight gain and her coarse skin improved. She did not experience any vasomotor symptoms during the sugar-free pill course.

Another MRI of the abdomen was performed few years later in view of the risk of malignancy and to confirm the absence of the rudimentary gonads. The MRI showed that the soft tissue posterior to the urinary bladder has increased in size and further developed into cervix and uterine parts. However, the size is still small compared to those in normal females. Still, there is no evidence of gonads seen.

When she got married, the patient did not reveal the real diagnosis to her husband because she was scared that he might not accept her genetic and phenotypic abnormalities. Nonetheless, the husband was told that she could not bear any child and he accepted it.
Considering the fact that her uterus had responded satisfactorily to the hormonal treatment, counseling was also given regarding the option of future fertility using oocyte donation. However, in view of the difficulty in explaining the situation to her husband, the patient opted not to proceed further.

Discussion

Swyer syndrome affects individuals with XY chromosomal make-up; nevertheless they have a female appearance. The exact incidence is unknown. It has been estimated to occur in 1 in 80,000 births.

The diagnosis of Swyer syndrome is made based on thorough clinical evaluation, detailed patient history, identification of characteristic findings (e.g., amenorrhoea and streak gonads), and a variety of tests including karyotyping. The height of the patient is particularly helpful in distinguishing patients with pure 46, XY gonadal dysgenesis from those with 45, XO/46, XY mosaicism but without the classic features of Turner syndrome.[4]

The chromosomal analysis in Swyer syndrome shows a male karyotype (46 XY). Mutations in the SRY gene have been identified in 15% to 20% of individuals with Swyer syndrome.[5] Mutations in the NR5A1 and DHH genes are also known to be associated with this condition.[6]

This case showed that the diagnosis was delayed and done only at the age of 27 years. A study by Michala et al.[1] also shows that many women experienced delay in reaching accurate diagnosis, often several years after the presentation to their general practitioners. It is suggested that health professionals should update their scientific knowledge and be aware of sexual development disorders.

Early diagnosis is important for a number of reasons: firstly, because of the risk of gonadal malignancy; secondly, early institution of hormonal therapy is vital for the induction of puberty; thirdly, HRT is required to prevent osteoporosis. [1]
The risk of tumour development in Swyer syndrome is significant. A 20% to 30% incidence of tumour in Swyer syndrome was reported.[7] The most common tumour involved in this condition is gonadoblastoma.[2] Dysgerminoma and embryonal carcinoma

were also reported.[2] Due to the risk of tumours, extensive search for the rudimentary gonads is needed and bilateral gonadectomy is advisable. As for this patient, since we could not detect any rudimentary gonads, she requires a close follow-up in the long run.

An interesting finding in this patient is that despite late induction of puberty and non-compliance to hormonal treatment, there is marked improvement in her uterine development. However, her uterine size was small than in normal controls. This finding was similar to the study carried out by Michala et al.[1] They demonstrated deficiencies in the management of the condition in terms of the timing and method of induction of puberty, which may be due to the inherent factors associated with the condition.[1] The small uterine size however did not appear to have adverse effect on the fertility outcome in Swyer syndrome.[1]

A small number of successful pregnancies have been reported in this group of patients.[1,3] Pregnancies were possible through oocyte donation and hormonal treatment. The presence of the XY genotype and the H-Y antigen does not affect the normal uterine and endometrial response. Thus, the possibility of maintaining normal pregnancy and delivery confirms the physiological ability of the uterus to accommodate and maintain successful pregnancy in patients with XY dysgenesis.[8]

In Malaysia, there is no official fertility law or Assisted Reproduction Technique (ART) Legislation so far. Oocyte donation was practised mostly in private hospitals among non-Muslim doctors and patients.

How does this paper make a difference in general practice?

- Creating awareness among general practitioners and also patients about this particular issue
- Highlighting the urgency of early diagnosis due to the risk of malignancy
- Providing information to primary care physicians to counsel patients about brighter fertility options
- Encouraging primary care providers to offer psychological and medical support by illustrating a well-managed case
- Encouraging primary care providers to co-manage such cases with tertiary centres; HRT can be given at the primary care level and referral is done only when there is a need, i.e., when mother and child need more detailed assessment

Conclusion

Early diagnosis of females presenting amenorrhoea is important. The treatment of Swyer syndrome requires multi-disciplinary teams that are able to provide multi-faceted care in terms of prevention of malignancy and osteoporosis, induction of puberty, fertility, and psychological support. The primary care physician needs to be aware of this condition and early referral to the tertiary centres is necessary.

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